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PROFESSIONAL VERSION

1st Edition









Health & Wellness Lab



Professional Version, 1st Edition

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Thrive: Physical Activity for Cancer Survivors

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What is POEM?

"

POEM is an opportunity for health professionals, school staff, community members, parents and children involved in the cancer experience to become comfortable with one principle: physical activity is safe and beneficial for a child with cancer. This is true from diagnosis, through treatment (even when in hospital) and for the lifetime of any survivor.

The word cancer on its own evokes fear and uncertainty. This manual provides the evidence for insisting on children being active kids in spite of a cancer diagnosis. It will help the reader realize that a medical condition that can require complicated, specialized care does not change the fact that children and adolescents need play, sport and movement. The fear and protective nature of parents is natural and expected – and we all play a role in overcoming that fear.

The information provided in this manual is a step towards helping everyone (including professionals) feel more comfortable with getting these kids movin' and groovin' again – as kids should.

Kurt Thompson, PT

Formerly Physiotherapist Hematology/ Oncology/ Transplant program Alberta Children's Hospital Calgary, Alberta Canada. "

"

Tremendous advances have been made over the last half century in treating childhood cancer. Through collaboration, most cases of childhood cancer are curable, and current efforts are directed towards one day curing all children and reducing the short and long term effects of curative therapy. Most survivors of childhood cancer have some long term consequence of their cancer or its treatment.

We are now moving closer to the goal of not just curing children, but giving them lives without limitations. We want young people with cancer to not only survive, but to have the capacity to live well. All of the efforts made towards these goals by children and adolescents, families and care providers need to be supplemented by healthy living. Physical activity is an essential component of healthy living. POEM is about helping families and professionals incorporate physical activity into the care of young people with cancer, and extend this activity to maximize survivorship or palliation. Physical activity can not only improve the lives of children or teenagers with cancer, but it can improve their lives after cancer- a life that should be long and fulfilling, without limits.

"

Gregory M.T. Guilcher MD, FRCPC, FAAP

Pediatric Oncologist Section of Pediatric Oncology and Blood and Marrow Transplant Alberta Children's Hospital Assistant Professor, Departments of Oncology and Pediatrics University of Calgary Faculty of Medicine Calgary, Alberta, Canada.

"

We all know the importance and benefit of physical activity in our daily lives. This should not be an exception for children, adolescents and young adults with cancer. The difficulty comes in knowing how to make sure their activities are safe given all the physical and emotional challenges they face. The POEM manual is an excellent guide to educate health care professionals and families on the theory and practicality of exercise and physical activity in this group. It is thorough, and takes into account the variety of treatment and recovery stages of an individual undergoing cancer therapy, yet it is also easy to read. I know that reading this book will impact the way I practice and look at physical activity in children, adolescents and young adults with cancer.

Tiffany Rent, RN, MN

Clinical Nurse Specialist Oncology/Neuro-Oncology Hematology/Oncology/Transplant Program Alberta Children's Hospital

"

As a parent with a child with cancer our entire world has changed forever. Being overwhelmed with feelings of helplessness are now part of our everyday. Treatment and procedures are not in our control. However there is one thing we as parents we can take charge of: helping and encouraging our kids to exercise. This manual will help guide you through this and answer many questions you may have.

After Lydia's brain cancer treatment was completed we struggled to find a sport she could participate in, we also had many reservations on how to go about getting her moving. Since starting the Pediatric cancer patients & survivors Engaging in Exercise for Recovery (PEER) program I watched my daughter learn how to gain strength, balance, coordination, confidence and most of all have fun exercising!

"

Angela Massiah Mom of Lydia and Veronica Lydia is 7 years old and is a cancer survivor



The professional version of this manual, upon which this family manual is based, was reviewed by Gregory Guilcher, MD; Tiffany Rent, RN and Kurt Thompson, PT, on behalf of the Section of Pediatric Oncology and Blood and Marrow Transplant at the Alberta Children's Hospital.

The three reviewers are supportive of the manual as a useful tool for professionals and families, and concur that the manual does not have any information that is contradictory with the Section of Pediatric Oncology and Blood and Marrow Transplant at the Alberta Children's Hospital. The three reviewers thus approve the POEM manual on behalf of the Section of Pediatric Oncology and Blood and Marrow Transplant at the Alberta Children's Hospital.

Chapters 5 (cardiotoxicity section) and 6 were reviewed and approved by Joyce Harder, MD, a cardiologist at the Alberta Children's Hospital.



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Preface

In light of advances in research and treatment protocols over the last 30 years, which have resulted in improved rates of survival, the field of physical activity and pediatric oncology forms an increasingly important area. It has been gaining recognition an innovative non-medical approach and adjunct to treatment. In fact, research has found physical activity may impact and mitigate a host of side effects experienced by childhood cancer patients and survivors. However, because a diagnosis of cancer during childhood and adolescence is rare, and advances in survival have been recent, this is an emerging field. Researchers are currently trying to determine the optimal frequency, intensity, time and types of physical activity for differing diagnoses and throughout the pediatric cancer experience. Although preliminary, we do know that physical activity is feasible, safe and beneficial if it is appropriately tailored to the cancer patients and survivors needs.

As researchers in this field we realized there is currently a gap between what we know from research, and what health care professionals, allied health care professionals, and families are implementing in pediatric cancer care.

Because we know that physical activity is a valuable component of pediatric cancer care, as well as an essential component in the healthy development of every child, we know more needs to be done to fill the gap. Therefore, we decided to create this manual in an attempt to better inform health care professionals, allied health care professionals, and educators about the benefits and considerations of physical activity during the pediatric cancer journey.

This manual represents the collective work of 27 international authors. Each author was invited to write his/her chapter based on their leading expertise in the area.

This manual contains 16 chapters, and several practical appendices covering broad topics which include: the benefits of physical activity, general recommendations for this population, practical advice for those engaging in physical activity with pediatric cancer patients, specific evidence for physical activity in several specific cancer groups (leukemia, hematopoietic stem cell transplant patients, solid tumours, brain tumours, palliative patients), tools used to assess physical activity, prototypes of current sustainable programs, alternative forms of physical activity interventions (yoga and technology enriched) and practical tips and recommendations to get more active.

This version of the manual is aimed at health care professionals, researchers and allied health care professionals.

For the purposes of the information to follow, the editors have pre-defined several of the terms that will be used throughout. First and foremost, the editors do acknowledge the differences between children and adolescents. However, for the purposes of this manual, pediatric will refer to both child and adolescent cancer patients and survivors. Second, patients refer to children and adolescents who are receiving active treatment for their malignancy, while survivors refer to children and adolescents who have completed treatment for their cancer. Third, although the terms exercise and physical activity are often used interchangeably, for the purposes of this manual, **physical activity (PA)** will refer to all activities that increase energy expenditure above resting as well as traditional forms of exercise. This broad definition was selected as a means to capture the many different types of physical activity that exist. Finally, quality of life (QOL) will be defined according to the World Health Organization, as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment.

To use this manual, note that bolded terms are used when a definition is in the glossary, or the first time an abbreviation is being used in the chapter. Text boxes are provided throughout to highlight important information. Additionally, appendices are present and are meant to provide practical information for the reader.

Please note: these are guidelines based on the best available evidence to date. They are general, and every child will be different. Therefore, these guidelines must be adapted on an individual basis around personal and medical characteristics. Before starting to work with patients, ensure they consult their oncologist or primary physician and obtain medical clearance. If you are a fitness professional or physician, be available for information exchange. It is recommended to start low and progress slowly, monitoring the patient or survivor carefully.

This manual is dedicated to all the brave children impacted by cancer, and their families.

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Chapter 1

Pediatric Oncology: An Overview

Gregory M.T. Guilcher, MD

Learning Objectives:

After completing this chapter you will know:

- ... how to define cancer and understand general principles of its staging.
- ... the incidence of cancer in children and adolescents in North America, rates of cure, and the prevalence of survivors of childhood cancer.
- ... the names of common types of cancer in children and adolescents.
- ...that the treatment of childhood cancer often requires multiple modalities of therapy, all of which involve short-term and long-term toxicities.
- ... the importance of physical activity in preventing and mitigating toxicities of cancer therapy.

Introduction

Cancer is the growth of cells in which normal regulation has been altered or inactivated entirely¹. **Malignant** cells proliferate without control, either due to abnormally increased growth signals or impaired mechanisms to inhibit or restrict cell growth and proliferation. Cancer cells often escape normal cell death, or apoptosis, yet do not grow into normal tissue structures **(differentiate)** and may even revert to a more primitive form of cell. Finally, cancer cells may not respect normal cell and tissue boundaries, and are prone to invade adjacent tissues or enter the bloodstream to access distant sites **(metastasis).** These abnormal cells ultimately grow to cause a mass or pressure effect on normal tissues, resulting in the symptoms and signs of cancer (refer to *Figure 1.1*). Cancer can present as local disease in the area of origin of the mass, or as advanced disease with dissemination to other areas of the body. Various staging systems have been developed, with more advanced staging representing more aggressive disease. Likewise, staging systems have typically been correlated with prognosis, with more advanced stages often requiring more intensive therapy. Some pediatric tumors (e.g.,



neuroblastoma) are further divided into low, intermediate and high-risk groups to incorporate biologic tumor markers with staging to again correlate with prognosis and the need for less or more intensive interventions.





Note. The hallmarks or characteristics that have been found to be important for cancer formation. These properties have been shown to play a fundamental role in tumor growth, survival and the generation of resistance to treatment in patients. Adapted from ².

Epidemiology of childhood cancers

Pediatric cancer comprises only 2% of all cancer cases, and the types of cancer seen in children differ from those diagnosed in adolescents and adults ^{1,3}. Refer to *Figure 1.2* and *Figure 1.3* for a summary of common childhood cancers ^{1,3-5}. While cancer is relatively rare in children, it remains the most common cause of death due to disease in children over the age of 1 year ¹. Approximately 1 in 7,000 children under 15 years of age in North America are diagnosed with cancer each year ¹. In Canada, an average of 900 new cases per year are identified in those under 15 years, and 1,300 cases annually in children under 19 years of age ¹. The incidence is highest in children 3 years of age and younger.







Note. Data taken from ^{4,5}. CNS: central nervous system tumor.

Figure 1.3. Cancer diagnoses in adolescents 15-19 years of age.



Note. Data taken from ⁴. CNS: central nervous system tumor.



Leukemias and lymphomas are the most common malignancies diagnosed in children, followed by **central nervous system (CNS)** tumors then various solid tumors. Embryonal tumors (arising from immature tissue) are more common in children compared to adults, while carcinomas (arising from epithelial cells) are common in the adult population and uncommon in the pediatric age range. Tumors of bone or muscle comprise a small proportion of childhood cancers, and can often impact musculoskeletal integrity due to either the tumor itself or its treatment.

While the causes of most childhood cancers remains unknown, approximately 10% of cases are associated with a known genetic cancer predisposition ^{1,5,6}. Although the role of environmental exposures have been explored, given that almost half of all childhood cancers are diagnosed by four years of age, this allows for little time to account for environmental exposures in the pathogenesis of childhood cancer. While much is left to be understood, several known risk factors, accounting for a small proportion of cases have been identified (refer to text box below).

Cure rates for childhood cancer in high-income countries now exceed 80%, and there are approximately 30,000 adult survivors of childhood cancer in Canada ^{1,5,7}. It is estimated that one in 300-350 young adults in North America are survivors of childhood cancer ³. Unfortunately, the reality is vastly different for those who live in low-income and developing countries. Children with cancer in these countries often do not survive due lack of access to timely diagnosis, care and essential medicines.

Known Risk Factors

- Acute Lymphoblastic Leukemia: Ionizing radiation; race; some genetic syndromes
- ✓ Acute Myeloid Leukemia: Chemotherapeutics; some genetic syndromes
- Brain tumors: Therapeutic ionizing radiation exposure; some genetic syndromes
- ✓ Hodgkin disease: Family history; infections
- ✓ Non-Hodgkin Lymphoma: Immune deficiency
- ✓ Osteosarcoma: Ionizing radiation; some genetic syndromes
- ✓ Ewing's sarcoma: Race
- ✓ Wilms' Tumor: Some genetic syndromes
- ✓ Rhabdomyosarcoma: Some genetic syndromes
- ✓ Hepatoblastoma: Some genetic syndromes, birth weight
- ✓ Malignant Germ Cell Tumors: Undescended testicles



Treatment of Childhood Cancer

Optimal treatment of cancer in children and adolescents often involves multiple types, or modalities of therapy. The goal of treatment is to maximize the chance of cure while minimizing both **short-term** and **long-term toxicities**. For those young people for whom cure is not believed to be achievable, therapy can be given to prolong life and maximize **quality of life (QOL)** - a goal which is a cornerstone of medical practice.

Treatment modalities typically include one or more of chemotherapy (or medical management), immunotherapy, surgery, radiation therapy and **hematopoietic stem cell transplant (HSCT)** (refer to *Chapter 8*). Therapies are chosen with consideration of multiple factors including: the best published data regarding effective modalities for a given tumor, the site(s) of the tumor, underlying medical issues, patient age, and known prognostic biologic characteristics of the tumor. In resource-limited settings, the costs of medications and access to radiation, surgical and diagnostic imaging facilities impact the therapy provided. The feasibility for the provision of some aspects of supportive care by families and health providers- factors such as the availability of intensive care support, access to inpatient beds, patient volume and associated clinic space, transportation and distance to health care facilities may all impact rates of survival. Intensive supportive care has greatly improved survival for children with cancer but is associated with tremendous financial costs and resources of time and space for provision of care. Also important are patient/family preferences and clinician experience with various therapeutic modalities. Finally, information regarding prognosis, short and long-term toxicities greatly influence treatment recommendations and informed decision-making.

Chemotherapy and implications for physical activity

Chemotherapy involves the administration of medicines by various routes to destroy

cancer cells. Chemotherapy has historically referred to cytotoxic medications or those drugs that are toxic to cells. Unfortunately, many such therapies greatly impact cells in other healthy tissues, particularly those cells that divide quickly ⁸. Medications are chosen which are effective to treat a given tumor, administered at the highest dose to achieve maximal tumor cell destruction,

Potential Side Effects

- ✓ Inhibit growth of health cells
- ✓ Fatigue
- ✓ Nausea
- ✓ Vomiting
- ✓ Diarrhea
- ✓ Immune suppression
- ✓ Loss of appetite

while still at a dose that can be tolerated with acceptable side effects. Generally such medications are given in combination to maximize the likelihood of destroying all cancer cells,



with as few overlapping toxicities as possible to minimize side effects. The combinations of chemotherapeutic agents chosen and the doses administered may require individualization, depending on the health of the child and the ability to tolerate the therapy. As many therapies often result in lower blood cell counts, such as anemia (low red blood cell or hemoglobin levels) which can cause low energy levels and leukopenia (low measures of white blood cells), which predisposes the child to infection (refer to *Chapter 5*) special precautions with respect to physical activity (PA) participation may be warranted. Other side effects relevant to PA include muscular deconditioning and osteopenia. Fatigue, even after cancer therapy has been completed, is common in children and youth undergoing chemotherapy. Several studies, including the large Childhood Cancer Survivor Study, have identified fatigue as not only prevalent in survivors of childhood cancer through adulthood, but as an identified barrier to participation in PA⁹⁻¹¹. Malnutrition is no longer accepted as an inevitable component of a diagnosis and treatment of cancer ¹². Energy requirements both at rest and during PA can be impacted by cancer and its treatment, and these effects can be carried into survivorship and adulthood ¹². Clearly adequate energy substrates through optimal nutrition has a relationship with fatigue and the ability to perform PA, and altered metabolic rates not only affect the performance of PA, but PA will impact metabolic rates as well. Thus, optimal nutrition during and after cancer therapy is important to promote normal growth and development and maximize QOL ^{12,13}.

There are several drugs especially relevant to PA and mobility (refer to *Appendix A* for a full list of common medications and side effects). Corticosteroids, commonly used to treat leukemias and lymphomas, cause central obesity, muscle and subcutaneous atrophy, **osteopenia/osteoporosis** and can even result in **osteonecrosis** (bone death)⁸. Vincristine and vinblastine are drugs used to treat many leukemias, lymphomas, brain and solid tumors. These drugs commonly cause peripheral neuropathy, which can be sensory or motor in nature. Methotrexate, used to treat many childhood cancers including leukemias, lymphomas and some bone tumors, can cause adverse effects on the central nervous system as well as osteopenia/osteoporosis. Some chemotherapeutic agents such as bleomycin and nitrogen mustard compounds are toxic to the lungs and can induce oxygen-diffusion abnormalities and pulmonary fibrosis (scarring). It has also been well established that a class of drugs known as anthracyclines are known to cause numerous cardiac late effects, including cardiomyopathies and arrhythmias, with the potential for cardiac failure (refer to *Chapter 6*). Future goals are to find more selective drugs with anti-tumor effect and fewer systemic side effects.



Radiation therapy and implications for physical activity

Radiation therapy can be a highly effective treatment modality for certain pediatric cancers ¹⁴. Radiation involves the use of photons, electrons or protons with precision to target

cancer cells. Typically radiation is used in combination with another treatment modality, and consideration is given to the child's age as well as the area (or field) to be radiated.

Radiation therapy is toxic to healthy tissues as well as cancer cells, so significant efforts are made to spare children radiation whenever possible. Growth and normal tissue development can be significantly impacted. Cognition is **Potential Side Effects**

- ✓ Local tissue and/or skin inflammation
- ✓ Fatigue
- ✓ Atrophy of tissue within the radiation field
- ✓ Radiation-induced second malignancy
- Neurocognitive delay (for cranial radiation)

vulnerable when the developing brain is exposed to radiation, and typically children under the age of three are spared cranial radiation, particularly to the cerebral hemispheres. Blood vessels, muscles and bones are also at risk, and each tissue has a different capacity to tolerate radiotherapy. Complex treatment plans are made to ensure tumor kill is optimal while sparing healthy tissue as much as possible, with efforts to avoid tissues and organs which are particularly vulnerable.

Cranial radiation carries the risks of growth and neurologic complications, and children who receive radiation to the brain are known to be at greater risk for obesity ^{14,15}. Learning issues might impact socialization and participation in organized activities. Radiation fields which include the lung or heart can carry risks of scarring to these organs, and cardio-respiratory long term effects can certainly impact the ability to perform PA ¹⁶.

Surgery and implications for physical activity

Most solid tumors require an attempt at surgical resection to maximize the chances of cure. Commonly resected lesions include CNS tumors, abdominal masses and musculoskeletal tumors. Thoracic primary tumors or metastases may also require surgical resection. The morbidity of such a surgery depends on the specifics of each individual case, but often such operations are complex and require specialized expertise.



Motor skills and PA tolerance are at risk of impact from such surgeries, either due to

potential injury from neurosurgical procedures, loss of lung volume or thoracic deformity from surgeries involving the chest cavity or functional and/or structural deficits from orthopedic surgical intervention. Communication between orthopedic

Potential Side Effects

 ✓ Many complications and side effects depend on the site of the tumor and specific surgical procedure (refer to *Chapter 5*)

surgeons, physiotherapists and qualified fitness instructors is essential to ensure the benefits of PA are maximized while avoiding activities that may put musculoskeletal structures at risk. Pathological fractures can have serious consequences both in terms of tumor control as well as resultant surgical interventions. For example, following a pathological fracture an amputation might be required whereas a limb salvage option might have been possible had the pathological fracture been prevented.

Immunotherapy and implications for physical activity

Immunotherapy involves harnessing immune mechanisms and responses to destroy

cancer cells. Such therapies are the focus of intense research, and are now becoming standard of care for diseases such as neuroblastoma and some lymphomas ¹⁷⁻¹⁹. The use of viruses to destroy cancer cells directly in addition to priming the child's immune system to

Potential Side Effects

- ✓ Allergic reactions
- ✓ Capillary leak syndrome
- Immune suppression
- Risk of secondary lymphoma

increase tumor kill is of growing interest and entering the realm of clinical trials ¹⁷. Children and young adults undergoing such therapy might be at risk for infection and special isolation precautions may be necessary, thereby impacting ability to engage in PA.

Hematopoietic stem cell transplantation and implications for physical activity

HSCT involves the infusion of blood stem or progenitor cells to facilitate recovery from high doses of chemotherapy and/or radiation, or as a form of cellular immunotherapy to correct an underlying blood or immune disorder. The stem cells may be re-infused into the same individual from whom they were collected (also known as autologous HSCT), and this strategy is typically used as a rescue from high doses of chemotherapy to allow such medication doses to be given safely and to facilitate recovery. Allogeneic HSCT, where the donor and recipient of



the blood stem cells are different people, is used to treat leukemias and to correct bone marrow failure (aplastic anemia) and various immunologic disorders (refer to *Chapters 8* for more

details). Given the intensity of both autologous and allogeneic HSCT, deconditioning is common and efforts to study the potential benefits of PA to promote recovery and perhaps improve immune cell function are underway ²⁰⁻²³.

Allogeneic HSCT carries a unique complication called **graft versus host disease**

Potential Side Effects

- ✓ Immune suppression
- ✓ Deconditioning
- ✓ Nutritional support often required
- ✓ GVHD for allogeneic HSCT
- ✓ Infertility
- Second malignancy

(GVHD), a condition in which the donor immune cells cause inflammation in host tissues that are identified as foreign ²⁴. In the acute form, GVHD can cause skin rash, diarrhea and/or liver abnormalities. While the chronic form is less commonly seen in children, it can be a devastating and a potentially fatal complication, which might require years of therapy before resolution ²⁵. Manifestations of chronic GVHD are many and can include fatigue, infection, anemia, joint stiffness, tightening of soft tissue structures with resultant decreased range of motion, as well as impaired lung function. Treatment of GVHD includes immune suppressing drugs, with steroids being one of the most effective agents. The side effects of corticosteroids can be significant, as previously discussed (refer to *Chapter 5* and *Chapter 8* for more details).

Summary of Cancer Therapy in Children

While cure rates for cancer in children and adolescents are generally relatively high, unfortunately cancer therapy at present is not without both short and long-term toxicities. In fact, few therapies are without acute side effects and such toxicities can be significant and dose or life-limiting. **Supportive care** is critical in the provision of good cancer therapy, and advances in supportive care have resulted in some of the improved cure rates seen in childhood cancer therapy over the last 50 years ²⁶. Extensive efforts are underway to identify those children who need more intensive therapy while sparing children who can be cured with less toxic treatment ¹.

Long-term effects of therapy are also common and often life-limiting in survivors of childhood cancer ^{27,28}. It is estimated that 60% of childhood cancer survivors will have at least one long-term side effect of therapy, many have multiple long-term morbidities and as many as 27% having a life-threatening complication ²⁸. Dedicated programs to follow survivors are essential in Canada and worldwide to address their many unique medical and psychosocial issues ^{7,29}.



Late Effects and Impact of Physical Activity

As previously mentioned, cancer therapy can have significant long-term effects on the ability to maintain an active lifestyle (refer to Chapters 15 and 16 for tips on how to become more active and overcome barriers to PA). Toxicity to the cardiovascular system is the most common long-term effect seen in survivors of childhood cancer therapy ^{27,28} (refer to *Chapters 5* and 6). Pulmonary toxicities might also impact PA tolerance ¹⁶. Fatigue is relatively common in childhood cancer survivors and is related to decreased activity, yet these survivors might be less symptomatic if physically active 9-11,30-32. CNS tumors are commonly associated with longterm neurologic deficits and sequelae such as visual loss, gross and fine motor deficits which can clearly impact PA levels ^{33,34} (refer to *Chapter 10*). Muscle weakness from steroid exposure, surgery or radiation is clearly related to strength and conditioning. Bone integrity may be compromised, either from a primary bone tumor or a surgical procedure required to resect such a lesion (refer to Chapter 5 and 9). Survivors of childhood acute lymphoblastic leukemia (ALL) are especially at risk of reduced bone mineral density, particularly due to steroid exposure with methotrexate implicated to a lesser extent ³⁵. The leukemia itself may damage bone integrity ³⁶. While all youth with a history of ALL are prone to long-term bone health issues, females, adolescents and those who become deficient in growth hormone (often due to



Finn, 7 years old

cranial radiation) are particularly at risk (refer to Chapter 7) ³⁷⁻³⁹. Sedentary lifestyle is a modifiable risk factor to prevent reduced bone mineral density ^{33,40,41}.



Obesity and childhood cancer

Obesity has become endemic in Western society over the last decades. Children and adolescents who are obese often experience increased toxicities of therapy and are less likely to survive some cancer therapies ^{42,43}. Moreover, survivors of childhood cancer who have received cranial radiation for leukemia are at higher risk of becoming obese or overweight compared to their healthy siblings ¹⁵. Survivors of HSCT are also at greater risk for obesity ⁴⁴. Historic measures of obesity, such as **body mass index (BMI)**, may underestimate disproportionate body composition in cancer and HSCT survivors. Specifically, some survivors might have normal or low BMI, yet their bodies are low in muscle mass and relatively high in fat content, a state called **sarcopenic obesity** ⁴⁵.

Future Directions: The Time for Action and Activity is Now

Children in Western society need a return to active living as part of everyday life and play. Children currently aged 10 years are the first generation in human history expected to have a shorter life expectancy than their parents ⁴⁶. The lifestyles and leisure activities in place by age 10 are often carried into later life, with their resulting benefits and/or associated risks ⁴⁶. All professionals who provide education and health care for children carry responsibility to promote and advocate for healthy living. Children and adolescents who undergo cancer therapy have already undertaken immense risk and persevered incredible challenges in an effort to live longer. Such a life should be as healthy as possible - survivors should not only be living but living well, and health promotion and disease prevention should be at the core of survivorship care. This focus on healthy living can start with a cancer diagnosis to not only increase the opportunity for cure but to also promote and establish lifelong healthy lifestyles. Prescriptions for PA have been shown to result in higher activity levels for patients and survivors, and such prescriptions can be given concurrently with cancer and survivorship care ⁴⁷.

The short and long-term toxicities of cancer therapies as they are provided today can result in barriers to active living. These toxicities include cardio-respiratory and musculoskeletal compromise, but these barriers are not insurmountable. PA interventions and the promotion of active living, which can mitigate complications of cancer therapy as well as improve physical, mental and emotional well-being, are essential in the provision of complete care of children and youth with cancer or who have survived cancer therapy. The time is now to recognize the critical importance of a simple but potentially lifesaving intervention - PA - that comes with little to no adverse effects yet offers tremendous benefits.



Take Home Message

Cancer in children and adolescents is relatively rare and cure rates are high. Current treatments still carry significant toxicities both short and long-term. Due to the intensity of these therapies and the significant time away from educational, social and athletic activities, children and adolescents who are diagnosed and treated for cancer are at high risk of physical deconditioning and may miss critical opportunities to develop healthy habits for active living. Physical activity is a safe and essential part of a healthy lifestyle, and activity during childhood cancer therapy can prevent and reduce the severity of complications, as well as promote healthy behaviors which are particularly important for this population with specific health risks.

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Chapter 2

The Benefits of Physical Activity in Pediatric Oncology

i) Health-related fitness and other physiological outcomes: Carolina Chamorro-Viña, PhD

ii) Fatigue: Julia Beulertz, PhD student & Freerk Baumann, PhD

iii) Psychosocial: S. Nicole Culos-Reed, PhD

vi) Neurocognition: Taryn Fay-McClymont, PhD

Learning Objectives:

After completing this chapter you will know:

Health-related fitness:

- ...the physiological late effects in pediatric cancer patients and survivors.
- ...the potential benefits of physical activity on physiological variables.

Fatigue:

• ...how fatigue may affect pediatric cancer patients and survivors on a physiological and psychosocial level.

• ...the potential benefits of physical activity regarding fatigue. Psychosocial:

• ...the potential benefits of physical activity on quality of life.

Neurocognitive:

- ...the neurocognitive late effects in pediatric cancer patients and survivors.
- ...the beneficial effects of physical activity on brain development and cognitive functioning, and how this relates to pediatric cancer patients and survivors.



Introduction

Progress in the treatment of most types of pediatric cancers is one of the greatest success stories of the late 20th century, with the five year survival rate increasing from less than 30% in 1960 to more than 80% today ¹. Unfortunately, the cancer treatments needed to achieve a cure may cause a myriad of short and long-term side effects, including second malignancies, cardiac and pulmonary impairment, musculoskeletal abnormalities, fatigue, neurocognitive deficits and social isolation ^{1,2}. These physical and psychosocial impairments have been linked to decreased physical performance, the ability to perform **activities of daily living (ADLs)** and decreased **quality of life (QOL)** ³⁻⁵.

Recently, **physical activity (PA)** intervention research has emerged as a promising adjuvant therapy to mitigate some of these side effects ⁶. There is growing evidence for the efficacy of PA to improve strength, **cardiorespiratory fitness**, symptoms of fatigue, and QOL ^{3,4,6-8}. Furthermore, it has been associated with enhancing normalcy for children with cancer, as their lives are often dramatically changed by their disease and treatments ⁹. For some patients, normalcy means resuming their lives where they had left off before their diagnosis ¹⁰. Importantly, none of the studies to date have reported any serious negative outcomes, even in immunocompromised patients ^{3,5,11,12}. It is widely accepted that PA is a key factor in the development of any healthy child, with participation in PA being associated with improved general health and disease prevention. Moreover, the link between PA and positive psychosocial development and mental health is well-established ^{3,9}. Thus, given the potential negative side effects associated with a cancer diagnosis and its associated treatments, PA is crucial in this special pediatric population. This chapter will discuss the benefits of PA with regards to outcomes related to **health-related fitness (HRF)**, fatigue, and psychosocial and neurocognitive functioning.

i) Health-Related Fitness and Other Physiological Outcomes

Health-related fitness is the ability to become and stay physically active. It has five components: cardiovascular fitness, muscular endurance, muscular strength, body composition and flexibility. Together, these components promote optimum health and prevent the onset of disease and problems associated with inactivity.

It is well known that HRF is affected by both cancer and its treatments ^{5,6}. For example, research has found that many pediatric cancer patients and survivors experience decreased cardiovascular fitness, muscular atrophy, limited range of motion, and an increased likelihood of



developing metabolic syndrome (e.g., obesity, diabetes) ³⁻⁶. These side effects might limit the individual's ability to be physically active (refer to *Chapter 5*) ⁶ and make the child prone to adopting a sedentary lifestyle. However, as PA is emerging as a promising complimentary therapy to mitigate several of the side effects caused by cancer and its treatment, greater efforts are being made to promote an active lifestyle among children affected by cancer ^{3,4,6,12}.

To our knowledge, only 14 studies to date have assessed HRF outcomes in pediatric populations (see *Table 2.1*). The studies identified were supervised, home-based, or a combination of a supervised and home-based program. The intervention period in these studies ranged from 8 weeks ¹³ to 2 years ¹⁴. The most common frequency reported was 3 times/week, but there was large variability in studies, ranging from 1 time/week ⁸ to 7 times/week ¹⁴. There was also a large variability in the duration of each training session ranging from 15 minutes/session ¹⁵ to 90 minutes/session ^{13,16}. However, 50-60 minutes/session was the most commonly reported duration. The majority of studies conducted their intervention with **acute lymphoblastic leukemia (ALL)** patients undergoing active treatment. A combination of moderate **aerobic training** along with **progressive resistance training** was the most common type of intervention. Other types of PA interventions included aerobic training only, aerobic training with an educational component and yoga ¹⁷. Importantly, no negative side effects were reported in any of the interventions. Preliminary results across these studies are promising as seen by improved cardiorespiratory fitness, strength, body composition, flexibility and physical function. These are described in greater detail below.

Cardiovascular fitness, also known as **aerobic fitness**, **cardio-respiratory endurance**, maximal aerobic power, or **maximal oxygen consumption (VO₂ max)**, is the ability of the body's circulatory and respiratory systems to supply fuel during sustained PA ¹⁸. It is measured as the amount of oxygen transported in the blood and pumped by the heart to the working muscles and as the efficiency of the muscles to use that oxygen. Good cardiovascular fitness has many health benefits such as decreased risk for: cardiovascular disease, stroke, high blood pressure, diabetes and other cardiopulmonary diseases and complications ¹⁸.

Unfortunately, as a result of cancer and its treatments, cardiovascular fitness is often decreased in pediatric cancer patients and survivors. It has been reported that pediatric cancer patients during the maintenance phase of treatment have a **peak oxygen consumption (VO₂ peak** 24 mL/kg⁻¹/min⁻¹) clearly below the expected VO₂ peak for age-matched healthy children (45 mL/kg-1/min-1) ^{13,16,19}. Several authors have corroborated this reduction in VO₂ peak ^{4,20-24}. The reduction in cardiovascular fitness will thus limit the child's capacity to perform ADL's without undue fatigue.



Fortunately, this decrease in the VO₂ peak seems to be modifiable. San Juan et al. reported an increase of 6 mL/kg⁻¹/min⁻¹ after only 16 weeks of aerobic and strength training in children with ALL during the maintenance phase of treatment (age range 4-7 years) ¹⁶. Increased aerobic capacity after varying training periods has also been reported by several authors ^{8,11,15,16,27}. This is very important because VO₂ peak is also an excellent indicator of health status and an independent predictor of mortality in both healthy and unhealthy populations ²⁸.

Muscular strength is defined as the maximum amount of force that a muscle can exert against some form of resistance in a single effort. The key to increasing muscular strength is by working against resistance ¹⁸. Muscular endurance is the ability of the muscle to continue to perform without fatiguing ¹⁸. Because muscular strength and endurance are so closely related, they will be discussed together.

Decreased muscular strength and endurance are common side effects of cancer and its treatments. Specifically, The evidence indicates that many pediatric cancer patient are forced to reach their maximum oxygen consumption in order to perform ADL's.

ADL's require between 9-18 mL/kg⁻¹/min⁻¹. For example, getting dressed requires 9.45 mL/kg⁻¹/min⁻¹. An activity such as playground games require 17.5 mL/kg⁻¹/min¹ and thus may be too challenging because they are close to the maximum oxygen consumption. Playing basketball games or climbing stairs (24.5 mL/kg⁻¹/min⁻¹) may be near impossible or exhausting because this activity would require the patient to be working at 100% of their VO₂peak^{3,25} and humans are able to tolerate this intensity for only a few minutes²⁶.

the use of corticosteroids, surgical procedures, or long periods of immobilization (such as those experienced during **hematopoietic stem cell transplantation (HSCT)**²⁹. Research has found resistance training is safe in pediatric cancer populations and also promotes improved muscular strength and endurance ^{3,6}. Perondi et al. reported an increase greater than 50% in the 10 **repetition maximum (RM)** test (bench press, leg press, leg extension and lateral pull down) after only 12 weeks of supervised PA in children with ALL ³⁰. Similarly, San Juan et al. reported an improvement of about 20% in muscular strength after an 8-week PA intervention in children with ALL during the maintenance phase of treatment, as well as in children treated with HSCT ^{13,16,31}. Strength improvements have also been reported by Tanir et al. ³⁴, Marchese et al. ³², Chamorro et al. ¹¹, and Keats and Culos-Reed ⁸. Rosenhagen et al. reported maintained strength during the neutropenic phase of HSCT ²⁷. This is an important finding, as a loss of strength is expected during this phase of treatment. No negative side effects due to resistance training have been reported in this population ^{8,11,32,33}. With regards to findings, supervised PA



interventions seem to better induce increases of strength compared with home-based interventions ⁴.

Body composition refers to the relative amount of muscle, fat, bone, and other vital components of the body ¹⁸. **Body mass index (BMI)** is a measure of relative weight based on an individual's mass and height and is a reliable indicator of body fatness for most children and



PEER: aerobic and strength training

teens. BMI is calculated in children in the same way as for adults, but interpreted differently. In children, the BMI value is compared to typical values for other children of the same age (refer to the Center for Disease Control and Prevention web site for more information ³⁴).

A high prevalence of overweight and obesity has been increasingly recognized in patients and survivors of pediatric cancer, mainly in ALL patients ³⁵⁻³⁷. This is concerning, as substantial weight gains are associated with a greater risk of development of comorbidities ³⁸. Equally important is substantial weight loss ³⁹. For example, in adult populations a BMI of less than 20 was associated with increased transplant-related mortality, decreased survival and decreased relapse free survival ⁴⁰. Losses in body weight during treatment may occur due to malnutrition and/or chemotherapy-induced

toxicities (such as mucositis and diarrhea)⁴⁰. To date, only two studies have reported on the effect of a PA intervention on BMI, fat mass and fat free mass in pediatric cancer patients and survivors. Chamorro et al. reported the BMI of children undergoing HSCT during the neutropenic phase of treatment ¹¹. Pre to post training, the intervention group increased their BMI while the control group experienced a decrease. However, the BMI remained within a healthy range. This was an important finding given the anticipated weight loss associated with treatment toxicity.

Author/Study Design	Population	Intervention	Result
Perondi et al. 2012 ³⁰ Quasi- experimental	ALL/ maintenance phase (6-16 yr) N= 6 IG=6	 Duration: 12 wk. Supervised in-hospital intervention Frequency: 60 min/ 2/ wk - PRT: 1st wk- 2 set x 15 rep of bench press, leg press, lat pull down, leg extension and seated row. 2nd wk ongoing: 4 set x 6-10 rep of same exercises describe above. - Aerobic training: 10 min warm up + 20 min at 70% of VO2 peak. 	- Strength ↑ 50 to 73 % in all the muscles tested with p<0.05.
Tanir et al. 2012 ³³ RCT	ALL/ in remission (8-12 yr) N= 40 IG=19	 Duration: 12 wk. Home –based intervention. Active ROM exercises: 3 times/day- 5/wk. Exercises: lying on back: hip flexion and extension, hip adduction and abduction, knee flexion and external and external rotation of the foot). PRT: 3 times/day 3/wk. Exercises: squatting (30 reps) and walking on the heels (10 rep x 3x back and forth). Aerobic training: 30 min 3/wk. Exercises: ride a bike, walk, run, jump and dance. Intensity not reported. 	 IG: ↑ aerobic capacity, functional capacity and strength (p<0.05). CG: ↔ aerobic capacity, functional capacity and strength
Marchese et al. 2004 ³² RCT	ALL/ maintenance phase (5-15 yr) N= 28 IG= 13	 Duration: 12 wks. 5 sessions of individualized supervised physical therapy + 4 months home-based exercise program. The home based exercise program consisted of functional exercises that children were able to incorporate into their daily routines based on consultation with parents and children. These included ankle stretching (held for 30 seconds /5 days a week), lower extremity strengthening (10 repetitions/3 days a week) and aerobic fitness on a daily basis. Intensity was not reported 	 - IG:↑ankle ROM and the knee extension strength (p<0.01). Aerobic capacity ↔. - CG:↔ aerobic capacity, strength and ankle ROM
San Juan et al. 2007 ¹⁸ Quasi- experimental	ALL/ maintenance phase (4-7 yr) N=7 IG=7	 Duration: 8 wk. Supervised in-hospital intervention Frequency: 90 min/ 3/wk PRT: 1 set of 8-15 repetitions of 11 types of exercises engaging the major muscle groups (bench press, shoulder press, leg extension, leg press, leg curl, abdominal crunch, low back extension, arm curl, arm extension, seated row and lateral pull down). 1-2 min rest period between exercises with stretching of the muscles involved in the last exercise. Aerobic training: the intensity and duration gradually increased during the program from 10 min at 50% of age predicted HRmax to 30 min at ≥70 % HRmax. 	- IG: ↑ functional capacity and strength (p<0.05).

Table 2.1. Physical activity interventions focus on health-related fitness outcomes.

 IG: ↑ functional capacity, aerobic capacity and strength (p<0. 05). VO2 peak increase a median of 6 ml.kg⁻¹ min⁻¹. 	 Aerobic capacity was lower in HSCT patients than in CG. IG: ↑ aerobic capacity and strength (p<0.05). 	 IG vs CG; ↑PA minutes and aerobic capacity (p<0. 05). IG and CG ↔ flexibility and upper body strength. 	 IG: 10 % ↑in the time spent on the bicycle ergometer. → Strength assessed by hand held dynamometer. CG: non reported Regular PA during isolation phase of HSCT is feasible, safe and counteracts the side effect of immobilization like muscular atrophy.
Same study as above with the same participants over 16 wk.	 Duration: 8 wk. Supervised in-hospital intervention Frequency: 90 min/ 3/wk FRT: 1 set of 8-15 repetitions of 11 types of exercise engaging the major muscle groups (bench press, shoulder press, leg extension, leg press, leg curl, abdominal crunch, low back extension, arm curl, arm extension, seated row and lateral pull down). 1-2 minute rest period between exercises with stretching of the muscles involved in the last exercise. Aerobic training: the intensity and duration gradually increase during the program from 10 min at 50% of age predicted HRmax to 30 min at ≥70 % HRmax. 	 Duration: 12 month. Home-based exercise intervention. Individualized exercise program based on the Physical Activity Pyramid for youth. The program was adjusted monthly based on the child's health and ability. Frequency: at least 3 sessions of 15-20 min of moderate-to- vigorous activity/wk. 	 Duration: approximately 34 days supervised intervention during the isolation phase of HSCT. In -hospital intervention. Frequency: approximately 50 min 3/wk. PRT/coordination training: This was individualized for each participant and included working the main muscles groups. Barbells, balls, bar and body weight was used to prescribe exercises. Aerobic training: Stationary bicycle ergometer with a minimal resistance of 6 watt for a minimum of 10 min. The resistance of the bicycle was increased in the next class only if participant reach 10 min. Intensity of training: Heart rate should not exceed [180- patient age] and breathing frequency has to be below 35 per minute. Participant train for a median of 18 minutes
Same as above	HSCT patients (IG:8±4 yr, CG: 7±3 yr) N= 15 IG= 8 HSCT CG= 7 healthy children	ALL (standard risk) (4-10 yr) N= 14 IG: 6	HSCT patients (15.3 ± 3.7 yr) N=23 IG: 13
San Juan et al. 2007 ¹⁵	San Juan et al. 2008 ³¹ Quasi- experimental	Moyer-Mileur et al. 2009 ¹⁷ RCT	Rosenhagen et al. 2011 ²⁷ Quasi- experimental

 1upper body strength flexibility and aerobic capacity (p<0.05) and this increment was maintain in the 3 and 12 month follow up assessment. 	- ↔ aerobic capacity.	 - ↔ aerobic capacity, strength, flexibility and BMI. - Just 4 participants finalized the study. The main reason for drop out was the fact that the program was so demanding. Children also perceived the training as bored. 	 - IG: ↑ BMI and weight (p<0.001). ↑ fat free mass and body fat (p<0.05) - ↑ Aerobic fitness and strength. - CG: ↔ BMI, body fat and weight with a trend to decrease.
 Duration: 16 wk with follow up assessment at 3 and 12 month Frequency: 90 min 1/wk Week 1- 8: 30 min educational sessions, 45 min aerobic training, 15 min of core strength training. Week 9-16: Variety of non-competitive PA. Informal lifestyle education was provided. 	 - Duration: 12 wk. Supervised 1/wk +Home –based intervention 2/wk - Frequency: 35 min 3/wk - Aerobic training: 30 min 3 /wk at 70-85% of the child's measured HRmax. - Stretching: 2-3 min 3/wk 	 Duration: 12 wk. Home –based intervention (2/wk) + supervised exercise session with physiotherapist (2/wk) Frequency: 45 min 4/wk Frequency: 45 min 4/wk Aerobic training: exercise intensity increase every 4 wk started at 66-77% HRmax and finish with >90% of HRmax. PRT and flexibility exercise were included but not described. 	 Duration: from the beginning of conditioning regimen until neutrophil engraftment (~30 days). Supervised in-hospital intervention Frequency: 50 min 5/wk (5/wk aerobic training + 2/wk strength training) PRT: 1 set of 8-15 repetitions of 6-10 types of exercise engaging the major muscle groups (bench press, shoulder press, leg extension, leg press, leg curl, abdominal crunch, low back extension, arm curl, arm extension, seated row and lateral pull down). 1-2 min rest period between exercises with stretching of the muscles involved in the last exercise. Aerobic training: range from 10 to 40 min depends of child status. Intensity controlled by heart rate monitor between 50%-70% of age predicted HRmax.
Mix cancer types (14-18 yr) N=10 IG: 10	Most of them ALL IG=(IG: 14±0.6 yr, CG:13±3.1 yr) N=6 IG=3	ALL survivors (6-14 yr) N=9 IG=9	HSCT in isolation phase (4-16 yr) N= 20 IG= 7 CG= 13 historical controls
Keats and Culos- Reed 2008 ¹⁰ Quasi- experimental	Shore and Shepard 1999 ⁶³ Quasi- experimental	Takken et al. 2009 ⁶⁰ Quasi- experimental	Chamorro- Viña et al. 2010 ¹³ Quasi- experimental

Hartman et al.	ALL	- Duration: 2 yr intervention. Home based -exercise program with	- BMI and percentage of body
2009 ¹⁶	(1-18 yr)	a individual physiotherapist follow up every 6 wk.	fat decrease to normal values
	N= 41	- Frequency: 7/wk	in the IG and the CG 1 year
RCT	IG= 20	- Parents were supplied with an exercise list enabling them to	post-treatment but these
		select exercises most appropriate for their child. Children had to	changes were more
		perform 1 time/day exercise to maintain hand and leg function and	pronounced in the IG (p<0,05)
		2/days jumping and stretching exercises.	
Wurz et al.	Mixed cancer	- Duration: 12 wk - Supervised group yoga program	 - IG: ↑ functional mobility
2014 ¹⁹	sample	- Frequency: 60 min 2/wk	(p=0,01)
	Out-patient (5-17 yr)	 Intervention: each session consisted in warm-up, standing 	
Quasi-	N=8	poses, group activities, supine/seated/kneeling poses, prone	(p=0,02)
experimental	IG=4	possess and a final resting pose.	- ↔ Ankle dorsiflexion ROM

Note. RCT: Randomized controlled trial; PRT: Progressive resistance training; N: number of participant; IG: intervention group; CG: control group; ROM: range of motion, BMI: body mass index; HRmax: Maximal Heart Rate; HSCT: hematopoietic stem cell transplantation; yr: year(s); wk: week(s); min: minute(s); ↔: maintain/ no change; ↓: decrease; ↑: increase/improve



Hartman et al. ¹⁴ (see *Table 2.1* for study details) reported an increase in BMI in the control group and in the intervention group during their last two years of maintenance therapy. However, one year after the cessation of the treatment both groups (control and intervention) experienced decreased BMI. Notably, the decrease was significantly pronounced in the intervention group ¹⁴. As survivors of ALL are at increased risk of become obese or overweight during early treatment phase and post treatment, interventions to manage body composition in this population should be promoted ^{37,38}. More research is necessary in this field to confirm the benefits of PA on body composition, however the preliminary evidence is promising.

Flexibility is the range of motion around a joint ¹⁸. Sufficient flexibility in the joints can help prevent injuries through all stages of life ¹⁸. Cancer therapy negatively impacts the musculoskeletal system; therefore, limited **range of motion (ROM)** is a common side effect. For example, reduce ankle dorsiflexion ROM is a common side effect of treatment with vincristine or cisplatin and is called **chemotherapy induced peripheral neuropathy (CIPN).** Children with diminished ankle dorsiflexion ROM will have their gait affected causing them to trip when walking or have difficulty to climbing stairs (refer to *Chapter 5* for more details on CIPN). Improvement in ankle ROM was reported by Marchese et al, in a 12 week home-based intervention ³². An improvement of flexibility was also reported by Keats et al. ⁸ and Wurz et al. ¹⁷ who found improvement in hamstring flexibility after the intervention. The findings in this area are still preliminary and more research is needed.

Other physiological variables impacted by PA

PA also seems to improve other physiological variables, such as **physical functioning** ^{13,19,41}, that are commonly negatively affected in children with cancer. Physical function is defined as the ability to perform tasks of daily living. This variable has been measured with different tools in pediatric oncology and only a few studies have addressed it ^{13,16,19,31,32,41}. The timed up and go test and the timed up and down stairs test are two of the most common tests reported ^{13,16,19,31}. Overall, PA seems to improve physical functioning, however more research is needed to confirm the preliminary evidence ⁵.

Notably, with regards to immune system recovery, there have been no negative effects reported to date. Two preliminary works performed by Ladha et al. ⁴² and Chamorro et al. ¹¹, demonstrated that moderate exercise does not have any deleterious effect on the immune system of children with cancer. Research must continue to explore the exercise dose issues (frequency, intensity, and mode) to determine the most appropriate and beneficial prescriptions to achieve immune system benefits.



To summarize, preliminary evidence indicates that PA is safe, feasible and beneficial throughout the childhood cancer journey. These results suggest PA promotes an improvement in cardiorespiratory fitness, muscular strength, muscular endurance, flexibility, body composition, and physical functioning. Early research suggests that exercise does not negatively impact immune function; however more work is clearly necessary. Future research on PA prescription will aid in understanding the potential improvements and develop the best possible interventions for this population.

ii) Fatigue

Fatigue has been argued to be an under-recognized and undertreated symptom in pediatric oncology ^{43,44}. Currently, data on the prevalence of fatigue in the pediatric cancer population is inconsistent. For example, Meeske et al. ⁴⁵ found that the prevalence of fatigue in survivors of childhood ALL fell within the general population limits. However, the bulk of the cancer literature has shown that **cancer-related fatigue (CRF)** is one of the most troubling and common symptoms experienced by children during and after treatment for cancer ^{43,44,46-52}.

CRF can be defined as an unusual sense of whole body tiredness, weakness, lack of energy, and an unusual need for rest ^{43,48,53}. Patients and survivors also may experience associated lifestyle changes, such as being socially isolated or unable to concentrate ^{43,48,53}. Fatigued patients and survivors characterize themselves as irritable, angry, unhappy and upset ⁴⁹. While adult survivors tend to describe fatigue as a loss of physical functioning during daily tasks such as short distance walking, climbing stairs or completing household tasks, children primarily report early fatigue during games and outdoor activities ⁴.

While the underlying mechanisms of CRF are not well understood ^{46,54}, it is most likely a multidimensional, multi-factorial and highly subjective phenomenon ^{43,45,53}. Regardless of the cause, CRF is a distressing symptom ^{48,51} negatively affecting the survivor's physical functioning and QOL ^{3,4,8,45,48,50,53-55}. Furthermore, CRF is related to a number of symptoms and survivor reported outcomes, including depression ^{45,55}, poor sleep quality ^{45,47,55}, and pain ⁴⁹. Additional factors associated with CRF include nausea, obesity, exercise-induced symptoms (i.e., shortness of breath with PA) and cognitive impairments ^{45,49,56}. Since fatigued survivors feel a loss of physical functioning, CRF often has a negative impact on the survivor's PA behavior ^{4,57}. At the same time, clinical PA programs may have the potential to reduce fatigue ^{5,6,58}. Several studies have examined the effects of PA interventions on survivors' fatigue scores and preliminary results are promising (*Table 2.2*).



Rosenhagen et al., ²⁷ found a positive trend in terms of fatigue scores during a PA intervention performed in the isolation phase of HSCT. Yeh et al., ⁵² found a positive effect of a PA program on fatigue with a sample of ALL survivors during maintenance therapy. This positive effect was also seen in a mixed sample of cancer survivors by Blaauwbroek et al..⁵³ and Keats and Culos-Reed⁸ found a positive effect of PA on fatigue with a mixed sample of childhood cancer survivors. While some of these PA programs were performed as a supervised intervention ^{8,27}, others were home-based programs ^{52,53}. Additionally, the form of PA varied from a 2-4 day in-hospital endurance training on a stationary bike ⁴⁷, to a 16-week group PA program including mixed exercises (endurance, strength, flexibility), ⁸ or a 10-week PA counseling program with feedback from a pedometer ⁵³. While these preliminary findings are promising, there are some inconsistencies in the research. For example, Takken et al. ⁵⁹ found a positive trend in fatigue-scores, but no effect on physical functioning in their study investigating the effects of a 12-week supervised and home-based PA program with ALL survivors. Similarly, Hinds et al., ⁴⁷ did not find any changes in fatigue within their 2-4 day supervised, in-patient endurance training with solid tumor and acute myeloid leukemia (AML) patients on a stationary bike. In light of the inconsistent findings across studies, Huang and Ness ³ suggest that the positive effects of PA programs on fatigue may require an improvement in the child's fitness condition (and/or motor performance).

To summarize, the preliminary literature in this area presents promising results regarding PA and fatigue. While PA programs may be beneficial for childhood cancer survivors suffering from fatigue, future research is necessary to determine how PA affects fatigue and what kind of PA is most advantageous.



Paul, Age 5



Table 2.2. Clinical physical activity interventions in pediatric oncology focusing on fatigue as one of the primary outcomes.

Authors	Population	Intervention	Results
Rosenhagen et al. 27	Stem cell transplanted patients N= 20 IG=10 (15.3 ± 3.7yr) CG:=10 (13.6 ± 4.0yr)	Supervised, in-hospital (isolation phase of PBSCT) IG: 34,1± 94days; 3/wk,50 min; cycle ergometer and additional strength/coordination exercises CG: no sports therapy	Fatigue ↑ (n.s.) in IG during intervention
Yeh et al. 52	ALL N= 22 IG=12 (11.01 ± 3.56yr) CG=10 (12.48 ± 3.86yr)	Home-based (maintenance chemotherapy) IG: 6wk; 3/wk, 30min; endurance PA at 40-60% of HRR with PA video CG: standard care	General fatigue score ↑ (p=0.02 per-protocol analyses) in IG vs. CG at 1- month follow up
Blaauwbroek et al. ⁵³	Mixed cancer survivors with fatigue N= 76 IG= 46 (29.8 ± 8.6yr) CG=30 (healthy controls)	Home-based (survivorship) IG:10 wk; telephone counselling and feedback from pedometer	Fatigue ↑ in IG during intervention (p<0.0005) and at follow up/wk 36 (p<0.0005)
Takken et al.	ALL N=9 IG=9 (9.3±3.2yr)	Supervised and home-based (survivorship) 12wk; 2/wk, 45-min, supervised (at 66->90% of HRmax) and 2/wk home-based	No significant changes in fatigue (improvement of 11%)
Keats et al. ⁸	Mixed cancer survivors N=10 IG= 10 (16.2 ± 1.6yr)	Supervised group PA (survivorship) 16wk;1/wk, 90min; education, endurance, strength, flexibility	Fatigue: general fatigue ↑ during intervention (p=0.01) and at 3-month follow-up; total fatigue and sleep/rest fatigue ↑ (p=0.01) at 12- month follow-up
Hinds et al. 47	Solid tumor, AML N= 29 IG=14 (13.08 ± 2.55yr) CG=15 (11.92 ± 3.24 yr)	Supervised, in-hospital (during medical treatment) IG: 2-4days, 2/days, 30min; endurance training on stationary bike	No effect on fatigue

Note. \uparrow : Improvement; N: sample size; IG: intervention group; CG: control group; HRR: heart rate reserve; yr: year(s); wk: week(s); min: minute(s); p: level of significance; (n.s.): not significant. Adapted from ⁵.



iii) Psychosocial

Treatments in pediatric oncology patients result in numerous negative physical and psychosocial outcomes, ultimately negatively affecting QOL ^{60,61}. A strategy to potentially mitigate many of the physical and psychosocial early and late effects is PA ^{3,5}. However, although this area of intervention research is growing, a majority of the studies to date have not included psychosocial outcomes. Of those that have included a psychosocial outcome, the focus has primarily been QOL using both self-report and parent proxy measures ^{8,13,27,31,32,41,62,63}. While this research has shown mixed results in terms of improvements over the course of an intervention, most studies have found improvements. Importantly, no studies have reported any detrimental psychosocial effects from PA. Growth in this area of research will help to address some of the primary methodological issues, including the sample sizes, populations (cancer types), and variation in the PA intervention in terms of frequency, intensity, time and type.

In the intervention studies that have found benefits in QOL measures, the findings support PA's positive impact on a number of different psychosocial domains, including role/social functioning, self-esteem, anxiety, mental health domains, comfort and resilience ^{8,27,31,32,41,63}. General psychosocial modules, such as those in the **Pediatric Quality of Life Inventory (PedsQL)**, also show improvement post-PA intervention (e.g., Keats et al., ⁸). Refer to *Chapter 12* for an overview of psychosocial instruments used in PA intervention research.

Yoga is an alternative form of PA that has been used as an intervention in pediatric oncology. The four studies to date performed in pediatric cancer population have focused primarily on the psychosocial benefits, including QOL, anxiety, depression, general well-being, self-efficacy/control, and self-esteem ^{17,64-66}. Generally positive psychosocial benefits have been seen, however the findings are limited to date in terms of sample sizes and variety of yoga interventions. Further discussion of this emerging yoga literature and a summary table of findings can be seen in *Chapter 14*. With regards to the benefits of traditional PA, a summary of the psychosocial benefits can be seen below in *Table 2.3*.



Table 2.3. Exercise and	psychosocial outcomes.
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Authors	Population	Intervention	Results
Rosenhagen et al. 27	Stem cell transplanted patients N=20 IG=10 (15.3 ± 3.7yr) CG=10 (13.6 ± 4.0yr)	Supervised, in-hospital (isolation phase of HSCT) IG: 34,1± 94days; 50 min; 3/wk ; cycle ergometer and additional strength/coordination exercises CG: no sports therapy	↑QOL (trend)
Gohar et al. ⁴¹	ALL; 2 weeks from diagnosis N=9 IG= 9 (2-14yr)	Supervised, in-hospital and home-based program; physical therapy 6-7mo	↑ QOL
Speyer et al.	Mixed cancer patients; during hospitalization N=30 IG= 30 (9-18yr)	Supervised, in-hospital; adapted physical activity >30 min;3/wk	Child-report QOL (domains: physical functioning, role/social-physical, self- esteem and mental health and behavior), ↑parent-proxy report QOL (domains: physical functioning, role/social-physical, self- esteem and mental health and pain)
San Juan et al. ³¹	Post-HSCT N=16 IG=8 (10.9 \pm 2.8yr) CG=8 healthy controls (10.9 \pm 2.8yr)	Supervised; endurance/ strength 8wk; 90-120 min 3/wk	↑ Comfort and resilience (self-report), ↑ Satisfaction and achievement (parent- proxy report)
Keats & Culos-Reed ⁸	Mixed cancer survivors N=10 IG= 10 (16.2 ± 1.6yr)	Supervised group exercise (survivorship) 16wk;90min; 1/wk; education, endurance, strength, flexibility	[↑] QOL (overall and domains: emotional, social, physical) and at 3-month and 12-month follow up, [↑] QOL (overall and domains: physical, emotional, psychological)
San Juan et al. ¹⁶	ALL during maintenance therapy N=7 IG=7 (4-7yr)	Supervised, in-hospital; endurance/ strength 16wk; 90-120min;3/wk	n.s.
Marchese et al. 32	ALL during maintenance therapy N=28 IG=13 (4-15yr) CG=15 (4-15y)	Supervised and home- based; physical therapy 4months	n.s



Shore & Mixed cancer entities Shepard 62 IG =6 CG= 11 healthy controls	Supervised and home-based 12wk; 30 min;3/wk	↓ Symptoms of anxiety
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Note. \uparrow : Improvement; \downarrow : decrease; ALL: acute lymphoblastic HSCT: hematopoietic stem cell transplant; leukemia; IG: intervention group; CG: control group; n.s.: not significant; QOL: quality of life; wk: week(s); yr: years.

Within this growing area of research, numerous methodological considerations should be addressed in future work that examines the potential psychosocial benefits of PA. First, choice of variables and the associated measurement tools should take into consideration consistency in tools and comparison across studies. While the PedsQL has been used as the primary measure of QOL, other questionnaires have also been utilized (refer to Chapter 12). With small sample sizes and limited research, being able to compare across studies that use the same measures would be advantageous. Second, considerations around the PA intervention could potentially strengthen the evidence for psychosocial benefits. Specifically, addressing the FITT principle (the frequency, intensity, time and type) of the PA intervention may increase the likelihood of impacting psychosocial outcomes, such as depression, anxiety, and general well-being or overall QOL. Finally, researchers should attempt to conduct multi-site studies to increase the sample size, and thus enhance the likelihood of finding both statistical and clinical significance in the psychosocial outcomes. The inability, through small sample sizes, to consider specific psychosocial domains versus the overall or general domains may be currently limiting our ability to truly understand the impact of PA on specific psychosocial outcomes in the pediatric oncology population. In addition, based on the small samples available, gualitative research that potentially provides more in-depth examination of exercise benefits in specific psychosocial domains should be employed.

iv) Neurocognition

Children with brain tumors or ALL, the most common forms of childhood cancer, are most at risk for neurocognitive late effects due to the use of central nervous system directed therapies, such as **cranial radiation therapy (CRT)**, and/or high-dose or intrathecal methotrexate and/or cytarabine (refer to *Appendix A* for a full list of common medications) ^{67,68}. Both CRT and high-dose or **intrathecal chemotherapies** have been linked to diffuse white matter loss and **demyelination** in the frontal lobe and posterior cortical and sub-cortical areas,



suppression of cell proliferation, and long-term cognitive executive deficits ^{69,70}. These processes often disrupt normal developmental processes in children and can cause marked negative cognitive sequelae that can appear for many years after treatment, negatively impacting their **QOL** and socialization ⁶⁹⁻⁷¹. **Cognitive executive deficits** often include deficits in processing speed, working memory, executive functioning (i.e., processes required to select, plan, organize, and initiate goal-directed activities, inhibit behavior, and shift from one mental set to another) and attention. Studies have demonstrated that over time these deficits negatively impact a childhood cancer survivor's intellectual and academic achievement largely due to a failure to progress at the same rate as their peers, rather than a loss of skills per se ⁶⁹⁻⁷².

While there are many studies that demonstrate neurocognitive deficits in childhood cancer survivors, very few studies address recovery or prevention of these deficits with remediation programs. Studies of pharmacologic therapies and cognitive remediation programs have demonstrated some benefits in regard to cognitive executive deficits, but the results have been mixed at best ⁷². There is a need for interventions that will have cognitive, physical, and social benefits for childhood cancer patients and survivors during therapy, recovery, and long-term.

Evidence from animal and human research demonstrates that PA may help to 'jumpstart' cell proliferation and foster plasticity in the neural environment ⁷⁰. PA has been shown to increase growth hormone, reduce inflammation, and increase microglia in the brain, and has beneficial effects on white matter tracts, the hippocampus and ultimately cognition ⁷³⁻⁷⁸.

Studies of healthy children confirm improvements in mood, cognition, and physical functioning with PA ^{75,79,80}. There is an accumulation of evidence demonstrating that PA has a beneficial effect on cognitive functioning in healthy children. A review of the literature by Tomporowski et al. ⁸⁰ demonstrated that gains in children's mental functioning due to PA training are seen most clearly on tasks that involve executive functions. Subsequent studies have demonstrated that acute PA actually enhances children's executive functioning ⁸¹. Research has also demonstrated that children who have higher levels of fitness show greater brain network efficiency and neurocognitive control, improved cognitive task performance, and better academic achievement ⁸²⁻⁸⁵.

While evidence regarding the benefits of PA in healthy children is accumulating, research is also demonstrating that pediatric cancer patients and survivors engage in less activity than their healthy peers ^{86,87}. Those survivors who have received CRT appear to be at particular risk of inactivity. A study of cardiorespiratory fitness in survivors of pediatric posterior fossa tumors who received CRT demonstrated that survivors were comparable to children with



chronic heart disease and other types of childhood cancer, but were less fit than children with cystic fibrosis and healthy controls ²⁴. Another study by Ness et al., ⁸⁸ documented specific deficits in muscle force production and PA tolerance among adult survivors of childhood brain tumors, with young age at diagnosis being the strongest predictor of weakness and poor fitness.

There is a dearth of studies specifically examining the beneficial effects of PA on cognitive functioning in pediatric cancer survivors. Rodgers et al., ⁷⁰ demonstrated that PA is capable of alleviating some of the CRT induced deficits in neurogenesis and cognition in rodents. For example, mice that were participated in PA after radiation demonstrated a 275% increase in new neurons and showed fewer declines in spatial memory compared to mice that did not have access to a running wheel ⁷⁰. A study by Wolfe et al., ²⁴ examined executive functioning and cardiorespiratory fitness in pediatric cancer survivors. They examined working memory in 9 adolescent pediatric posterior fossa tumor survivors who received CRT. Even though the sample size was relatively small, and the average time since treatment was nearly ten years, they found that higher cardiorespiratory fitness was associated with better working memory ²⁴.

Overall, the literature on neurocognitive benefits of PA in pediatric cancer patients and survivors is in its infancy, but evidence is beginning to mount in terms of positive and long-term effects of PA on cognition in children. While we know that pediatric cancer survivors suffer deleterious neurocognitive and physical sequelae of cancer treatments, we do not yet understand how to best intervene to prevent these late effects. By understanding the beneficial effects of PA on brain development and cognition in healthy children and animals, we can begin to elucidate the positive effects PA may have on preventing or ameliorating some of the negative neurocognitive sequelae we observe in pediatric cancer survivors.



Owen, 5 years old



Take Home Message

- Physical activity is safe and feasible. Preliminary results suggest it promotes an improvement in cardiovascular fitness, muscular strength, muscular endurance, flexibility, range of motion and improved physical functioning without affecting immune system functions.
- Cancer-related fatigue is a common symptom in pediatric oncology, affecting patients and survivors on a physiological and psychosocial level. Further research is necessary to better understand the role for physical activity interventions on fatigue.
- The limited research to date suggests that physical activity potentially enhances quality of life and specific psychosocial domains. Future research is necessary to more clearly elucidate potential benefits and outline effective methodologies and measurement tools.
- Evidence is beginning to accumulate that demonstrates that physical activity may have beneficial effects on neurocognitive functioning in pediatric cancer patients and survivors.

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Chapter 3

Physical Activity Across the Pediatric Oncology Trajectory

Julia Beulertz, PhD student & Freerk Baumann, PhD

Learning Objectives:

After completing this chapter you will know:

- ...why physical activity is important in childhood cancer populations.
- ...potential reasons for inactivity in childhood cancer populations.
- ...potential therapeutic physical activity strategies and their benefits on physiological and psychosocial outcomes.

Introduction

Physical activity (PA) plays a vital role in the physiological and psychosocial development of children. Adequately developed physical fitness (i.e., strength, endurance, flexibility) enables children to engage in **activities of daily living (ADLs)** ¹. There is a reciprocal relationship between PA (and its success and enjoyment) and subsequent **physical functioning**. As such, impaired physical functioning may lead to an inactive lifestyle and reduced levels of PA ². These reduced levels of PA may contribute to continued impaired physical functioning and various chronic health conditions (i.e., cardiovascular disease, several cancers, diabetes, osteoporosis, obesity, mental health disorders) ³.

There are several existing PA guidelines for children and youth. According to the World Health Organization ⁴, Children and youth aged 5-17 should accumulate at least 60 minutes of moderate-to-vigorous intensity PA daily. Most of the daily PA should be aerobic. Vigorous-intensity activities should be incorporated at least 3 times per week ⁴. Specifically, within the field of pediatric oncology, much of the research has been based on the former **Center for Disease Control (CDC)** guidelines for PA. According to CDC guidelines, 30 minutes of moderate intensity PA on 5 days of the week or 20 minutes of vigorous intensity PA on 3 days of the week are recommended for children and adolescents ^{5, 6}. However, it should be noted that



these guidelines have recently been updated to 60 minutes or more of moderate to vigorous PA daily⁷. Refer to *Appendix B* for PA guidelines

Inactivity in childhood cancer survivors

Research suggests that pediatric cancer survivors tend to be inactive ^{5, 6, 8-10}. Crosssectional studies generally find that only approximately 50% of childhood survivors meet the CDC guidelines for PA mentioned above ^{5, 6, 9}. Additionally, childhood cancer survivors are more likely to be inactive compared to healthy controls ^{5, 6, 8, 10} and the intensity of activities tends to be lower ¹⁰. However, there is some inconsistency in findings between researchers, with some reporting levels of activity similar to those reported by healthy children ^{11, 12.} Because healthy children often do not meet general PA guidelines ¹³, this may be an unexpected finding.

Several possible reasons for inactivity exist. Some research suggests this inactivity may be due to the cancer and its associated medical treatment and side effects, while other research suggests the low self-confidence of survivors regarding PA is the culprit ¹⁰. Finally, it has been posited that the overly cautious approach towards PA by parents, physicians and educators may underlie the low rates of PA ^{8, 10}. Most likely, it is the interplay of several factors that are responsible for the high levels of inactivity (refer to *Figure 3.1*).

Figure 3.1. Direct and indirect relations between chronic health conditions and inactivity.



Note. Translated from ².



For example, the disease and its subsequent treatment may result in overprotective behaviors, increased worry/anxiety, social isolation, and a lack of knowledge regarding safe or appropriate PA, together leading to lower levels of activity. Lower levels of PA further impair physical functioning, which in turn contributes to an inactive lifestyle ². While all patients and survivors are at risk, activity rates vary by diagnosis. Bone tumor, leukemia and **central nervous system (CNS)** tumor survivors have been reported to be the most inactive ^{10, 14}. Additional predictors of inactivity include more than 20 **gray (Gy)** cranial radiation ⁵, specific chemotherapeutic agents (i.e., vinca-alkaloide, platinum, anthracycline; refer to *Appendix A* for full medication list) ⁶, amputations ⁶, female sex ^{5, 11}, neurocognitive problems ⁹, and those experiencing **cancer-related fatigue (CRF)** ¹⁵. Because childhood cancer is associated with impairments in **health-related fitness (HRF)** and physical functioning, a sedentary lifestyle after treatment may worsen the detrimental effects of the disease and its treatment ¹². Given that childhood cancer survivors may suffer from various late-effects, PA should play a vital role in pediatric oncology in order to reduce both the short and long-term side effects ¹.

Physical Activity Interventions in Pediatric Oncology

In order to reduce inactivity and maintain or improve physical functioning of childhood

cancer survivors, modified PA programs may be beneficial. PA interventions designed to maintain or improve HRF and physical functioning (specifically targeting disease-related impairments) may be conducted by allied health care professionals or exercise specialists with a background in pediatrics and chronic conditions (or cancer-specific training) ¹⁶.

Over the last 15 years, several studies on therapeutic PA programs in pediatric oncology have



Participants exercising at the PEER program at the Gordon Townsend School in the Alberta Children's Hospital



been published. Most of these studies have been conducted with **acute lymphoblastic leukemia (ALL)** survivors during the maintenance phase of medical treatment ¹⁷. In general, increasing evidence on the feasibility of PA programs in pediatric oncology has been reported ^{17.}

In addition, all studies investigating the effect of PA on immunological parameters suggest that PA in pediatric oncology can be safely undertaken ¹⁸⁻²¹. Two recent reviews on PA interventions in pediatric oncology suggest there is evidence for the benefits of PA on muscle strength, flexibility, aerobic capacity, physical functioning, fatigue and **quality of life (QOL)** ^{17, 22}. *Appendix 3.A* presents a summary of research results regarding PA interventions with childhood cancer patients. For detailed information including evidence levels of PA intervention studies in pediatric oncology see Baumann et al.,¹⁷.

Physical activity during medical treatment

During the **isolation phase** of **hematopoietic stem cell transplantation (HSCT)**, supervised endurance and **progressive resistance training** programs have not shown any adverse effects ^{18, 23}. Maintenance or improvements in **aerobic fitness**, muscle strength, body mass, QOL and fatigue have also been reported during this phase of treatment ^{18, 23}. In addition, moderate-intensity PA training during hospital stays for HSCT did not show any negative effect on immune cell recovery ¹⁸.

The research on PA programs conducted during in-patient medical treatment have included supervised interventions ²⁴⁻²⁶ or combined supervised and home-based ^{21, 27, 28} interventions. Positive effects have been found for different physiological and psychosocial parameters, including motor function and QOL ^{24, 26, 27}. Importantly, no negative effects on immune parameters have been reported ²¹. Most programs included mixed PA focusing on endurance, strength and flexibility. A supervised yoga program has also shown benefits ²⁴. Notwithstanding, some inconsistencies in the research have been found. For example, a 2-year PA program for survivors treated for ALL was not more beneficial when compared to standard care in terms of bone mineral density, motor performance and ankle dorsiflexion. However, the authors note that this was most likely due to unsatisfactory compliance ²⁸.

PA programs during later phases of treatment, such as the **maintenance phase** of treatment for ALL, have included supervised ^{19, 20, 29, 30}, home-based ^{31, 32}, or combined supervised and home-based PA programs ³³. The form of PA conducted within these studies varied considerably from a 30 minute acute PA intervention ¹⁹ to a 12-month enhanced activity



program ³². Regardless, positive effects were found on fatigue, endurance, ankle dorsiflexion, functional mobility, level of activity and strength ^{19, 20, 29-33}.

Physical activity during survivorship

During survivorship, research has generally focused on supervised programs ³ or a combination of supervised and home-based programs ^{34, 35}. *Appendix 3.B* provides an overview of PA interventions during survivorship. Positive effects have been found on QOL, fatigue, activity and HRF parameters. The duration of programs varied from 12 to 16 weeks and all programs included some form of aerobic, resistance and/or flexibility training ^{3, 34, 35}.

Conclusion

PA programs during most phases of medical treatment, as well as during survivorship, appear beneficial in terms of physiological and psychosocial parameters. However, as most studies were conducted with ALL patients, best evidence is only provided for this patient group. In addition, small sample sizes and a large variety in intervention designs and outcome parameters limits the evidence. Therefore, future research with different childhood cancer populations and larger sample sizes is necessary. In addition, studies should aim to determine the best intervention design (focusing on optimal duration, intensity and type of PA) across all phases of medical treatment and survivorship.

Take Home Message

Given low rates of activity in pediatric oncology, physical activity interventions are necessary. According to current research results, physical activity interventions are feasible, safe and beneficial for childhood cancer patients and survivors. However, research evidence is limited and future studies are required.



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Appendix 3.A

Physical Activity Interventions During Medical Treatment

Author	Demographics	Intervention	Results
	Di	uring Isolation Phase of HSC	т
Rosenhagen et al. ²³	IG: n=10 CG: n=10 (HSCT-patients)	Supervised, in-hospital; endurance/ PRT 34.1 ± 94days; 3/wk; 50 min	Acceptance: approved Grip Strength: ↑ (NS in IG) QOL: ↑ (NS in IG) Fatigue: ↑ (NS in IG)
Chamorro-Vina et al. ¹⁸	IG: n=7 CG: n=13 (HSCT-patients)	Supervised, in-hospital; endurance/ PRT 3wk; 5/wk; 50min	Adherence: >90% Transplant Outcomes: no differences Aerobic Fitness: ↑ (p=0.034 in IG) Strength: ↑ (p=0.018 in IG) Immune System: no negative effect on immune cell recovery Weight/BMI/body Fat: ↑ in IG vs. CG during intervention
	Duri	ng In-Patient Medical Treatr	nent
Gohar et al. ²⁷	IG: n=9 (ALL; 2 weeks from diagnosis)	Supervised, in-hospital and home-based program; physical therapy 6-7mo	Adherence: 98% Motor Function: ↑ QOL: ↑
Geyer et al. ²⁴	N=6 (mixed cancer types; after induction phase)	Supervised, in-hospital; yoga 2 mo; 5 yoga sessions	QOL: ↑ (p=0.016)
Shore and Shepard ²¹	PG: n=6 (mixed cancer entities; after induction phase) CG: n=11 (healthy)	Supervised and home- based; endurance and PRT 12wk; 3/wk; 30min	Immune Function: ↓ but reduction remained insufficient to cause concern for health Endurance: ↑ Anxiety: ↑
Speyer et al. ²⁶	N=30 (mixed cancer entities; during hospitalization)	Supervised, in-hospital; adapted physical activity >3/wk; 30min	QOL: ↑ (p=0.001 – p< 0.0001)
Hinds et al. ²⁵	IG: n=14 CG: n=15 (solid tumor, AML; during hospitalization)	Supervised, in-hospital; endurance 2-4days; 2/days; 30min	Adherence: 84.5% Sleep: ↑ (p=0.05 in IG vs. CG) Fatigue: no effect
Hartman et al. 28	N= 41 IG: n=20 (ALL-patients during all phases of medical treatment)	Supervised and home- based; physical therapy 2yr	Adherence: unsatisfactory DF-ROM: not more beneficial in IG vs. CG BMI/body fat: normalized faster in IG after intervention



Author	Demographics	Intervention	Results
	Durii	ng Post-Transplant Phase o	fHSCT
San Juan et al.	N= 16 IG: n=8 (post- BMT) CG: n=8 (healthy)	Supervised; endurance/ PRT 8wk; 3/wk; 90-120 min	Adherence: 70% Functional Mobility: ↑ (p<0.05 in IG vs. CG during intervention) Strength: ↑ (p<0.05 in IG) Endurance: ↑ (p<0.05 in IG vs. CG during intervention) QOL: ↑ (p<0.05 in IG vs. CG during intervention)
		During Maintenance Therap	у
Yeh et al. ³⁰	N= 22 IG: n=12 (ALL)	Home-based; endurance training 6wk; 3/wk; 30 min	Adherence: 67-83% Fatigue: ↑ (p=0.02 in IG vs. CG at 1-mo follow-up)
Ruiz/San Juan et al. ^{20, 29}	N=7 (ALL)	Supervised, in-hospital; endurance training/ PRT 16wk; 3/wk; 90-120min	Immune Status: no adverse effects on IGF, IGFBP, GH Adherence: >85% VO2peak: ↑ (p<0.05)
Author	Demographics	Intervention	Results
Moyer-Mileur et al. ³¹	N= 13 IG: n=6 (ALL)	Home-based; nutrition and exercise 12mo; >3/wk; 15-20min	Level of Activity: ↑ (p=0.14 in IG vs. CG during intervention) Endurance: ↑ (p=0.09 in IG vs. CG during intervention)
Ladha et al. ¹⁹	N= 10 IG: n=4 (ALL) CG: n=6 (healthy)	Supervised; endurance training 30min	Immune Function: similar neutrophil reponse in IG and CG
Marchese et al.	N= 28 IG: n=13 (ALL)	Supervised and home- based; physical therapy 4mo	DF-ROM: ↑ (p<0.01 in IG vs. CG during intervention) Strength: ↑ (p<0.01 in IG vs. CG during intervention)

Note. IG: intervention group; CG: control group; mo: month(s); wk: week(s); yr: year; N: number of participants; min: minute(s); IGF: insulin-like growth factors; IFGBH: IGF-binding proteins; GH: growth hormone; DF-ROM: ankle dorsiflexion range of motion; PRT: Progressive resistance training; QOL: Quality of life (or sub-dimension of QOL); SCT: stem cell transplantation; N/n: sample size; NS: not significant; p: level of significance; BMD: bone mineral density; BMI: body mass index; VT: ventilator threshold; ↑: improved; ↓: worsen.



Appendix 3.B

Physical Activity Interventions During Survivorship

Author	Demographics	Intervention	Results
Takken et al. ³⁵	N=9 (ALL)	Supervised and home- based; endurance/PRT 12wk; 4/wk; 45 min	Feasibility: can be appreciated No significant changes in strength, exercise capacity, functional
Keats and Culos-Reed ³	N=10 (mixed cancer entities)	Supervised, group- based; endurance training/ PRT/ flexibility 16wk; 1/wk; 90min	Adherence: 81.5% QOL: \uparrow (p=0.01) Fatigue: \uparrow (p=0.01) Activity: \uparrow (p=0.12) Endurance: \uparrow (p=0.31) Strength: (abdominal: p=0.13; upper body: p=0.04) Flexibility: (right: p=0.03/left: p=0.01)
Sharkey et al. 34	IG: n=10 (mixed cancer entities)	Supervised and home- based 12wk; 2-3/wk; 45-60min	Level of Activity: ↑ (p<0.05 from t1-t2)

Note. IG: intervention group; N: number of participants; mo: month(s); wk: week(s); min: minute(s); PRT: Progressive resistance training; QOL: Quality of life (or sub-dimension of QOL); N/n: sample size; p: level of significance; \uparrow : improved; \downarrow : worsen.


Chapter 4

General Physical Activity Recommendations for Pediatric

Oncology

Tim Takken, PhD & Marco van Brussel, PhD

Learning Objectives:

After completing this chapter you will know:

- ...the impact of treatment modalities on physical fitness levels.
- ...the potential role of physical activity and exercise training to enhance cardiopulmonary and musculoskeletal functioning.
- ...physical activity guidelines provided should be personalized, supervised, and should take into account potential cardiotoxic therapy exposure.

Introduction

Childhood cancer takes place during a fundamental phase of life in which remarkable physiological, anatomical, and psychological transformations occur and the foundation for adult behavior, lifestyle and health status is established ¹. Failure to participate in **physical activity (PA)** during an average of 2 years of therapy at an age when children are usually introduced to leisure time PA and sports may have significant implications for future PA, health outcomes and ultimately **quality of life (QOL)**¹.

Intensive treatment, including combined treatment modalities such as chemotherapy, surgery and radiotherapy is frequently necessary in children with cancer. These treatment modalities might not only influence the abovementioned transformations and participation in PA, but are frequently accompanied by a wide spectrum of short and long-term adverse events, including diminished neurological function, cognitive dysfunction, impaired cardiac and pulmonary function, decreased bone density, musculoskeletal sequelae and secondary malignancy. Furthermore, impaired physical fitness is a well-known adverse effect of the



disease itself, the treatment, hypoactivity, and deconditioning ²⁻⁵. Impaired physical fitness typically includes reduced aerobic capacity, decreased muscle strength and flexibility.

PA has the capability to enhance cardiopulmonary and musculoskeletal function, perhaps preventing lasting deficits in aerobic fitness, if incorporated during or soon after treatment ^{6,7}. Furthermore, PA may decrease the effects of muscle atrophy and **cachexia** due to both cancer and the toxicity of cancer therapy through suppressing inflammatory responses, enhancing the immune function, rate of protein synthesis and anti-oxidant enzyme activities ⁸. This chapter will discuss general exercise and training recommendations for aerobic fitness, strength and flexibility in pediatric cancer survivors, based on existing literature.

Aerobic Training

Determining the **aerobic fitness** in survivors with cancer is of great clinical relevance, as this variable is a powerful predictor of mortality in people with or without disease ⁹⁻¹². Many children, adolescents, and even young adults who survived cancer are reported to have lower aerobic fitness (up to 20-30% less) than healthy controls ^{3,4,13,14} and this is especially true during the treatment phase ¹⁵. Although various intervention studies indicate evidence for improvement in **cardiorespiratory fitness** ¹⁶, a recent review of **randomized controlled trials (RCTs)** indicates only small benefits ⁷. However, due to the small number of RCTs and their low methodological quality, outcomes of **clinical trials (CTs)** may also be used to determine the efficacy of aerobic training in children with cancer. For example, the study by San Juan et al. indicates significant improvements in **aerobic fitness (VO_{2peak})** in children with **acute lymphoblastic leukemia (ALL)** after a 16-week intra-hospital supervised PA intervention



during the maintenance phase of treatment ¹⁷. *Table 4.1* depicts general aerobic exercise recommendations adapted for pediatric cancer patients and survivors. These recommendations are based on existing literature in healthy children ^{18,19} and have been adapted based on the literature ⁷ and our own clinical experience with aerobic training. For further general pediatric PA guidelines refer to *Appendix* D.



Table 4.1. General recommendations following the **Frequency**, **Intensity**, **Time and Type** (F.I.T.T.) principle for children and adolescents for aerobic exercise and adapted for pediatric cancer survivors.

F.I.T.T.	Cardiovascular (aerobic) training	Interval training
Frequency	2-5 times/week	2-3 times/week
Intensity	Moderate to heavy ($\dot{V}O_{2_{peak}}$ 40 to 85%)	3-5 minutes of light to moderate baseline PA ($\dot{V}O_{2peak}$ 20 to 59%) interrupted 6-8 times by 1-3 minute bouts of very intense PA ($\dot{V}O_{2peak}$ > 85%)
Time	20-70 minutes	In total 20-70 minutes
Туре	Running, jumping, cycling, swimming, football (ie, soccer)	Running, jumping, cycling, swimming

Note. FITT: frequency, intensity, time and type of exercise; $\dot{V}O_2$: oxygen uptake. **Interval training** can be used alternatively with aerobic training. Data compiled from ¹⁸ and ¹⁹.

Progressive Resistance Training

Childhood cancer therapy also impacts the musculoskeletal system. Compared to healthy controls, studies have shown that treatment can result in impaired bone and muscle strength both during active treatment and for years following the completion of therapy ^{4,20,21}. Muscle atrophy and reduced muscle strength are common among cancer survivors ^{4,20,22-24}, due to the catabolic effects of several chemotherapeutic agents such as vincristine and corticosteroids (refer to *Appendix A* for a full list of common medications). Encouragingly, intervention studies targeting these impairments during the maintenance phase in children with ALL are promising ^{17,25}. Similar results were also found for children with mixed cancer diagnoses ²⁶. However, when only considering RCTs, no significant effects of exercise training on muscle strength have been reported in the limited research to date ⁷. Given the low methodological quality of the existing RCTs, CTs should also be considered in order to determine the true efficacy of strength training on muscle strength and its effect on bone development.

Bone mineral density (BMD) is accrued during childhood. In theory (strength) training could have a positive effect on the accrual of bone in pediatric cancer survivors ²⁷. *Table 4.2* depicts general strength training recommendations for pediatric cancer patients and survivors.



These recommendations are based on existing literature in healthy children ^{28,29} and have been adapted based on the literature ^{18,30} and our own clinical experience with resistance training in children with childhood cancer.

Table 4.2. General recommendations following the F.I.T.T. principle for strength training adapted for pediatric cancer survivors.

F.I.T.T.	Strength (Resistance) Training	
Frequency	2-3 times per week	
Intensity	High (50-70% of maximal voluntary contraction)	
Time	2-3 minutes per each principal muscle group (about 8-20 repetitions) in total 20-30 minutes (can be interchanged with aerobic training and games)	
Туре	Push-ups, sit-ups / crunches, pull-ups, handgrips, squats, climbing, martial arts, rowing etc.	

Note. Adapted from ³⁰.

Flexibility Training

In pediatric oncology, flexibility can be affected because of contractures due to long-term hospital admission or due to diminished neurological function (e.g., diminished ankle dorsiflexion range of motion) as an adverse effect of pharmacological treatment. Effects of exercise training on flexibility were recently reviewed by Braam et al., ⁷. The authors reported that flexibility has been assessed in three RCTs, with conflicting evidence. In one study, the active ankle dorsiflexion method was used to assess flexibility and in the second study, the passive ankle dorsiflexion test was used ⁷. No statistically significant difference between the intervention and control group was identified with the active ankle dorsiflexion test, whereas with the passive test method a statistically significant difference in favour of the exercise group was found ³¹. The third study assessed body flexibility by the use of the sit-and-reach test, and no statistically significant difference between the intervention and control group was identified, the role of flexibility in **activities of daily living** (ADLs) cannot be understated. In fact, flexibility is one of the variables included in the definition of health related-fitness by the **American College of Sport Medicine (ACSM)**.



Practical Tips

Health Care Professionals:

- ✓ Inform your patients about the benefits of PA.
- ✓ Inform your patient about contradictions to PA, if any (refer to *Chapter 5*).
- ✓ Provide educator or fitness professional with relevant medical information
- \checkmark Maintain open communication with educators and fitness professionals.
- ✓ Follow gender and age-specific hematological parameters (e.g., white blood cell counts, platelets, hemoglobin, hematocrit).

Educator and Fitness Professionals:

- ✓ Ask for medical clearance from appropriate health care professional (e.g., oncologist/ orthopaedic surgeon/ cardiologist). Refer to Appendix H.
- ✓ Ask for relevant medical information (e.g., current health status, medical treatment and co morbid conditions). Refer to Appendix G.
- ✓ Know any contraindications to PA. Refer to *Chapter 5.*
- Moderate aerobic fitness training, combined with strength training, is safe and may be of benefit.
- ✓ Structured, personalized, supervised (in hospital) training is recommended for the most effective training results.
- ✓ Testing by an experienced exercise physiologist is recommended for detecting and assessing potential anthracycline cardiomyopathy before start of PA or training program.
- ✓ Ask participants to update their medical information if their health status changes.
- ✓ Maintain open communication with medical staff.
- ✓ Keep it fun to improve rates of participation and adherence.
- ✓ Adapt PA to each individual's needs.

Intervening During and After Treatment

It is expected that children who survived cancer will have lower fitness levels during (chemo) therapy than during remission and will have less energy to perform PA³³. When in remission many children wish to be free of cancer and its treatment. Thus they often lack interest in participating in organized PA therapy ³³ offered at the hospital. Therefore, the feasibility of PA programs seem to be the highest during the last phase of therapy or as soon as possible when the disease moves into remission ³³. Many studies regarding exercise training in pediatric cancer patients and survivors are performed with ALL during the maintenance phase



of therapy ^{17,25,34}. However, based on the currently available evidence from RCTs and CTs it is not yet possible to draw definitive conclusions regarding the optimal timing of the intervention.

Programming Options

After initial treatment completion, home-based, 1:1, and group-based PA programs in community settings have all been examined ⁷. None of these options have been proven to be

superior in a head-to-head comparison trial ⁷. However, structured, personalized, supervised inhospital PA programs seem to be the most effective and safe training approach to increase the functional capacity of childhood cancer survivors on treatment, with possible subsequent improvement of their muscle strength, functional mobility and hence their QOL ^{16,33}. Little



information is available to develop specific guidelines for each cancer type; however, currently the literature suggests the importance of developing PA that is individually tailored.

Current Limitations

Overall, current evidence is positive regarding the impact of exercise training on muscle strength and cardiorespiratory fitness, when all types of study designs are considered ¹⁶. However, only small benefits on cardiorespiratory fitness and flexibility and no statistical improvements in muscle strength were found when merely RCTs and CTs were taken into account ⁷. It is important to note however, that the current evidence (and its generalization) is limited due to methodological limitations of the reviewed studies ⁷. Furthermore, the aforementioned exercise programs (all designs) have mainly been conducted in children with hematological malignancies (e.g., leukemia) and effects might differ for other types of pediatric cancers, where research is still lacking.

Although the effects of training are promising, additional RCT should focus on high methodological quality and child-specific features for the acquirement of evidence-based and clinically applicable PA recommendations for pediatric cancer patients and survivors. The latter is needed because evidence-based guidelines for the optimal design for exercise interventions are lacking.



Current Guidelines

It is crucial to realize that there are currently no universally accepted training guidelines for children with cancer. Therefore, we recommend using the so-called F.I.T.T. principle; Frequency, Intensity, Time, and Type, as a basic framework for developing an individualized, disease-specific training program. As variations between the different factors determine the efficacy of training, the key is to determine the most important contributing factors for each child taking into account all the various anthropometric and disease-specific limitations. Nonetheless, general recommendations can be given (*Table 4.1* and *Table 4.2*). However, cancer and treatment specific PA contraindications should be taken into consideration (refer to *Chapter 5*). Healthcare professionals, clinical exercise physiologists and other exercise professionals could assist in designing appropriate PA programs for improving physical fitness, attenuating fatigue, and improving QOL in children surviving cancer ³⁵.

When considering physical training programming, it is important to keep in mind the possibility of higher fatigue values, slower recovery times, and slower adaptation times in children with cancer. The guidelines provided should be personalized, supervised, and should take into account potential cardiotoxic therapy exposure (refer to *Chapters 5 and 6*) ³⁶. Exercise training should be developmentally and age-appropriate, enjoyable and involve a variety of activities to maximize motivation and adherence ³⁷. Children and adolescents are more likely to enjoy short-term, high-intensity exercises, because they usually offer the necessary variety and better mimic the usual daily activity pattern of children (refer to *Chapter 16* for tips to increasing PA). Furthermore, training programs should continue for about 12 consecutive weeks. After these 12 weeks, a comprehensive re-evaluation should be made ³³.

Take Home Message

Exercise training seems feasible and effective in pediatric cancer survivors and could prevent lasting deficits in physical fitness and function. Training programs should be carefully adapted to the potential of every patient taking into account all the various anthropometric and disease-specific limitations. Although there are currently no universally accepted training guidelines for children with cancer, general recommendations for training are provided in this chapter.



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Chapter 5

Practical Aspects of Physical Activity in Pediatric Oncology

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Learning Objectives:

After completing this chapter you will know:

- ...the side effects related to cancer treatments that affect a person's physical activity.
- ...the areas of emphasis and areas of caution when participating in physical activity for each side effect.
- ...when symptoms during physical activity warrant a referral to a medical professional.

Introduction

This chapter will address common side effects and conditions related to cancer and its treatment among various pediatric oncology populations. The sections covered include: i) **chemotherapy-induced peripheral neuropathy (CIPN)**; ii) osteopenia/osteoporosis; iii) osteonecrosis; iv) cardiac; v) pulmonary toxicity; vi) hypertension; vii) pancytopenias; viii) bone tumor effects; ix) sensory impairments; and x) chronic graft-versus-host disease. Each section will describe areas to emphasize and areas to exhibit caution when participating in **physical activity (PA)**. It will become evident that most forms of PA can be safely performed if the impact of cancer and its treatments are taken into account. The evidence to date suggests that in most cases, the benefits for PA outweigh the possible risks.

i) Chemotherapy-induced peripheral neuropathy

CIPN is a common, yet often unrecognized side effect in children and adolescents with cancer ^{1, 2}. Both children in active treatment and survivors of pediatric cancer may suffer from symptoms related to CIPN that may impact their ability to engage in PA. These side effects may include sensory symptoms such as numbness, tingling, pain or loss of position sense (i.e.,



proprioception), and motor symptoms including weakness and disruptions in coordination.

Because neurotoxic agents known to cause CIPN are frequently used in the treatment of multiple pediatric cancers, health professionals must assess the impact CIPN has on a person's ability to participate in PA in order to prescribe a successful, sustainable PA program (refer to *Table 5.1*).

CIPN is characterized by damage to the peripheral nervous system from a chemotherapeutic agent, with each agent manifesting slightly different pathologic changes and symptomatic effects ³.

Table 5.1. Chemotherapy agent and pediatric cancer types.

Chemotherapy Agent Known to Cause CIPN	Pediatric Cancer Type
Vincristine	ALL, Lymphomas, Solid tumors, Brain tumors
Cisplatin	Brain tumors, solid tumors, bone tumors
Taxanes	Rare tumors
Epithilones	Refractory solid tumors
Bortezomib	Refractory or recurrent tumors
Thalidomide	Medulloblastoma or hepatocellular carcinoma

Note. ALL: acute lymphoblastic leukemia. Adapted from ¹.

The pediatric modified-total neuropathy scale is reliable and valid in children and adolescents with non-**central nervous system (CNS)** cancers and may be used to quantify neuropathy symptoms. Refer to *Table 5.2* for a summary of the tool.

Recent evidence measuring CIPN in children with non-CNS cancer during treatment with vincristine or cisplatin, found that 50% of patients had sensory impairments and 90% demonstrated distal weakness indicating motor neuropathy ⁴. Unfortunately, these impairments may persist, as documented by Ramchandren et al. ⁵ who reported that 29.7% of children 7.4 years off treatment for **acute lymphoblastic leukemia (ALL)** demonstrated nerve conduction abnormalities ⁵. The frequency and persistence of CIPN therefore warrants careful consideration.



A pediatric cancer patient or survivor may be unaware of the motor and sensory effects of their chemotherapy and may overestimate their ability to participate in certain types of PA. Hartman et al. found that 77% of children (n=53, mean age 5.2 years) treated with vincristine overestimated their motor performance ⁶. Additionally, 48% of children and adolescents undergoing testing for neuropathy reported functional deficits such as tripping when walking or difficulty with buttons, and 98% demonstrated distal muscle weakness in clinical testing ². Because self-report data are unreliable and may fail to reveal important deficits, medical professionals recommending PA for these patients should use clinical tests to assess neuropathy and its potential impact on motor performance. It is often appropriate to refer to a physical therapist to assess this deficit, as even minimal deficits can affect a person's ability to safely participate in PA. Fortunately, many functional limitations may be identified and addressed by physical therapy ^{7,8}.

Scoring	 ✓ Graded scale for 8 areas (scored from 0 – 4); for a maximum score of 32 ✓ Scores of 0 – 4 Normal ✓ Scores of > 4 Neuropathy
	 ✓ Sensation symptoms ✓ Pain, numbness, tingling
	 ✓ Functional symptoms ✓ Buttons, walking, stairs
	✓ Autonomic systems

	 Autonomic systems Light-headedness, temperature change 	
Clinical Tests	Test	Equipment
	 ✓ Light touch 	 ✓ Semmes Weinstein monofilaments
	✓ Pin sensation	 ✓ Medipin[™]
	 ✓ Vibration 	✓ Biothesiometer
	✓ Strength	 ✓ Manual muscle test
	✓ Reflexes	✓ Reflex hammer

Note. Summary of Peds-mTNS summarized from ².



Areas of emphasis in patients and survivors with chemotherapyinduced peripheral neuropathy

The following areas must be emphasized to improve the physical function and PA capacity of a person with CIPN (refer to Table 5.3). Ankle range of motion (ROM) is often reduced in pediatric cancer patients and survivors and may be addressed by stretching (refer to Appendix 5.A)⁷. Younger children should have their caregiver stretch the gastrocnemius-soleus muscle complex with knee extended to optimize muscle length. School-age children and adolescents can stretch independently at a wall or on a step. Patients and survivors of ALL who have less than 5 degrees of active ankle dorsiflexion (DF) ROM are more likely to demonstrate decreased walking efficiency even 10 years post treatment compared to those with greater ankle ROM⁸. This relationship emphasizes the need to address ankle ROM when attempting to improve PA capacity. Additionally, CIPN causes peripheral weakness most often in the wrists, hands, ankles, toes and ascending proximally if severe ^{2, 9}. Therefore, strength training of these muscles is important to allow success in PA. Balance training (refer to Appendix 5.B) should also be incorporated into a PA program secondary to its relationship to CIPN in children on treatment^{2, 10}. The combination of strength and balance training has been demonstrated to reduce the risk of falls with adults with diabetic peripheral neuropathy, although this has not yet been studied in individuals with CIPN¹¹. The mode and duration of PA should be chosen with CIPN in mind, as some patients or survivors may not be able to increase their heart rate with activities that require muscular endurance from the ankles. For example, biking may be better than jogging or fast walking for aerobic exercise as their ankles may fatigue prior to challenging the cardiovascular system. Walking shorter distances however, may be beneficial for strengthening the ankles prior to onset of muscular fatigue (refer to Appendix B for general pediatric PA guidelines).

Areas of caution in patients and survivors with chemotherapyinduced peripheral neuropathy

Although the importance of PA is established for pediatric oncology patients and survivors, one must consider certain areas of caution when exercising with CIPN (refer to *Table 5.3*). There may be an increased risk of falling and supervision by a caregiver or professional may be required ¹⁰. Fortunately, many patients and survivors have a mild form of CIPN and only high-level activities such as a contact sport over uneven surfaces would warrant caution. Depending on the duration of PA, muscular fatigue of the ankle may cause tripping or an



inefficient gait pattern. Orthotics or athletic ankle bracing may be required depending on the type of PA chosen. If a person with even mild CIPN has had a history of ankle sprains prior to or during treatment, it is essential they wear an external ankle support during PA that would challenge the ankle ^{12, 13}. Activities such as walking long distances, walking over uneven surfaces, running, or sporting activities may require ankle support. Hand weakness from CIPN may also impede strength training with barbells or other weighted devices, however an exercise band could be used instead. Throwing and catching or sport specific skills such as setting in volleyball could be affected when hand weakness is present.

Despite the impairments that may be present due to CIPN, both children on treatment and post-treatment can be safe and successful participating in a PA program. Medical professionals should assess CIPN specifically, address functional impairments through rehabilitation services, recommend appropriate PA supervision, and provide comprehensive patient education.

Table 5.3. Areas of emphasis and caution in patients and survivors with chemotherapy-induced peripheral neuropathy.

	Emphasize:
\checkmark	Ankle flexibility
✓	Strengthening of ankles, toes, wrists, and hands
v	Balance training
v	Mode of PA appropriate to raise HR (e.g., biking, swimming, waiking with orthotics)
	Practice Caution:
✓	Exercises that require more ankle flexibility than is present (as foot structure may be compromised)
\checkmark	Strength training requiring hand grip
\checkmark	PA over uneven surfaces
✓	Advanced balance activities
~	Activities that require ankle muscular endurance (as ankles may fatigue prior to challenging the cardiovascular system)

ii) Osteoporosis, Osteopenia (or low bone density)

Children and adolescents whom are currently going through cancer treatment or whom have completed treatment have multiple risk factors that lead to osteopenia, or decreased bone density ¹⁴. Measurement in children/adolescents for bone density is different than in adults because they have not yet reached peak bone mass. The International Society of Clinical



Densitometry defined osteoporosis in infants to adolescence in 2013 as the following: the finding of a vertebral compression fracture in absence of disease or high-impact trauma, or a

history of clinically significant fractures in addition to bone mineral density (BMD) Z-score \leq -2.0 ¹⁵. The Zscore refers to a measurement of standard deviation (SD) comparing the BMD to age and gender-matched normal values ¹⁶. Clinically significant fractures are

Refer to the Bone Mineral Density Childhood Study website for more information on normative values and a Z-score calculator at http://www.bmdcspublic.com¹⁷.

defined as two or more long bone fractures by age 10 years, or three or more long bone fractures at any age up to age 19 years. The International Society of Clinical Densitometry does not recommend using the term osteopenia, but recommends the term "low bone density" for children without a clinically significant fracture history with a BMD Z-score \leq -2 S.D. Chemotherapy with agents such as methotrexate and corticosteroids, anthracycline treatment causing gonadal dysfunction, as well as cranial radiation are cancer treatments known to cause low BMD ^{14, 18, 19}. Persons who receive \geq 9 g/m² of corticosteroids or \geq 40 g/m² of methotrexate are at higher risk for low BMD as in some patients with leukemia ²⁰. Cranial radiation >18 gray (Gy) can also cause growth hormone dysfunction that can lead to low BMD ²¹. In addition to these toxicities, reduced PA during and after treatment is also to blame. Fortunately, much can be done with PA to decrease this known late effect of cancer treatment. Often, bone density is not assessed unless there is a history of fracture or pain issues. Therefore, areas of emphasis and caution need to be considered in any PA prescription. Refer to *Table 5.4* and *Table 5.5* for specific recommendations.

Areas of emphasis in patients and survivors with low bone mineral density

In a child with cancer, **weight-bearing exercises** are essential both during treatment and post-treatment to build bone density that is needed into adulthood. Since 60% of osteoporosis risk is determined by the bone mass in early adulthood ²², and much of that bone mass is formed around age 12 in girls and 14 in boys ²³, a child must not wait until treatment completion to begin PA. Research in children with and without cancer has demonstrated the impact of weight-bearing exercises on bone density and the positive impact into adult bone health ^{22, 24}.

In a population where low bone density is a risk factor, even more emphasis must be put on the type of weight-bearing exercise required to build bone mass. In healthy children and pre-



adolescents, jumping from a 61 cm height box over 100 repetitions for at least a 7-month time period, 3 times per week, increased bone mass ²⁵. If the frequency was reduced to 2 times per week at 75 jumps per session, the benefit to bone strength was not seen ²⁶. In addition, higher bone mass is observed in adolescents that play high-impact sports such as basketball, handball, or gymnastics than athletes that swim or adolescents who do not participate in sports ²⁷. In patients and survivors of pediatric ALL, physical performance was related to bone mineral density as well ²⁴. Therefore, if it is safe in regards to a person's other possible deficits of low blood counts (pancytopenia), balance, weakness, neuropathy, or osteonecrosis, children with cancer or survivors should engage in high impact exercises at least 3 times per week as recommended by the U.S. Department of Health and Human Services for all children for bone strengthening ²⁸. If time or endurance is an issue, emphasis should be put on the frequency of high impact exercise (>3 times per week), rather than the duration, to maximize benefit to the bone ²⁹.

In the pediatric oncology population with a risk of low bone density, it is also necessary to emphasize PA that targets balance training and strength training to reduce risk of falls and therefore decrease the risk of fracture ²⁹. Core strengthening and PA such as Yoga or Tai Chi are good examples. In children whose gait (walking) is affected, such as some patients with brain tumors or severe peripheral neuropathy, gait training with a physical therapist is needed to promote safety and confidence as ambulation deficits have been related to lower bone density ¹⁸. In general, pediatric cancer patients and survivors need to feel safe and strong in their ability to challenge themselves with a high impact exercise to build bone.

Areas of caution in patients and survivors with low bone mineral density

It is a balance between an emphasis on load-bearing exercise and reducing risk of falls and fracture secondary to low bone density (refer to *Table 5.4*). Caution should be taken with participation in contact sports secondary to risk of trauma. However, depending on severity of low bone density and functional status, this may be allowed as contact sports often provide the force through a bone that would increase bone strength.



Table 5.4. Areas of emphasis and caution in patients and survivors with low bone mineral density.

	Emphasize:
✓	Weight-bearing exercises
\checkmark	Progressive resistance exercise focused on strength development
\checkmark	Balance training
✓	Core strength
	Practice Caution:
✓	Contact sports
\checkmark	Activities or sport that could increase the risk of a fall

Areas of emphasis in patients and survivors with osteoporosis

Due to the difference in definition of osteoporosis between the pediatric population and adult population, recommendations may differ as well. Strength and balance training are very important in patients and survivors with osteoporosis of any age (refer to *Table 5.5* and *Appendix 5.B*). Depending on the person's physical status, exercises must be carefully modified to allow safe training. An exercise program for all survivors of pediatric cancer with osteoporosis should include flexibility, muscle strength, core stability, cardiovascular training, and gait ³⁰. Core strength and stability should be emphasized to protect the spine in persons with osteoporosis; trunk extension strength is priority in an adult survivor of pediatric cancer ³⁰. In pediatrics and adolescents, current recommendations include weight-bearing exercise (possible high impact) and vibration therapy although the value of this intervention is just now being investigated ^{23, 31}. Consultation with a physical therapist is beneficial to individualize person's exercise program dependent on pain and a person's mobility status.

Areas of caution in patients and survivors with osteoporosis

If the person is an older adult survivor of pediatric cancer, and is known to have osteoporosis, high impact exercises that cause bouncing or jerky movements such as running or jumping should be avoided ^{32, 33}. Exercises or sports that cause spinal flexion and rotation or twisting, should also be avoided in adult survivors as these increase compression of the spine and increase the risk of vertebral compression fractures ^{32, 33}. For example, some yoga or stretching poses that involve spinal flexion could increase risk of vertebral fractures and are not



safe in persons with osteoporosis 30 , and thus a modified protocol should be applied (refer to *Table 5.5*). Adults with osteoporosis who have a history of vertebral compression fractures are at higher risk for future compression fractures 30 .

Care must be observed with heavy lifting or lifting overhead ³². For the child or



Balance training at the PEER program

adolescent survivor of pediatric cancer with osteoporosis, caution must also be observed, however activities prohibited in adults may be allowed secondary to the possibility of building bone at this age. Weight-bearing exercises as tolerated are recommended ¹⁹. For example, in a child with a history of fracture and low BMD, running and jumping or sports may be allowed if strength and balance is normal. If a child's balance or strength is limited,

weight-bearing exercises must be individualized and restricted where balance loss may occur to ensure safety and reduce fracture risk. Please consult the oncologist, orthopedic surgeon, or physical therapist to determine what is safe for an individual considering the complicated picture of multi-system deficits.

Table 5.5. Areas of emphasis and caution in patients and survivors with osteoporosis.

	Emphasize:
✓ ✓	Core strength Brograssive registence exercises with an emphasis on strength
• √	Gait steadiness
✓	Balance
	Practice Caution:
~	Exercises causing spinal flexion, rotation, or side-bending
✓ ✓	Exercises that promote spinal movement and/or induce pain High impact activities
~	Unsupported balance activities



iii) Osteonecrosis

Osteonecrosis (ON) is a disabling complication in children and adolescents exposed to corticosteroids during cancer treatment ³⁴⁻³⁶. It is defined as the death of a segment of bone. Approximately 33% of children with ALL or non-Hodgkin lymphoma are affected, with the highest risk in children older than 10 years of age ^{37, 38}. Children who have had a **hematopoietic stem cell transplant (HSCT)** are also at higher risk ³⁹. ON is multi-articular, affects weightbearing bones, and occurs most often in hips and knees ³⁷. The condition may be asymptomatic; however if severe, it can lead to pain, decreased mobility, and deterioration of the joint requiring joint replacement ^{36, 37, 40}. Little is known about the prognosis of ON, however in one study in patients with ON of the knee, 21% eventually had a **collapsed joint** ⁴¹. Risk of joint collapse was associated with older age, lesions that extended to the articular surface at diagnosis, and pain at presentation ⁴¹. ON results in changes to a joint that requires individualization of a PA program to protect the bone, strengthen the muscles around the joint or joints, and reduce pain.

Restrictions are made by the orthopedic surgeon, oncologist, or physical therapist, and depend on the severity of the disease and symptoms of each affected patient. Weight-bearing may be restricted to reduce pain or to reduce progression of joint deterioration ^{36, 37}. Restrictions are specific to each individual and communication is necessary with medical team for proper exercise prescription.

Areas of emphasis in patients and survivors with osteonecrosis

It is important to emphasize ROM and strength in persons with ON (refer to *Table 5.6*)^{34, 42, 43}. ROM of the involved joint should be completed actively if possible, and passively if pain is elicited. Other joints may also lose ROM secondary to compensated movement patterns, so flexibility should be challenged through PA if possible. Strengthening may decrease the stress through the affected bones by increasing support around a joint. **Open chain strengthening**, progressing to strengthening in a weight-bearing pain-free position, is appropriate for a person with ON ³⁴.

Aerobic activity is also important in children or adolescents with ON, despite the complexity of balancing weight-bearing activity that increases bone density and the possible requirement of decreased weight-bearing secondary to pain from a bone lesion ⁴². If a painful joint is an issue, bike riding or aquatic PA may be appropriate. Occasionally, an orthotic device



may be used to divert stress around an ON lesion in the knee to allow walking for longer periods of time as well.

Areas of caution in patients and survivors with osteonecrosis

Caution is necessary when considering PA options for a cancer patients and survivors with ON (refer to *Table 5.6*), however through collaboration with the oncologist, orthopedic

surgeon, and physical therapist, it is possible to create a PA prescription that provides the benefits of exercise with minimal risk. Foremost, it is important to avoid exercise that increases pain through an area of known

Avoid exercises that increase pain through an area of known osteonecrotic lesion. Pain should NEVER be ignored!

osteonecrotic lesion. Pain may be intermittent or inconsistent, however it should not be ignored. Although the use of crutches may decrease pain through a hip or knee, it may also put additional stress through a shoulder that could be affected. In general, persons with ON should think of pain as their guide and keep in frequent follow-up with medical providers for symptom management.

Table 5.6. Areas of emphasis and caution in patients and survivors with osteonecrosis.

	Emphasize:
✓ ✓ ✓	Pain-free PA ROM Progressive resistance training starting with open-chain and progressing to strengthening in a weight-bearing, pain-free position
	Practice Caution:
✓ ✓ ✓	PA in the presence of pain Individual orthopedic weight-bearing precautions High impact activity

iv) Cardiotoxicity

Patients and survivors of pediatric cancer are at risk for **cardiac dysfunction** secondary to the direct effects chemotherapy or radiation ^{44, 45}. Since the combination of strength training and aerobic conditioning has been demonstrated to be beneficial in adults with **congestive heart failure (CHF)**, both must be emphasized in pediatric cancer patients and survivors ^{46, 47}. For more details regarding cardiotoxicity, please refer to *Chapter 6*.



Areas of emphasis in patients and survivors exposed to cardiotoxic therapies

It is important to emphasize aerobic and strengthening components of exercise in patients and survivors exposed to cardiotoxic therapies (refer to *Table 5.7*). Strength training should be completed at a frequency recommended for healthy adults or children which is typically three times per week ^{28, 48, 49}. For general pediatric strength and aerobic PA guidelines, refer to *Appendix D*. A person should use a weight they can lift 10 times with ease ^{43, 46.} This level of training will maximize strength, while reducing breath-holding or **valsalva maneuver** that could cause stress to the heart. Persons should use correct strength training techniques, breathing through the movement, lifting through their full range of motion, and engaging muscles through the lifting and lowering of the weight ^{50.} The Children's Oncology Group recommends consulting with a cardiologist if a person had over 300 mg/m² of anthracyclines and is interested in heavier strength training (refer to *Chapter 6* for more information on cardiotoxicity) ⁵⁵.

It is generally accepted that aerobic exercise is both safe and necessary in cancer patients and survivors ^{43, 46, 51, 52}. Although there is much more to be learned in regards to aerobic exercise and cardiotoxicity, early research has demonstrated that patients and survivors with subclinical cardiac dysfunction have a safe physiological response to aerobic exercise ⁵³. Moderate aerobic activity is recommended 60 minutes per day for children and adolescents ^{28, 46, 49} (for general pediatric PA guidelines, refer to *Appendix B*). Prior to the initiation of a regular exercise program in patients who are at high risk of cardiotoxicity, it is recommended that the child undergo a full evaluation by their physician or cardiologist. This may include a formal treadmill stress test ⁵⁴. **Heart rate (HR)** and **blood pressure (BP)** should be monitored during exercise session (e.g., at the beginning of the session, in the middle and at the end), and the program may need to be modified if an abnormal HR or BP response (e.g., no change in HR with effort, falling >10 in systolic BP, >250 mmHg systolic BP, >125 mmHg diastolic BP) is noted ⁵⁴. Notice that the abnormal response described in this section is from adult literature due to the lack of published guidelines for pediatric patients ⁵⁴.



Areas of caution in patients and survivors exposed to cardiotoxic

therapies

Although exercise is generally safe and beneficial for cancer patients and survivors, one should understand symptoms of cardiac dysfunction with those at risk. Refer to *Table 5.7* for detailed areas of caution. Additionally, see the textbox below for an overview of symptoms related to cardiac dysfunction.



Table 5.7. Areas of emphasis and caution for patients and survivors exposed to cardiotoxic therapies.

	Emphasize:
√ √	Aerobic exercise monitoring vitals (if history of symptoms) Progressive resistance training with ability to lift weight at least 10 repetitions (i.e., using a lighter weight)
	Practice Caution:
✓ ✓ ✓ ✓	Strength training with heavy loads Isometric training Valsalva maneuver Exercise with cardiac dysfunction symptoms (refer to above text box)

v) Pulmonary toxicity

Pediatric cancer patients and survivors with a history of radiation, thoracic surgery or chemotherapy with alkylating agents are at risk for pulmonary toxicity ⁵⁵. Pulmonary late effects include **pulmonary fibrosis**, **interstitial pneumonitis**, and **restrictive lung disease** ^{55, 56}. Symptoms may include dyspnea, shortness of breath, chronic cough, wheezing, or exercise



intolerance ⁵⁶⁻⁵⁸. Although these symptoms may be rare, it is important to understand that a

Symptoms:

- DyspneaShortness of
- breath
- ✓ Chronic cough
 ✓ Wheeting ⁵⁵⁻⁵⁷
- ✓ Wheezing ⁵⁵⁻⁵⁷

person with cancer could have both cardiac toxicity and pulmonary toxicity resulting in decreased exercise tolerance.

Research into the effect of PA in people with and without cancer who have pulmonary diseases has demonstrated benefits in PA tolerance and quality of life ⁵⁸⁻⁶¹. In general, pulmonary rehabilitation programs include aerobic conditioning, flexibility and

progressive resistance training ⁶², so it should be assumed that cancer patients and survivors at risk should participate in these important components of PA at current recommended levels, while paying

If a person demonstrates symptoms of exercise intolerance or pulmonary toxicity, vitals such as heart rate, blood pressure, and oxygen saturation should be monitored by a trained professional (e.g., Certified Exercise Physiologist, physical therapist, nurse or physician).

particular attention to areas of emphasis and caution (refer to *Table 5.8*). Normal oxygen saturation is between 95-100%. If saturation is below 92%, or abnormal changes in vital signs occur, referral back to the primary physician is necessary for further testing. Participants may be on supplemental oxygen. With clear parameters from a pulmonologist and monitoring of **exertional dyspnea**, portable oxygen should not be a reason for a person to avoid participating in an exercise program.

Table 5.8. Areas of emphasis and caution in patients and surivors with pulmonary toxicity.

Emphasize:	
✓ Aerobic conditioning	
✓ Flexibility	
✓ Progressive resistance training	
Practice Caution:	
 ✓ Exercise intolerance ✓ Exertional dyspnea 	

vi) Hypertension

Children and adolescents with cancer are at risk for hypertension during and posttreatment. This clinical finding is seen with patients with multiple diagnoses including ALL and those requiring HSCT ⁶³⁻⁶⁵. Persons with renal toxicity from agents such as ifosfamide,



carboplatin, and cisplatin may experience hypertension as a late effect ⁴³, or persons in

treatment with corticosteroids may have hypertension acutely secondary to fluid retention. In addition, pediatric cancer patients and survivors are at higher risk for metabolic syndrome, with arterial hypertension as a key component ^{43, 66}.

Measurement in children/adolescents for hypertension are different than in adults. Pediatric hypertension has been defined as **systolic BP (SBP)** and/or **diastolic BP (DBP)** that is at or above the 95th percentile (Refer to *Appendix C*).

Areas of emphasis in pediatric cancer patients and survivors with hypertension

Although there is a paucity of exercise trials investigating blood pressure in pediatric cancer patients and survivors, much can be learned from the study of adults and children with hypertension of other etiology. Refer to *Table 5.9* for areas of emphases in people with hypertension. In general, the American College of Sports Medicine recommends persons with hypertension to complete aerobic exercise almost daily at a moderate intensity or 40-60% of their **oxygen uptake reserve**; for at least 30 minutes ⁶⁷. For exercise at higher intensity, exercise stress testing may be recommended if other cardiovascular risk factors are present. Fortunately, children and adolescents with hypertension without any other cardiovascular risk factors can engage in PA at high or intense levels without risk of a cardiovascular implication such as a stroke or myocardial infarction ⁵⁹⁻⁶¹. Aerobic activity should be supplemented by progressive resistance training as well ^{67, 68}. Strength training is considered safe in this population ^{61, 62}. It is critical to stress weight loss in a child that has hypertension and obesity, as research has demonstrated a greater reduction in blood pressure when there is a decrease in body mass index ⁶⁹.

Areas of caution in pediatric cancer patients and survivors with

hypertension

Competitive sports are encourage, however children and adolescents with hypertension

Pediatric blood pressure norms are available at: http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.pdf; additionally, refer to *Appendix C*⁶⁹. greater than the systolic pressure of 99% + 5 mm Hg should undergo exercise stress testing ⁷⁰. Adults with

uncontrolled hypertension and atherosclerotic coronary artery disease have a risk of sudden



death with high/intense PA. Exercise stress testing is therefore recommended for adult survivors of pediatric cancer exercising at a high level with hypertension that is not under control ⁷¹.

Table 5.9. Areas of emphasis and caution in patients and survivors with hypertension.

	Emphasize:
> >	Aerobic training at a moderate intensity Progressive resistance training
✓	Weight loss if needed
	Practice Caution:
√	Competitive sports in patients and survivors with uncontrolled hypertension
v	exercise stress testing first
\checkmark	Valsalva maneuver
\checkmark	Power lifting

vii) Pancytopenias: Anemia, Thrombocytopenia, and Leukopenia

Pancytopenia is a disorder consisting of **anemia** (low hemoglobin), **thrombocytopenia** (low platelets) and **leukopenia** (low white blood cell count) ⁷². Mild forms of pancytopenia are common among all children with cancer either as part of their primary disease (as in leukemia) or as an effect of chemotherapy or radiation⁷². Severely low blood counts will be seen most frequently among children undergoing HSCT.

Symptoms should drive PA prescription, not absolute counts, unless critically low. Some safety precautions are good to keep in mind as guidelines, but clinical reasoning must play a role, weighing risks versus benefits accordingly. This is especially

Symptoms must drive PA prescription! Keep safety precautions in mind as a guideline, but be prepared to modify to each patient and/or survivor.

relevant in children who have been very ill, or in hospital. PA, particularly during hospital admissions, plays a role in helping parents overcome fears about the safety of PA during cancer treatment. This can lead to better choices with respect to future levels of activity/sports participation. Each cytopenia is extremely common among children with cancer. These types of cytopenias will be addressed individually.



Anemia

Anemia can be defined as a reduction in circulating blood hemoglobin below age-related normative values, impacting a person's ability to carry oxygen to their tissues ⁷³. Refer to *Table 5.10* for normal values among various age groups ⁷⁴. Typical signs and symptoms of anemia include:

- \checkmark Lethargy, weakness, increased need for sleep.
- ✓ Shortness of breath on exertion
- ✓ Headache, irritability, poor mental concentration (can impact school performance)
- ✓ Poor appetite
- ✓ Pallor
- ✓ Increased resting heart rate (tachycardia)

Areas of emphasis in patients and survivors with anemia

PA recommendations during periods of anemia must take into account a person's symptoms, or lack thereof. *Table 5.11* highlights the areas of emphasis and caution. Evidence indicates that there are no adverse effects associated with resistance training or aerobic training during periods of anemia so long as symptoms are managed and blood transfusions are administered when symptoms are present ⁷²⁻⁷⁵.

Although there is considerable variability in how well children tolerate anemia, most cancer patients and survivors will require blood transfusions if their hemoglobin drops below 80 g/L for symptom control ⁷⁵. While anemic, heart rate at rest and with exertion will be higher due to decreased efficiency of the blood's ability to carry oxygen ⁷⁵⁻⁷⁸. Education will help the child and family adjust their activity expectations if they are undergoing chemotherapy, so that they understand why they fatigue faster and feel overall less energetic. Adolescents are often more reliable at self-monitoring their levels of fatigue and sensing when their hemoglobin is lower, but younger children may require more monitoring. The use of **rating perceived exertion scale** (**RPE**) and HR monitor would be appropriate in this group (see *Appendix F* for a sample RPE scale).

Given that chemotherapy-related anemia is usually transient, it is important that PA be encouraged to avoid long-term deconditioning ^{77, 78}. An individually tailored balance of rest and activity will help prevent a decline in functional strength and endurance ^{77, 78}.



Table 5.10. Lower limits of normal blood hemoglobin.

Age (years), Sex	Lower Limit of Normal Hemoglobin (grams/liter (g/L)
0.5 – 4.9	110
5.0 – 7.9	115
8.0 – 11.9	120
12.0 – 17.9, Female	120
12.0 – 14.9, Male	125
15.0 – 17.9, Male	130

Note. Adapted from Brugnara 75

Areas of caution in patients and survivors with anemia

When hemoglobin is known to be low but not below 80g/L, exercise intensity will be guided by symptoms. Heart rate monitoring may be necessary when re-initiating exercise if a child has been inactive for some time. It is important that exercise is not initiated or be terminated in the presence of headaches, dizziness, changes in levels of consciousness and/or nausea ⁷⁵⁻⁷⁸.

Table 5.11. Areas of emphasis and caution in patients and survivors with anemia.

	Emphasize:
\checkmark	Encourage PA within a tolerable range for the patient
\checkmark	Educate on the effect of anemia on PA
√	Use RPE scales and heart rate monitors
	Practice Caution:
✓	Hemoglobin < 80 g/L with symptoms of lightheadedness, dizziness, nausea, generally unwell or change in level of consciousness. Wait for blood transfusion prior to resuming PA
✓	Hemoglobin < 80 g/L, asymptomatic. Do PA with cautious, low-intensity exercise, monitoring for symptoms
1	If nonticipant has examine and has been inective, monitor UD responses during excession

✓ If participant has anemia and has been inactive, monitor HR response during session

Thrombocytopenia

Thrombocytopenia is defined by a platelet count below the lower normal limit of 150-400 x 10^{9} /l ⁷³. Generally, the risk of severe spontaneous hemorrhaging is rare unless the platelet



count is below 10 x 10^{9} /l, except if platelet function is additionally compromised or other coagulopathies are present ⁷⁹. Typical signs and symptoms are described in the textbox and *Table 5.12* highlights the areas of emphasis and caution ⁷³.

Signs and Symptoms of Thrombocytopenia

- ✓ Increased frequency and severity of bruising
- Signs of microvascular bleeding (spotted bruising), categorized based on its size
- ✓ Spontaneous bleeding (typically mucosal: oral, nasal, rectal)
- Bleeding out of proportion to tissue trauma

Areas of emphasis in patients and survivors with thrombocytopenia

In all cases of low platelets, proper form and technique should be emphasized in order to avoid injury. Resistance training should be progressive and supervised to maximize safety and minimize risk of a bleed or unnecessary bruising. If using exercise equipment, use of extra padding over hard surfaces can be helpful in avoiding painful bruising, such as adding padding or a pillow to the seat of a stationary bike ⁷⁵⁻⁷⁸.

Areas of caution in patients and survivors with thrombocytopenia

Studies caution against high intensity PA (e.g., contact sports), and maximal PA stress testing if platelets are below 50×10^{9} /l ^{76, 79, 80}. However, moderate resistance and aerobic training is generally safe to continue until platelet count is as low as 20×10^{9} /l ⁷⁵⁻⁷⁸ and low-intensity PA can often continue with a platelet count as low as 10×10^{9} /l ^{76, 77}. Most centers will consider prophylactic platelet transfusions when the count drops below the $10-20 \times 10^{9}$ /l range or even higher, depending on the underlying condition, largely at the discretion of the physician ⁷³. If uncertain, wait until a transfusion or speak with the physician before proceeding with a PA program.

Table 5.12. Areas of emphasis and caution in patients and survivors with thrombocytopenia.

Emphasize:

- ✓ Supervised progressive resistance training
- Minimize the risk of bleeding or unnecessary bruising (e.g., perform supported balance activities and avoid high impact activities)



Practice Caution:

- ✓ Platelets < 50×10^9 /L- Avoid high risk activities (e.g., contact sports);
- ✓ Platelets 10-20 x 10⁹/L May require platelet transfusion. Can still exercise at low intensity. Extra care to avoid tissue trauma
- ✓ Platelets < 10 x 10⁹/L- Require transfusion. Higher risk of spontaneous bleeding. Do not perform PA until transfusion

Leukopenia

Leukopenia refers to a white blood cell count below normal range for age (and is often referred to as immune system suppression)⁷³. As white blood cells refer to a group of distinct but complementary types of immune function cells, the absolute number of white blood cells is not on its own clinically relevant to PA except as a marker of immune system health, which is usually low⁷³.

For the purposes of identifying those at higher risk of infection, it is more useful to look at **absolute neutrophil count (ANC)**, as neutrophils are considered the "first responders" of our immune system and crucial in fighting off infection ^{81,82}. Neutropenia is considered mild, moderate or severe when ANC is below 1.5×10^9 /L, 1.0×10^9 /L and 0.5×10^9 /L, respectively ⁸³. Neutropenia accompanied by fever is a medical emergency for the child undergoing treatment for cancer due to a compromised ability to fight infection ⁸¹⁻⁸³. In terms of PA, a fever with temperature greater than 38 degrees Celsius is usually a contraindication to PA ^{75, 77}. For additional areas of emphasis and caution refer to *Table 5.13*.

Areas of emphasis in patients and survivors with leukopenia

Proper hand hygiene, wiping down PA equipment between uses, and keeping immunosuppressed children away from others who are feeling unwell are strategies, which aid in keeping the neutropenic child free of infection ^{73, 77}. Some authors recommend avoiding pool exposure during severe neutropenia ⁸⁴. If in doubt, consult their oncologist, as neutropenia is not the only factor involved in risk of infection. For example, the integrity of their skin and mucosal membranes also plays an important role ⁷³.



Areas of caution in patients and survivors with leukopenia

Studies examining the effects of PA during immunosuppression have shown that PA (both resistance and aerobic training) is safe to be performed in the absence of fever ^{75, 77, 78}.

Safety Precautions when Working with Immunocompromised Patients:

- ✓ Focus on individualized sessions
- \checkmark Never attend a session if you are sick
- Measles and chickenpox immunizations are highly recommended
- ✓ Sterilize all the equipment before and after the session
- ✓ Use the appropriate safety gear at your local institution (e.g., masks, gloves and gowns)
- ✓ Keep your nails short
- ✓ Wash your hands before and after the session

Preliminary data by Chamorro-Vina et al. ⁸⁵ suggest that mild to moderate aerobic and resistance training during the neutropenic phase following HSCT (neutrophil count < $0.5 \times 10^9 \mu$ L) does not increase the risk of adverse events. Also Ladha et al. ⁸⁶, in a sample of ALL survivors, reported no effect of a single acute PA bout on white blood cells, monocytes or

eosinophils, indicating no adverse effects on immune response. It is worth noting that moderate levels of aerobic training are safer for this population as high intensity training has been shown to cause a decline in immune function in healthy individuals ⁸⁷. After prolonged or intensive exercise bouts, many components of the immune system reflect physiological stress and immunodepression. This period commonly lasts 3-72 hours, and commonly is known as the "open window" ⁸⁸. One should keep in mind that moderate training in a detrained individual undergoing cancer treatment will be at a much lower intensity than a well-trained individual. However, because these are preliminary studies, more research is necessary. We cannot currently generalize the safety to the entire pediatric cancer population therefore common sense and consultation with all members of the health care team should be required.

Table 5.13. Areas of emphasis and caution in patients and survivors with leukopenia.

	Emphasize:
√	Low to moderate aerobic training
~	Progressive resistance training
	Practice Caution:
~	Neutrophil count < 0.5 x 10 ⁹ /L indicates severe neutropenia. Follow safety precautions
\checkmark	Some suggestions to avoid aquatic sports and high intensity exercise
\checkmark	Avoid exercise if fever >38 degree Celsius



viii) Bone tumor effects: post-surgical considerations in

osteosarcoma

Osteosarcomas are the most common malignant tumors and derived directly from bone tissue. Survival rates from osteosarcoma have improved dramatically over the last 30-40 years with significant advances in surgical and chemotherapeutic options ⁸⁹⁻⁹¹. Please refer to *Chapter 9* for more details.

Surgical options vary based on the site(s) involved, but in the lower extremity amputation or limb-sparing techniques are used to offer the best possible functional outcomes ⁹¹⁻⁹⁴. Functional outcomes vary by limb sparing procedures as compared to amputation ⁹⁵. With regards to PA post-surgery there may be important considerations. Specifically, 82% of limb salvage patients and 91% of amputation patients will require a **prosthesis** or brace. Fifty three percent of limb salvage patients and 83% of amputation patients will require an **assistive device** for ambulation. With regards to activities of daily living, there will be variation, depending on the procedure. During ambulation, a proportion of patients will limp (89% limb salvage; 78% amputation) and have difficulty climbing stairs (33% limb salvage; 31% of amputation) and a low proportion of patients will participate in sports (38% limb salvage; 39% amputation). The majority of these patients will eventually be capable of driving a vehicle (90% limb salvage; 92% amputation) ⁹⁵.

Other forms of cancer affecting bone health

Several types of cancer may infiltrate bone. Some originate from soft-tissue cancers and may grow into nearby bony structures, as in Ewing's sarcoma or rhabdomyosarcoma ^{89, 90}. Metastatic disease can also infiltrate bony structures and cause pathological fractures ^{89, 90}. Metastatic disease in a bone that has not fractured can be considered much like a primary tumor mass in that it will weaken that bone, placing it at high risk of fracture. By following the same guidelines for osteoporotic patients as outlined in the Osteopenia and Osteoporosis sections, one can tailor safe PA prescription for that individual, depending on the site of bone involvement. This is important in maintaining quality of life and functional independence among palliative patients as well.



Areas of emphasis in patients and survivors of osteosarcoma or other bone malignancy

Table 5.14 highlights areas of emphasis in this population. However, it is important to note that surgery to remove a malignant mass is more extensive than a surgery to re-surface joints. Soft tissues that have been infiltrated by the tumor will be removed and surrounding blood vessels and nerves may be damaged. The amount of bone removed in osteosarcoma is related to the size of the tumor mass. The hardware used varies on the location of the tumor. These can involve ^{84, 91-94}:

- ✓ a metal rod and nail replacing as much as half of the resected femur or tibia; or
- ✓ the entire femur being replaced, requiring an adjacent knee replacement with a component nailed into the tibia;
- ✓ amputation; or
- ✓ rotationplasty, a procedure where the femur is removed and the lower leg is surgically attached to the hip, which turns a person's foot functionally into their knee ⁸⁴.

The involved bones are skeletally immature therefore some components are built with the ability to be expanded to accommodate for growth. If growth is properly accommodated for, issues of leg length discrepancy and associated pelvic asymmetry can be avoided. Otherwise, one can expect this asymmetry to cause eventual back pain and associated scoliosis ⁹⁶. A leg length discrepancy of 2 centimeters or less typically has no functional impact ⁹⁷. A surgery to remove an osteosarcoma may involve as much as 2 years of physical and/or occupational therapy.

It is important to protect the joints and operated limb while bones and muscles heal due to delayed healing and increased risk of infection because of chemotherapy ^{91, 98}. Immobilization and limited weight bearing post-operatively play a significant role in the development of disuse atrophy ⁹⁸. Familiarity of a person's surgery and post-operative precautions will assist in setting realistic goals and expectations. As an example, patients and survivors who have had their vastus medialis head of the quadriceps muscle resected as part of tumor removal may appear "stiff-kneed" compared to the other side ⁸⁹. This is due to a decreased ability to control the knee during initial heel-strike. It may not be possible for such a patient or survivor to achieve perfect gait symmetry ⁸⁹. Conversely, a patient or survivor who had both vastus lateralis and intermedius but retained vastus medialis tend to have greater motor control at the knee, highlighting the importance of vastus medialis in load absorption ⁸⁸. The orthopedic surgeon is



the best source for identifying what has been removed and what limitations or features are inherent within the prosthetic reconstruction ⁸⁵. Consultation with the physical therapist or occupational therapist will also be beneficial to determine mobility safety. For a detailed overview of different surgical procedures, the reader is encouraged to read ⁹⁸.

Table 5.14. Areas of emphasis in patients and survivors with osteosarcoma.

✓ Improving range of motion within surgical limitations, followed by: ✓ Progressive resistance training in functional patterns ✓ Gradual weaning-off of ambulatory aids to encourage muscle use of the lower extremities ✓ Full body symmetry during gait (Note: asymmetry can hint at range or strength impairments) ✓ Balance and coordination training ✓ Progressive return to sport or work with physician clearance

Areas of caution in patients and survivors of osteosarcoma or other bone malignancy

Table 5.15 summarizes common safety precautions that are prescribed by the orthopedic surgeon – note that this may vary considerably. These precautions are surgeon-lead and should be reviewed when developing a therapy plan as well as determining activity and sports restrictions ^{92, 95}.

Though seen less frequently, osteosarcoma within the humerus presents unique challenges given the complexity of the shoulder girdle. For a detailed overview of precautions, expected outcomes, areas of emphasis during early and late rehabilitation categorized by tumor and surgical approach (proximal humerus, total humerus, elbow replacement), the reader is encouraged to review Punzalan and Hyden's article ⁹⁴. Additionally, it is thought that patients and survivors with a prior history of osteosarcoma should be aware that they are predisposed to lower BMD and, consequently, at higher risk of fracture throughout their bodies ⁹². At a mean follow-up of 16 years after therapies in patients and survivors who were disease-free, 20.8% were considered osteoporotic and 43.7% were considered to have low bone density when compared to age-matched normative data ⁹². It may be worthwhile for a person with previous history of osteosarcoma who wishes to take on a new sport or high-risk activity to request from their physician a BMD scan to determine their fracture risk. For other PA recommendations and precautions refer to osteopenia and osteoporosis within this chapter.

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Tumor Site/ Procedure	Expected Outcomes	Precautions	Functional Impact	Orthotic Recommendations
Proximal Femur	Normal gait; tends to be less functionally limiting than above knee amputation or hip	Total hip replacement precautions: avoidance of hip flexion past 90 degrees, extremes of internal or external rotation and adduction	Difficulties dressing due to forward bending/ hip flexion restrictions. Avoid crossing the legs in sitting or standing. Limited sports participation if abductor muscles removed.	Hip abduction brace. If hip abductors are resected with tumor or if an allograft is used, then hip, knee, ankle and foot orthosis may be prescribed.
Distal Femur	Good functional gait, some return	dislocation. Limited total knee arthroplasty restrictions:	Due to lack of ligamentous support at the knee, likely not	Continuous passive motion (CPM) therapy early post-
	to limited sports activity. Use knee support as needed.	knee flexion and sports limitations at surgeon's discretion.	able to participate in stop- and-go and contact sports. Better gait performance if vastus medialis muscle spared, even if intermedius and lateralis bellies of the quadriceps were removed.	operatively in some cases. Supportive bracing until quadriceps strong enough to support body weight.
Total Femur Reconstruction	Functional gait long-term. Common to have trunkal lurch sideways towards	Combined total hip and knee precautions. Often no active hip abduction for months post- operatively to avoid	Very limited sports participation. Often restricted generalized hip movement in first few months to allow for scarring around prosthesis to	Supportive bracing as described for hip and knee above.
	operated side due to weak abductor muscles.	abductor muscles from detaching from prosthesis.	protect against dislocation.	

Drovimol Tibio 100		Vace immedilization for	- coatby schobilitation aired	l loo of knoo immobilization
	gait, some return	6-12 weeks with	Letiguity renabilitation given long period of immobilization.	splint until quadriceps able to
	to limited sports	protected weight bearing	Tend to have slower gait than	sustain knee extension in gait.
	activity,		distal femur resections and a	
	preferably with		pattern of knee	
	supportive knee		nyperextension during stance	
Eibular Autoaraft	Cood finational	Non woicht booring noot		l loo of knoo immobilizor duo
After Mid-Shaft	dout unictional	non weight beaning post-	Provinged and slow	to duadricens disruption to
Femur Tumor	to sports	progress to partial weight	leads to significant muscle	avoid hamstrings contracture.
Resection ¹⁰⁰	participation if no	bearing approximately 2	atrophy. Commonly 2-3 years	must be cautious about torque
	complications in	months post-op and full	before fibula hypertrophies to	of the limb's weight
	the first 2 years	weight bearing around 9	size of femur. Cautious return	concentrating at the ends of
	post-op	months	to sport with progressive loading	any brace.
Van Ness	Excellent	Protected weight bearing	Often able to return to	Initial use of low-grade
Rotationplasty ³²	functional return	during period of bone	activities and sports in the	compression stocking to
	after prosthetic	healing. Progressive	long term.	control swelling/ shape for
	training	weight bearing.		readiness into prosthesis.
Extracorporeal Irradiation and Re-	Functional gait	Protected weight bearing with progressive weight	Can take 2-3 years for irradiated bone to heal	Depends on area operated.
Implantation		bearing.	completely. Limited high- impact activities.	
Considerations for	Bone healing will be	e slowed by cancer therapies	s: not the usual 6-8 weeks for bo	ne healing. The risk of infection
all	is higher due to imr especially if referrin	nunosuppression. Excellent of on to community programs	communication with surgical and s. If uncertain, consult the primar	l oncology teams is necessary, v physician.
	-) -)		-

Note. Compiled from 89-90, 92, 94, 99-101


ix) Sensory impairments

Refer to *Table 5.16* for areas of emphasis and caution if a patient or survivor is experiencing sensory impairments.

Skin sensation

Invasive surgeries carry a risk of damaging cutaneous nerves, resulting in altered, decreased, or absent sensation at or near the surgical site. In 2000, Spicer and colleagues ¹⁰² found sensory deficits in the anterior surface of the knee in 50% of patients undergoing anterior crucial ligament (**ACL**) reconstruction. Surgeons make an active effort to identify and protect sensory cutaneous nerves, given that painful neuromas can arise from surgical nerve injury ¹⁰³. Unfortunately, the aggressive nature of osteosarcoma may make it difficult to avoid all cutaneous nerves. Though anecdotally a rare occurrence, it is still worthwhile assessing a patient's sensation. Depending on the extent of nerve injury, this may include deficits in ¹⁰⁴:

- ✓ sensation of hot/cold (a potential risk for burns if inattentive, e.g., in the use of a hot pack during rehabilitation);
- ✓ discrimination of deep, light, or pinprick sensation;
- ✓ joint proprioception, which may appear as incoordination or clumsiness; and
- ✓ sensation of different forms of pain.

Nerve injury may also lead to sensation of pain from an otherwise non-painful stimulus. Pain then inhibits muscle activation and may prevent functional use of the affected limb. Sensation plays a role in joint and limb protection in healthy populations. As an osteosarcoma patient or survivor may be unable to feel what their body is doing, early re-introduction into PA and sports should be supervised closely to identify faulty movement patterns.

Ototoxicity

Ototoxicity refers to damage to the cells within the inner ear responsible for hearing and balance and is a moderately common side effect of cisplatin chemotherapy in osteosarcoma ¹⁰⁵. It typically affects hearing loss in the high frequency ranges and, rarely, within ranges related to speech among osteosarcoma patients and survivors ¹⁰⁵. Hearing loss rarely occurs at doses less than 260mg/m² and typically presents bilaterally ¹⁰⁵. Some authors suggest screening only those who receive greater than 400mg/m² ¹⁰⁶. Unfortunately doses this high are necessary for other forms of cancer. In a study examining the impact of cisplatin chemotherapy on ototoxicity in medulloblastoma patients, where the median dose was 412.5 mg/m² (with a range of 200-600), 25.9% of their 35 study participants required hearing support ¹⁰⁷. It is worthwhile being



aware of the potential for hearing impairment among persons undergoing treatment for cancer as this may affect safety.

In animal models, ototoxicity affecting hearing occurs long before damage can be perceived in the vestibular system, suggesting that much higher doses of cisplatin among children with cancer may lead to balance issues ¹⁰⁸. Vestibular impairment, although not studied yet, could theoretically be related to ototoxicity in children with osteosarcoma. This situation would necessitate increased reliance on visual and somatosensory input for balance ¹⁰⁹. This would put them at higher risk for falls in low-light situations and/or uneven terrain as their vestibulo-spinal reflexes would be dampened ¹⁰⁹. Referral to a vestibular rehabilitation specialist is warranted in this case for training of compensatory strategies. When prescribing PA, ensure balance issues are taken into account to avoid risk of falls.

Table 5.16. Areas of emphasis and caution in patients and survivors with sensory impairments.

	Emphasize:				
\checkmark	Education regarding risks of impaired sensory input; teach frequent skin checks particularly				
	in hard-to-see areas				
\checkmark	Stress importance of proper alignment of joints during PA				
\checkmark	Progressive balance training for increased use of unimpaired sensory systems				
	······				
	Practice Caution:				
\checkmark	Careful when applying hot or cold to a limb with impaired sensation due to risk of burn/				
	frostbite				
\checkmark	Monitor skin and/or surgical scar condition in first year after surgical resection of tumors, as				
	impaired sensation can make it difficult to feel if skin or scar tissue is breaking down or				
	getting infected				
\checkmark	If unable to learn proper alignment through activity, consider bracing for additional support				
•	and prevention of injury				
./	When training over upoven terrain during return to sport, gradual progressive drills are				
v	important to quoid foulty movements				
	Important to avoid faulty movements				

x) Graft-versus-host disease

Graft-versus-host disease (GVHD) can be acute or chronic (refer to Chapter 8).

Chronic graft-versus-host disease (**cGVHD**) is a frequent cause of morbidity and subsequent mortality following allogeneic HSCT. Its pathophysiology is characterized by impaired immune tolerance mechanisms, which can cause chronic inflammation and subsequent scar formation ¹¹⁰. cGVHD usually begins between three months to two years after transplantation. Generally



the clinical manifestations of cGVHD do not differ significantly between children and adults ¹¹⁰⁻

Table 5.17. Common organs affected by chronic graft versus host disease.

Skin	Can evolve from a rash to deep sclerotic changes that constricts much like a severe burn might		
Eyes	Changes in tear duct function with associated dryness and/or conjunctivitis		
Oral mucosa	Ulcerations, gingivitis, destruction of salivary glands		
Liver	Liver damage may lead to stasis, cirrhosis		
Gastrointestinal tract	Nausea and vomiting, chronic diarrhea, malabsorption		
Genitals	Ulceration or fissuring, often accompany changes in oral mucosa		
Lung	Progressive, irreversible obstructive and/or fibrotic changes and increased risk of severe infections		
Joints and fasciae	Fasciitis, potentially limiting mobility in large joints. Rheumatoid symptoms in the joints		

Note. Compiled from ^{110, 111, 113, 114}.

It is worth noting that cGVHD often impacts a few, and not all, of the organ systems listed above. The severity among impacted systems may also vary. The prevention of cGVHD is primarily controlled through the use of steroids ¹¹⁰.

Areas of emphasis in patients with chronic graft versus host disease

As with other forms of disease requiring sustained doses of steroids, patients may experience multiple side effects ¹¹⁰, and this it is important to recognize these when tailoring a PA program for children with cGVHD. *Table 5.18* provides PA recommendations for this population based on associated complications. Unfortunately, there is a paucity of literature looking at PA interventions in this population, and more research is needed in this specialty area. A recent animal study looking at mice given allogeneic HSCT showed favourable outcomes after an 11-week moderate-intensity treadmill program ¹¹⁵.



Table 5.18. Physical activity recommendations based on cronic graft versus host disease impact.

Organ system	Recommendation
Skin and fasciitis: scarring over joints and deep into tissues	Conservative approach of stretching program shown to be superior to surgical interventions; refer to rehabilitation specialists when available.
Changes to nerve and muscle physiology: proximal musculature steroid-induced myopathy extremely common	Emphasize use of shoulder and hip muscle groups as part of strengthening program; develop endurance.
Joint pains associated with rheumatic changes	Emphasize strengthening muscles around painful joints to improve joint protection.
Fibrotic lung changes leading to impairments to gas exchange; oxygen dependence; steroid myopathy severe enough to impact muscles of respiration	Teach rate of perceived exertion (refer to <i>Appendix F</i>); maintain normal breathing as able; may need to teach relaxation/ breathing exercises as breathlessness can be very anxiety-provoking, may lead to panic attacks. Consult respirologist.
Osteoporosis	Strengthening of surrounding musculature. See osteoporosis in this chapter.
Pancytopenia	Refer to pancytopenia in this chapter.

Note. Compiled from ¹¹⁰⁻¹¹⁵.

Children with cGVHD must have a slow, gradual re-introduction into PA. Often these children have been ill for long periods of time and their parents have a great deal of fear about "pushing too hard". Early sessions with a child with cGVHD should focus on low-intensity activity that is meaningful and rewarding. This will help gradually alleviate the fear of activity in both the child and the parent.

Areas of caution in patients with chronic graft versus host disease

The list of precautions for children with cGVHD depends on which systems are affected by the condition. Generally most systems will not directly pose a danger to the child in terms of PA, but rather may limit their ability to participate, such as in the case of skin or fascial contractures or scarring that limit range of motion ¹¹⁰. However, certain organ involvement requires extra caution, as detailed below:

Bone – osteoporosis and/or osteonecrosis. Refer to Osteoporosis and Osteonecrosis sections.



Lungs – particularly significant if oxygen exchange is impaired, some children will require continuous supplemental oxygen supply. The presence of portable oxygen tanks does not mean they cannot participate in PA. Refer to Pulmonary Toxicity section for details on safety for this population. Though not a treatment related toxicity per se, the changes that can occur as a result of cGVHD can closely resemble other etiologies of lung tissue damage ¹¹⁰.

Because of the complex nature of this condition, experts in this area recommend that patients with cGVHD seek services from a specialized center familiar with graft-versus-host disease after bone marrow transplantation ¹¹⁰.

Conclusion

Patients and survivors of pediatric cancer are at risk for multiple side effects during treatment and for years into adulthood. Although it is critical to understand the complexities of cancer treatment and the resulting side effects, it is important to note that children currently in treatment and patients and survivors of pediatric cancer are able to engage in PA safely with minimal risks. In most cases, the advantages of PA outweigh the risks. In order to plan a safe PA program for children with cancer, we encourage that the general and specific PA recommendations described in this chapter are followed. For all risk factors and side effects of cancer treatment, it is crucial to assess symptoms of PA tolerance pre, during and post exercise. Supervision is recommended when starting a PA program, during intense cancer treatment periods, and when making any significant program changes. If symptoms are present, refer back to the oncologist or primary physician for further testing. Finally, it is essential to individualize the PA program for the interests and age of the person to optimize long-term compliance that will promote a healthy adulthood.





Kinley, 6 years old

Take Home Message

It is generally safe and beneficial for patients and survivors of pediatric cancer to perform physical activity, being aware of a few precautions depending on the treatment regimen and side effects. Awareness of the areas of emphasis and caution for physical activity regarding the side effects of cancer treatment will assist medical professionals in optimizing a person's success in a physical activity program.

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Appendix 5.A

Ankle Stretches for Patients and Survivors of Pediatric Cancer with or at Risk for Chemotherapy-Induced Peripheral Neuropathy

Exercise	Target population	Picture	Variations	Equipment	Instructions
Caregiver- Assisted Gastrocne mius- Soleus Stretch	Children below age 7 years or unable to do independent stretch		Supine, Prone, Seated	None	With child's knee extended, stretch ankle back into dorsiflexion (toes towards knee) avoiding any twist or collapse of arch. Hold 30 seconds.
Gastrocne mius- Soleus Wall Stretch	Persons older than age 7 with or without arches in standing		Flexed knee to target soleus muscle	Wall or counter	Standing facing wall. Step one leg forward. Face toe toward wall. Lean forward with both heels on ground maintaining arch in foot. Should feel stretch through calf and back of knee. Hold 30 sec.
Gastrocne mius- Soleus Stair Stretch	Persons older than age 7 with arch in standing		Both legs, or one leg at a time	Stair with railing	Stand with balls of feet on edge of stair holding onto the railing. Drop heels down below the step and hold for 30 sec. Should feel through calf and back of knee.



Appendix 5.B

Balance Exercises for Children, Adolescents, and Adults With or at Risk for Chemotherapy-Induced Peripheral Neuropathy

Difficulty	Exercise	Picture	Age	Variations	Equipment	Instructions
Easy to Moderate	Standing with feet together	No picture.	≥ 2 years	Adding arm challenges; Add unsteady surfaces	Bosu, couch cushion, or air mattress	Stand on unsteady surface while doing another activity with arms
Easy to Moderate	Walking on a line		≥2 years	Heel touching toe; Backward; Stepping over obstacle; Hands on hips	Tape line or balance beam	Walk forward on a line with stepping off. Increase difficulty by variations.
Moderate to Difficult	Single leg stance		≥ 3 years	Increase difficulty with hands on hips; Add arm challenges or head movements; Add unsteady surface for higher level skill	Support surface (doorway, chair, counter)	Stand on one leg for as long as possible and add additional challenge if able >10 seconds if older than 5 years



Chapter 6

Physical Activity and Cardiotoxic Therapies

Saro Armenian, DO, MPH

Learning Objectives:

After completing this chapter you will know:

- ...the magnitude of risk associated with treatment-related congestive heart failure in survivors of childhood cancer.
- ...the pathophysiology of cardiac injury as well as clinical and treatment-related modifiers of congestive heart failure risk.
- ...the current state of knowledge regarding the risk and benefits associated with physical activity in survivors exposed to cardiotoxic therapies.

Introduction

The National Cancer Institute defines cardiotoxicity in general terms as "toxicity that affects the heart" (www.cancer.gov/dictionary/). However, the mechanism with which certain cancer-directed treatments cause cardiac injury can be quite complex, often manifesting as clinically evident cardiovascular disease years after completion of therapy. Cardiotoxicity is one of the most serious chronic complications of pediatric cancer therapy and may manifest as cardiomyopathy, pericarditis, congestive heart failure, valvular heart disease or premature coronary artery disease ¹.

During the past two decades, research on cancer survivorship issues has revealed that chemotherapy induced-cardiovascular complications (such as coronary artery disease, stroke, and especially **congestive heart failure** (**CHF**)) have emerged as a leading cause of morbidity and mortality in long-term survivors of childhood cancer ². In fact, childhood cancer survivors are at a 15-fold increased risk of developing CHF ³ and are at 7-fold higher risk of premature death due to cardiac causes ⁴, when compared with the general population. Treatments used in adult and pediatric oncology populations that have been associated with cardiotoxicity include ^{5,6}:



- i) Chemotherapeutic agents that include but are not limited to anthracycline, cyclophosphamide, cytarabine, cisplatin and isofosfamide; and
- ii) Radiotherapy where the heart is in the field of treatment.

i) Chemotherapeutic Agents

These are associated with the development of acute or chronic cardiovascular adverse effects that could impact **quality of life (QOL)** of children with cancer and limit future treatment

options. Anthracycline antibiotics are the best known class of chemotherapeutic drugs associated with cardiotoxicity. These agents, especially doxorubicin, have long been a key component of therapy for hematological and solid tumors in children and are still use in nearly 60 % of childhood cancer. Anthracycline–induced cardiotoxicity can manifest as either asymptomatic or clinical as a CHF. There is a strong dose-



PEER participant working balance

dependent relation between anthracycline chemotherapy exposure and CHF risk. The incidence of CHF is <5% with cumulative anthracyclines exposure of <250 mg/m²; approaches 10% at doses between 250 and 600 mg/m²; and exceeds 30% for doses >600 mg/m² ^{2,5,7,8}. This risk is higher in females, among those who are treated at a younger age (<5 years of age), are exposed to chest radiation, and who develop cardiovascular risk factors such as hypertension and diabetes after completion of therapy (*Table 6.1*)². The most frequently used analogs of anthracyclines include doxorubicin and daunomycin (see *Appendix A* for a list of common medications and *Appendix 6.A* to see anthracycline conversion formulas)⁸.

i) Radiotherapy

Radiotherapy where the heart is in the field of treatment can result in a number of longterm complications including constrictive pericarditis, cardiomyopathy, valvular heart disease, coronary artery disease, and conduction abnormalities ¹. Exposure to mediastinal radiation is associated with valvular fibrosis or insufficiency in 40% to 60% of Hodgkin lymphoma survivors, whereas conduction defects are present in as many as 75%. Although clinically evident CHF is



rare following mediastinal radiation alone, when present it is primarily in the form of diastolic

dysfunction, as opposed to systolic disease seen following anthracycline exposure.

These survivors have emerged as a significant population at high risk for preventable heart disease ¹. In childhood cancer survivors, there is often a long (>10 years) latency between cardiotoxic exposure and clinically evident Those children exposed to doses >250 mg/m² of anthracycline are at the highest risk to develop cardiotoxicity.

cardiac disease ^{2,6}. In fact, it is well recognized that there is a variable period of asymptomatic cardiac dysfunction that precedes clinically overt signs and symptoms (*Table 6.1*) ⁹. For anthracycline-exposed survivors, the asymptomatic stage is characterized by **left ventricular** (**LV**) systolic dysfunction which manifests as decreased **ejection fraction** (**EF**; lower limit of normal: 50%) or **shortening fraction** (**SF**; lower limit of normal: 27%), a clinical picture similar to dilated **cardiomyopathy** ^{2,6}. Individuals who receive anthracyclines and chest radiation may have a combination of dilated and restrictive **cardiomyopathy** that results from **myocardial fibrosis** and due to ionizing radiation ^{2,6}.

Signs and Symptoms	Therapeutic Exposures Associated with Increased Risk	Clinical Risk Factors
Signs:	Anthracycline chemotherapy	Younger age at treatment (<5
 ✓ Edema ✓ Rales Symptoms: 	Dose-dependent increase in risk (lifetime cumulative incidence, %)	years old)
	$(-220 \text{ mg/m}^2)(5\%)$	Female sex
 ✓ Dyspitea ✓ Fatigue 	✓ (5%) ✓ 250-600 mg/m² (10%) ✓ >600 mg/m² (>30%)	Cardiovascular risk factors (hypertension, diabetes)
	Chest radiation exposure in which the heart is in the field of treatment	

Table 6.1. Clinical signs and symptoms and risk factors associated with CHF.

Note. The definition for symptomatic CHF is taken from ⁹. Risk classifications are taken from ^{2,7,10}. Refer to *Appendix 6.A* to see anthracycline conversion factors.

Recognizing the importance of screening for and early detection of asymptomatic disease, the Children's Oncology Group as well as other international organizations have



developed clinical practice guidelines that recommend annual comprehensive history and physical examinations be performed on all survivors treated with cardiotoxic therapies, paying close attention to signs and symptoms of cardiac disease ¹¹⁻¹⁴. In addition, screening echocardiograms should be performed, ranging from annually to every 5 years, depending on CHF risk (*Table 6.2*).

Table 6.2. Children's Oncology Group's recommended frequency of echocardiogram or MUGA scan for childhood cancer survivors.

Age at Treatment [†]	Chest Radiation	Anthracycline Dose ^{††}	Recommended Frequency
< 1 year old	Yes	Any	Every year
	No	<200 mg/m ²	Every 2 years
		≥200 mg/m ²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m ²	Every 5 years
		≥100-<300 mg/m ²	Every 2 years
		≥300 mg/m²	Every year
≥5 years old	Yes	<300 mg/m ²	Every 2 years
		≥300 mg/m ²	Every year
	No	<200 mg/m ²	Every 5 years
		≥200-<300 mg/m²	Every 2 years
		≥300 mg/m ²	Every year
Any ag	e with decrease in se	rial function	Every year

Note. Taken from ¹¹. [†]Age at time of first cardiotoxic therapy. ^{††}Based on equivalent mg of doxorubicin/daunomycin.

However, given that a substantial proportion (up to 50%) of childhood cancer survivors

treated with cardiotoxic therapies could have asymptomatic disease, clinicians are hesitant to make recommendations regarding limitations of PA, due in part to concerns for worsening cardiac function that may result from increased **cardiometabolic** demand on the heart.

Up to 50% of childhood cancer survivors treated with cardiotoxic therapies could have asymptomatic disease.



Physical Activity after Cardiotoxic Therapy Exposure

Patients with normal cardiac function at risk of cardiotoxicity

There is considerable evidence supporting the advantages derived from regular moderate PA in the general population^{15,16}. The current joint guidelines for healthy adults from the American Heart Association (**AHA**) and the American College of Sports Medicine for adults (**ACSM**) recommend 30 to 40 minutes of aerobic exercise five times per week and strength training twice per week ¹⁵. Studies in limited numbers of childhood cancer survivors have found that despite having lower exercise capacity, evidenced by lower peak myocardial oxygen consumption^{17,18}, survivors can attain significant improvements in muscle strength and flexibility, cardiopulmonary fitness, and overall physical function when engaged in aerobic PA ¹⁹. While specific recommendations regarding PA in childhood cancer exposed to cardiotoxic therapies exist, most are consensus based or centers own experience ^{1,11,20}. Given the well-documented benefits of PA in the general population as well as in non-oncology populations at risk for CHF due to genetic disorders, regular PA is recommended for survivors treated with anthracyclines and/or chest radiation who have normal LV systolic function ^{1,9,21-23}.

The **Children Oncology Group- Long Term Follow up Guidelines (COG-LTFG)** has offered a few recommendations and contraindications for children undergoing cardiotoxic therapies (refer to *Table 6.3* and *Table 6.4*).

Table 6.3. Children Oncology Group- Long Term Follow up Guideline: Physical activity recommendation for children undergoing cardiotoxic treatments.

Recommendations

- Patients beginning an exercise regimen for the first time should be encouraged to promptly report to their physicians symptoms of tiredness or difficulty in breathing that do not resolve with rest.
- ✓ Aerobic exercise is generally safe and should be encouraged.
- High repetition weight lifting involving lighter weights is more likely to be safe. The numbers of repetitions should be limited to that which the survivor can perform with ease.



Table 6.4. Physical activity contraindications for children undergoing cardiotoxic treatments.

Contraindications

- ✓ Intensive isometric exercise such as weight lifting, wrestling should be avoid in those patients defined in table 6.2 (as those who need screening every one or two years).
- ✓ Patients and survivors who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with cardiologist.

With regards to limitations in the intensity of PA, the AHA ²² and the European Society of Cardiology (**ESC**) ²³ provide no restrictions in activity for individuals who are at risk for cardiac decompensation due to genetic disorders (i.e., familial dilated cardiomyopathy, hypertrophic cardiomyopathy) but have normal cardiac function (abnormal genotype, normal phenotype).

Patients with asymptomatic cardiac disease

No specific guidelines for children with cancer and asymptomatic cardiac disease exist. However, the approach to managing heart failure in children with heart disease caused by chemotherapy or radiation doses not differ substantially from managing heart failure caused by idiopathic, genetic or other acquire causes of cardiomyopathy ². Cardiology consultation is recommended for survivors with asymptomatic cardiomyopathy to define limits and precautions for PA (i.e., limited or no participation in competitive sports with high cardiometabolic demand such as body building, rock climbing, windsurfing, ice hockey) ²⁰. For individuals with

asymptomatic cardiac dysfunction, there are specific recommendations regarding allowable activities (high, moderate, low-intensity) that are based on severity of existing cardiac dysfunction ²². Due to anecdotal reports of cardiac deterioration in childhood cancer survivors during intensive isometric exercise, cardiology consultation may be reasonable for high risk survivors who plan to be engaged in such high

These resources will help physicians determine which type of PA will be suitable or not for each patient:

- ✓ Williams et al., 2007 [21]
- ✓ Maron et al., 2004 [22]
- ✓ Pellicia et al., 2006 [23]

intensity PA, as defined by the AHA and ESC ^{22,23}. It is important to note that existing recommendations for PA in childhood cancer survivors remain consensus-based, and that more studies are needed.



Future Directions

Studies are needed to prospectively evaluate the safety and efficacy of interventions to improve physical fitness, as well as to define optimal levels of PA to maintain benefit in childhood cancer survivor at risk for premature cardiovascular disease. Outcomes of interest should include improvement in cardiac function, reversal of pathologic cardiac remodeling, improvement in health-related QOL, and other self-reported outcomes such as fatigue and vitality.

Take Home Message

Cardiovascular complications such as congestive heart failure have emerged as a serious side effect of cancer-directed therapies used in children with malignancies. These survivors and their healthcare providers should be made aware of their long-term cardiovascular disease risk, and the importance of engaging in regular aerobic physical activity to improve overall fitness and long-term wellbeing.



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Appendix 6.A

Anthracycline Conversion Factors

The risk of developing cardiotoxicity by anthracycline is usually described by the cumulative doses of doxorubicin. There is a paucity of literature to support isotoxic dose conversion; however, the following conversion charts can be used as a guideline to assess the patient's risk to develop cardiotoxicity, but clinical judgment should be the key factor to determine the risk for the patient.

Chemotherapy Agent	Conversion Factors
Doxorubicin	Multiply total dose x 1
Danourubicin	Multiply total dose x 0.833
Epirubicin	Multiply total dose x 0.67
Idarubicin	Multiply total dose x 5
Mitoxantrone	Multiply total dose x 4

Note. Taken from the Children Oncology Group- Long-term Follow-up Guidelines for Survivors or Childhood, Adolescent and Young Adult Cancers



Chapter 7

Physical Activity and Leukemia

Alejandro San Juan Ferrer, PhD, Physiotherapist; Carolina Chamorro-Viña, PhD &

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Learning Objectives

After completing this chapter you will know:

- ...more about a diagnosis of leukemia during childhood.
- ...the potential side effects of the treatment of leukemia.
- ... the role of physical activity as a beneficial tool for patients and survivors of leukemia.
- ...the precautions childhood cancer patients and survivors must take to safely engage in physical activity.

Introduction

Leukemia is a progressive, malignant disease of the blood-forming organs, marked by the distorted proliferation and development of leukocytes and their precursors in the blood and bone marrow. Hematological tumors derive from two normal cell lineages: **lymphoid** (e.g., lymphocytes B and T, **natural killer (NK)** cells, and plasma cells); and **myeloid** (e.g., granulocytes, erythrocytes, thrombocytes, macrophages and mast cells). Leukemia is the most common childhood cancer, representing 31% of all cancers among children less than 15 years of age ¹.

Acute lymphoblastic leukemia

Acute lymphoblastic leukemia (ALL) represents approximately 25% of all cancers among children less than 15 years of age, and 75% of children diagnosed with leukemia ¹. ALL survivors usually present with bone marrow failure (e.g., bleeding, infection and abnormal blood



counts) that is clinically manifested as fatigue, bruising, and increased rate of infections (refer to *Chapter 5*)^{2}. ALL childhood survivors have a relatively high survival rate and more than 90% of children with standard risk disease can now expect to be cured ³.

Acute myeloid leukemia

Acute myeloid leukemia (AML) represents approximately 4% of all cancers among children less than 15 years of age ⁴, and 20% of children diagnosed with leukemia ⁴. AML is a heterogeneous group of diseases, 70% of myeloid leukemia is acute and the remainder includes chronic and/or sub-acute myeloproliferative disorders ⁴. Often present with infiltration of the blood, bone marrow and other tissues by neoplastic cells of the hematopoietic system ². Up to 65% of pediatric AML survivors experience long-term side effects ⁵.

Common Treatments and Phases

Acute lymphoblastic leukemia

ALL treatment is usually composed of three phases:

1) **Induction**: The goal of this first phase of treatment is to induce morphologic **remission** and to restore normal **hematopoiesis**². Drugs commonly used include vincristine, corticosteroids (prednisone/dexamethasone and L-asparaginase), with or without anthracyclines, and in conjunction with **intrathecal therapy (IT)** (including methotrexate, cytarabine and hydrocortisone) ⁶. Refer to *Appendix A* for full medication list. This induction phase aims to induce complete remission in 4-6 weeks ⁷.

2) **Central nervous system (CNS)-**directed treatment with **consolidation** (or intensification) therapy. Approximately 3% of patients have detectable CNS involvement at diagnosis. However, unless specific therapy is directed toward the CNS, the majority of children will eventually develop overt CNS leukemia. Therefore, all children with ALL typically receive systemic combination chemotherapy with some form of CNS prophylaxis ⁸. The consolidation or intensification phase lasts for 1-2 months and aims to prevent CNS relapses and to reduce the systemic minimal residual leukemia burden ². It consists of the combination of IT chemotherapy and CNS-directed systemic chemotherapy; cranial radiation is reserved for select situations ⁸. The type of CNS-therapy that is used is based on a patient's risk of CNS-relapse, with higher-risk patients receiving more intensive treatments ⁸.



3) Maintenance therapy: This last phase of treatment is prolonged, lasting as long as 2-3 years. It consists of daily oral 6-mercaptopurine and weekly oral methotrexate. In some protocols, pulsed applications of glucocorticoids, vincristine and IT chemotherapy are also administered ⁷. Some leukemia patients at higher risk may receive more intense maintenance chemotherapy and IT. The objective of maintenance therapy is to help lower the risk of cancer recurrence after it has disappeared following initial therapy.

Acute myeloid leukemia

AML treatment is usually divided into two phases:

1) Induction: As in ALL, induction phase aims to induce complete remission, and therapy regimens commonly use cytarabine and an anthracycline (e.g., daunorubicin), in combination with other agents (e.g., etoposide and/or thioguanine) ⁹.

2) Consolidation (or intensification) therapy: The objective of this phase is to kill any remaining tumor cells using more intensive treatment over several months. Chemotherapy drugs are usually used and high doses of cytarabine (ara-C) and daunorubicin may also be added. The use of some form of CNS-directed treatment (IT chemotherapy with or without cranial irradiation) is considered a standard part of the AML treatment and it has been incorporated into most protocols for childhood AML treatment ¹⁰. IT chemotherapy is usually given every 1-2 months, until the consolidation phase is completed. This phase may also include allogeneic or autologous **hematopoietic stem cell transplant (HSCT)** depending on the treatment protocol and survivor's risk ¹¹. Unlike ALL, maintenance therapy is usually not included in pediatric AML protocols or for acute promyelocytic leukemia. A major challenge in the treatment of childhood AML is to prolong the duration of the initial remission with additional chemotherapy or HSCT ⁴.

Hematopoietic stem cell transplantation

HSCT is another treatment option for certain types of AML and ALL. This procedure involves infusion of cells (hematopoietic stem cells; also called hematopoietic progenitor cells) to reconstitute the hematopoietic system of a patient (refer to *Chapter 8* for more information).



Potential Treatment Side Effects and Implications for Physical Activity

Early side effects in survivors of childhood cancer are experienced during or shortly after treatment (e.g., surgery, radiotherapy, chemotherapy). These may include increased risk of infections, hemorrhagic and thromboembolic complications, nausea and/or vomiting, loss of appetite, allergic reactions, skin changes, fatigue, pain, or temporary hair loss ^{7.} Late-effects (long-term side effects) occur months or years after treatment and may affect most body systems. These effects may also increase the risk for secondary malignancies ¹². Refer to *Table 7.1* for a list of late-effects.

Cancer treatments can affect physiological systems that in turn might impact PA

participation. Specifically, impaired lung function, decreased blood oxygen transport capacity, diminished cardiac output and thus blood supply to body tissues (e.g., exercising muscles), reduced cardiorespiratory fitness to low levels (e.g., 50-70% lower level of **maximal oxygen consumption (VO₂max)** versus age and sex-matched healthy children), and the resultant fatigue, even during normal **activities of daily living (ADLs),** may all limit PA



Training aerobic capacity at the PEER program

participation. Cancer treatments may also induce gastrointestinal toxicities which can interfere with nutrition and thus with energy supply to muscles, thereby decreasing muscle mass (with greater decreases noted in HSCT survivors), while increasing adiposity and total body mass. These side effects in conjunction with other factors may be related to or promote a sedentary lifestyle. The reasons for lower PA in childhood cancer patients are not entirely clear; however, three potential explanations have emerged in the literature ¹⁴ (refer also to *Chapter 3*). The first, a physiological explanation, postulates that survivors of cancer are less active as a result of adverse consequences of cancer treatment side effects. The second argues that childhood cancer survivors are subject to an insidious "spectrum of disuse" as a result of an overly cautious approach towards PA fostered by concerned parents and physicians and this may lower children's self-confidence ¹⁵. Finally, another interesting point of view is that expressed by Oeffinger et al.¹⁶. They showed that the timing of the diagnosis and the length of the treatment



often coincide with a period of life when children are introduced to organized sports, such as soccer ¹⁶. Therefore the child with a cancer diagnosis would miss out on this critical period and therefore not be introduced to numerous leisure time PAs.

Table 7.1. Main late-effects in pediatric cancer.

System	Example of late side effects
Cardiovascular	Cardiomyopathy , congestive heart failure , arrhythmia, subclinical left ventricular dysfunction, valvular disease, atherosclerotic heart disease, myocardial infarction, pericarditis, pericardial fibrosis, and hypertension.
Pulmonary	Pulmonary fibrosis, interstitial pneumonitis, restrictive/obstructive lung disease, pulmonary dysfunction.
Musculoskeletal	Osteopenia, osteoporosis, osteonecrosis, reduced/uneven growth, reduced function/mobility, hypoplasia, fibrosis, radiation induces fracture (doses ≥ 40Gy), scoliosis/kyphosis (trunk fields only), secondary benign or malignant neoplasm, muscle weakness, fatigue.
Digestive	Hepatic dysfunction, veno-occlusive disease, hepatic fibrosis, cirrhosis, cholelithiasis, peptic ulcer, pancreatitis.
Endocrine/Metabolic	Growth hormone deficiency, precocious puberty, hypo and hyperthyroidism, thyroid nodules/cancer, Radiation doses ≥ 40Gy: hyperprolactinemia, central adrenal insufficiency, gonadotropin deficiency, lower metabolic cost.
Urinary	Glomerular toxicity, tubular dysfunction, renal insufficiency, hypertension, hemorrhagic cystitis, bladder fibrosis, dysfunctional voiding, neurogenic bladder, bladder malignancy.
Immune/Hematologic	Leukopenia, thrombocytopenia, anemia.
Neurocognitive	Neurocognitive deficits (executive function, attention, memory processing speed, visual motor integration), learning deficits, diminished intellectual quotient, fatigue.
Nervous System	Leukoencephalopathy, spasticity, ataxia, dysarthria, dysphagia, hemiparesis, seizures, motor and sensory deficits, brain tumor, peripheral sensory or motor neuropathy, pain, cerebrovascular complications (stroke, Moya disease, occlusive cerebral, vasculopathy).
Psychosocial	Social withdrawal, educational problems, depression, anxiety, posttraumatic stress, dependency, fatigue.

Note. Translated from ^{13.}



Physical Activity and Leukemia Research Summary

Searching the PubMed database for current literature regarding PA interventions among pediatric leukemia survivors, nine studies ¹⁷⁻²⁷, with a total of 155 participating children were identified (refer to *Appendix 7.A*). Out of all study participants, a total of 141 children were diagnosed with leukemia, 133 of these children were diagnosed with acute ALL. Eight out of nine included studies focused on ALL-patients exclusively, while only one study included leukemia survivors after bone marrow transplantation ²³. Thus, considering the overall research on PA interventions in pediatric oncology, current literature provides most data for ALL-patients.

The results of all included studies suggest that PA interventions with pediatric leukemia patients and survivors are feasible ^{17, 26, 27} and safe ^{19, 22}. Patients participated regularly (adherence between 60-98%) and no adverse effects or complications related to the PA intervention were reported in any publication. In addition, all studies presented some positive effect on physical functioning (e.g., strength, **aerobic capacity**, functional mobility, motor performance, ankle dorsiflexion ^{17, 18, 20-25}, level of activity ²¹, **body composition** ¹⁸, fatigue ^{17, 27} and **quality of life (QOL)**) ²³.

The setting in these studies differs considerably. While three studies were conducted as supervised programs ^{19, 22-25}, two studies were conducted as home-based programs ^{21, 27} and four studies included a combination of supervised and an additional home-based intervention ^{17, 18, 20, 26}. All studies conducted within the hospital were supervised ²²⁻²⁵. Most studies were conducted during medical treatment and maintenance therapy ^{19-21, 23, 25, 27}, while only one study focused on children affected with leukemia during survivorship ²⁶. The duration of programming varied from six-weeks up to two-years. One study even investigated the effects of an acute PA bout (30 minutes) on immune parameters ¹⁹. However, most studies explored an 8-16 week PA intervention. Regarding the form of PA, the studies differed considerably as well. While one program included **aerobic training** exclusively ²⁷, seven studies analyzed the effect of a combined PA program including stretching, resistance, aerobic and coordination as well as physical therapy, education and lifestyle/ recreational activities ^{17, 18, 20, 21, 23, 25, 26} (studies ²² and ²⁴ were done from extracted data from the intervention program of study ²⁵).

Overall, the results indicate that PA interventions with pediatric leukemia patients and survivors are feasible and safe. They also suggest a positive effect on physiological and psychosocial outcomes. However, a comprehensive evaluation of the existing data is very challenging given the large heterogeneity of the studies in terms of outcomes, form of PA, duration and setting.



Physical Activity Recommendations

Prior to initiating any new PA program, all childhood cancer survivors should first consult with their physician, as individual treatment factors and overall health status may impact their ability to safely participate in activity. Refer to *Table 7.2* for an example of objectives and PA recommendations and refer to *Appendix 7.B* for a sample group-based PA program.

Table 7.2. Objectives and physical activity recommendations during the different phases of cancer treatment for acute lymphoblastic leukemia patients.

Treatment Phase	Objective	PA Recommendation
Induction	Coping with side effects of cancer diagnosis and treatments. The goal is to prevent physical deconditioning.	In-hospital physiotherapy (aka physical therapy (PT)) and supervised PA.
Consolidation	Continue coping with side effects of cancer diagnosis and treatments. The goal is to continue preventing physical deconditioning.	In-hospital physiotherapy/PT and supervised PA.
Maintenance	Continue coping with the side effects of cancer diagnosis and treatments. The goal is to continue preventing physical deconditioning and start the process of rehabilitation as soon as possible (with the goal of recovering normal levels).	In-hospital or community-based supervised PA to rebuild physical fitness capacity to normal or close to normal levels. PT if needed.
Survivorship	Health promotion. The goal is to optimize overall health and quality of life.	Community-based PA programs. PT if needed.

Note. Compiled from 28 , as well as the authors own experience.

Physical Activity Precautions

While no detrimental effects of PA in children and adult cancer patients/survivors have been reported ^{29,30}, it is important to acknowledge that under some conditions certain precautions must be taken when prescribing PA. Refer to *Table 7.3* and *Chapter 5* for specific recommendations.

In addition to any medical contraindications or precautions, the side effects caused by the disease and treatment (e.g., extreme fatigue and/or muscle weakness, dyspnea, nausea, pain), may make it difficult for the patient/survivor to complete a PA session. In this situation, the



patient/survivor should reduce the intensity and duration of PA. In the event that these symptoms do not subside with reduced activity, the patient /survivor should consult with his/her physician as soon as possible.

Table 7.3. Precautions for physical activity prescription in childhood leukemia patients and survivors.

Pathology/Condition	Precaution
Fever	Temperature > 38°C: Avoid intense and strenuous PA.
	Temperature > 40°C: Avoid all PA.
Pancytopenia	Refer to Chapter 5.
Cachexia	Monitor weight loss. Engage in less aerobic and more
Loss of over 35% premorbid weight	of caution and supervise PA if cachexia is of concern.
Primary or metastatic bone cancer (increased risk of bone fractures)	Refer to Chapters 5 and 9.
Ataxia and dizziness	Avoid high impact PA.
	Avoid contact sports and activities that have a high risk of crash and falls and/or that require additional balance and coordination (e.g., treadmill walking, outdoor cycling).
CIPN	Refer to Chapter 5.

Note. Adapted and translated from ¹³. CIPN: Chemotherapy-induced peripheral neuropathy.

Future Research

The available literature presents several limitations that need to be addressed to improve the quality and level of evidence of future research (e.g., lack of control group, incomplete randomization, blinded measurement, small population sample). Moreover, PA interventions should be adapted based on the varied cancer diagnoses (e.g., solid tumors), therapy phases (e.g., induction), current health (e.g., severe anemia), and stage of survivorship to ensure safety and determine the potential positive effects of PA across the pediatric cancer trajectory.



Take Home Message

Physical activity programs are safe and necessary in this pediatric population. The literature has shown that physical activity has positive effects on muscle strength, cardiorespiratory fitness and quality of life. Physical activity during induction and consolidation phases of treatment should be supervised and preferably located at hospitals equipped with a child appropriate gymnasium. Once children move into later phases of treatment (e.g., maintenance), home-based physical activity programs and community programs are recommended. Once the child has reached normal or close to normal levels of conditioning according to their age, children should be encouraged to follow an active lifestyle and slowly be reintegrated into community and school-based physical activity.



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Appendix 7.A

Clinical Physical Activity Interventions in Children with Leukemia

Authors	Population	Intervention	Results
Yeh et al. 27	IG=12 (ALL) CG=10 (ALL) maintenance therapy	Home-based IG: 6wk; 3/wk, 30min; at 40- 60% of HRR; endurance CG: standard care	Feasibility: Adherence 67-83% Fatigue: general fatigue score ↑ in IG vs. CG (p=0.02)
Gohar et al. ¹⁷	N=9 (ALL) intensive medical treatment	Supervised, in-hospital and home-based ~ 6-7 mo; 5/wk; physical therapy program (mixed exercises)	Feasibility: 98% Physical functioning: Gross motor function ↑ (~35%) Fatigue: ↑ (~15%)
San Juan et al. ^{24, 25} Ruiz et al. ²²	N=7 (ALL) maintenance therapy	Supervised, in-hospital and 20-wk detraining 16wk + 20wk detraining; 3/week, 90-120 minutes Endurance: 30min. at 50- 70% HR _{max} Strength: 1 set, 8-15 repetitions,11 exercises	Immune status: no major effects on IGFs, IGFBPs and GH -> exercise can be safely undergone Adherence: > 85% Physical functioning: VO_{2peak} ↑ (p<0.05); VT ↑ (p<0.05); strength ↑ (p<0.05); functional mobility ↑ (p<0.05); passive DF-ROM ↓ (p<0.05) QOL: no differences
Hartman et al. 18	IG=20 (ALL) CG=21 (ALL) completed medical treatment	Supervised, in-hospital (every 6wks) and home- based IG: 2yr exercise program (mixed exercises) CG: standard care	Physical functioning: Motor performance \uparrow in IG; BMD _{TB:} \downarrow in IG during intervention (p=0.03) and \uparrow at follow up (p=0,004); passive DF-ROM \downarrow in IG; BMI \downarrow in IG during intervention and \uparrow at follow up; body fat \uparrow in IG during intervention and \downarrow at follow up Unsatisfactory adherence
Moyer- Mileur et al. ²¹	IG=6 (ALL) CG=7 (ALL) maintenance therapy	Home-based IG: 12mo; >3/wk; 15-20 min physical activity (mixed) and educational sessions CG: standard care	Physical functioning: PACER laps ↑↑ in IG (~80%) Activity: Pedometer steps ↑ in IG (~140%); minutes ↑ in IG (~140%)
Takken et al. 26	N=9 (ALL) survivorship	Supervised, community- based and home-based 12wk; 4/wk, 45-min, at 66- >90% of HR _{max} (mixed exercises)	Feasibility: 60% Physical functioning: no significant changes (muscle strength (-10/+10%), exercise capacity (VO _{2peak}) (+3%), functional mobility (-1/+4%), fatigue (- 11%))



San Juan et al. 23	IG=8 (leukemia) CG=8 (healthy matched controls) ~8.9 ± 4.5 mo post HSCT	Supervised, in-hospital 8wk; 3/wk, 90-120min Endurance: 10-30min at 50- 70% HR _{max} Strength: 1 set, 11 exercises, 8-15 repetitions	Adherence: 70% Physical functioning: Functional mobility \uparrow in IG (p<0.05); strength \uparrow in IG (p<0.05); endurance (VO _{2peak}) \uparrow in IG vs. CG (p<0.05) QOL: comfort and resilience \uparrow in IG vs. CG (p<0.05); satisfaction and achievement \uparrow IG vs. CG (p<0.05)
Ladha et al. ¹⁹	IG=4 (ALL) CG=6 (healthy matched controls) maintenance therapy	Acute, supervised intervention 30min, intermittent run-walk on a treadmill at 70-85% of VO _{2peak}	Immune system: no negative neutrophil response; neutrophil response is similar to that of healthy children
Marchese et al. 20	IG=13 (ALL) CG=15 (ALL) maintenance therapy	Supervised (5 sessions) and home-based IG: 4mo exercise program (physical therapy; mixed exercises) CG: no exercise recommendations	Physical functioning: active DF-ROM ↑ in IG vs. CG (p<0.01); knee extension strength ↑ in IG vs. CG (p<0.01)

Note. \uparrow : improved/ better; \downarrow : deteriorate/ worse; N: sample size; IG: intervention group; CG: control group; IG vs. CG: comparison between cohorts; ALL: acute lymphoblastic leukemia; p: level of significance; min: minute(s); d: day(s); wk: week(s); mo: month(s); yr: year(s); QOL: Quality of life; BMI: body mass index; BMD: bone mineral density; HRR: heart rate range; HRmax; maximum heart rate; DF-ROM: dorsiflexion range of motion; VT: ventilator threshold; PACER: progressive aerobic cardiovascular endurance run; HSCT: Hematopoietic stem cell transplan



Appendix 7.B

A Practical Example of a Group-Based Physical Activity Session

Characteristics of the program:

- ✓ Group-based
- ✓ Age: 4-9 years
- ✓ Diagnosis: leukemia patients during maintenance therapy

	Objective	Example		
		"Fire, Water, storm"		
Warm-Up	Prenaring for exercise	The child/children is/are moving (either walking or running) around the gym. The therapist now shouts one of several predefined warnings ("fire", "water", "storm"). The players have to react accordingly.		
	r repaining for excisible.	Fire: lay flat on the ground or a gymnastics mat		
Duration:	Increase heart rate above	Water: climb on a bench		
~10 min. Intensity:	resting (but in a comfortable	Storm: hold on to a stable surface (e.g., wall bars)		
RPE 2-4	zone) and increase the body	Then, the next round starts.		
	temperature.	Variations:		
		 Add more warnings. Have the children choose the warnings. Add several running exercises. 		
		Other examples		
		Low-intensity games (e.g., running/walking games).		
	Aerobic Training	Biathlon		
Workout	WorkoutImproving endurance.Similar to the winter-sport " cross-country skiing and rif includes "shooting" and rur			
Duration:	Increase heart rate above	course (e.g., a 20m loop), a penalty loop (e.g., a 10m loop) and a "shooting range" (e.g., a gymnastics mat		
~30 min. resting. Ensure the child is		tennis balls and a box) have to be arranged.		
Intensity: RPE 4-6	able to maintain conversation	children must run (e.g., 3 loops of the running course) and then go to their shooting range. There,		
	(able to talk) while exercising.	they have to "shoot" (e.g., get 3 tennis balls into a box). Each missed shot must be atoned for by		



		running one penalty loop.
		After shooting (and running the penalty loop(s)) children repeat the circuit.
		Variations:
		 Alternate shooting in lying and standing position. Alternate length of running course and penalty loop. Alternate way of "shooting". Relay: Play in teams.
		Other examples
		Running, jumping, catching, dribbling, kicking, or relay games.
	Resistance Training	"Jungle adventure"
	Improving muscular endurance, muscular	Arrange a number of climbing/balancing stations and connect them with gymnastic mats. Arrange one empty treasure chest (e.g., a box) at one end of the course. Arrange small items along the course (e.g., (medicine) balls, bean bags, weights etc.).
	strength and bone density.	Children must "save their treasures" and carry all items through the jungle course to their treasure chests without touching the floor.
		Variations:
		 Vary climbing/balancing stations. Vary items the children have to carry.
		Other examples
		Circuit training, climbing course, jumping, throwing and catching.
		Weather massage
Cool-Down	Proparing to cool down and	One child is lying on a gymnastics mat or sitting on a chair in a relaxed position. The therapist will massage according to the weather conditions the child is choosing.
Duration: ~10 min	return to quiet activities. Return the heart rate to	Rainy: thrum with your finger tips softly on the child´s back
Intensity: RPF 2-3		Sunny: put the palm of your hand softly on the child´s back to have him/her feel the warmth of your hands
_	baseline/resting.	Lightning: paint a lightning flash on the child's back
		Windy: stroke with your finger tips over the child's back
		Cloudy: stroke with the palm of your hand over the child's back
		Variations:



	1.	Have two children massage each other.
	2.	Have all children massage the therapist.
	3.	Vary from "weather massage" to "pizza massage" etc.
	4.	Tell a story including several weather changes.
	Other exa	mples
	Relaxatior exercises.	n games and/or stretching and or breathing

Note. min: minutes; RPE: Intensity according to the RPE Scale (Scale from 1-10). See *Appendix F* for RPE Scale



Chapter 8

Physical Activity in Children Treated with Hematopoietic

Stem Cell Transplantation

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Learning Objectives:

After completing this chapter you will know:

- ... the types and phases of hematopoietic stem cell transplant.
- ... the potential side effects of hematopoietic stem cell transplant.
- ... the benefits of physical activity for children treated with hematopoietic stem cell transplant.
- ... the precautions to take when prescribing or engaging in physical activity for this population.

Introduction

Hematopoietic stem cell transplant (HSCT), formerly referred to as a bone marrow transplant, is a unique procedure that has become standard of care for hematological malignancies, and congenital or acquired disorders of the hematopoietic system ¹. This procedure involves the infusion of **hematopoietic stem cells (HSCs)** to reconstitute bone marrow function in patients ². The use of HSCT to treat pediatric cancer has increased in the last decade and the survival is as high as 65-74% ³. However, those patients treated with HSCT are considered to be in the high-risk group to develop longterm complications ⁴. Among these side effects are muscular atrophy, fatigue, diminished cardiovascular functioning, immunosuppression, and **graft versus host disease (GVHD)** ^{3,5}.

Physical activity (PA) has recently been studied as a complementary tool to boost the recovery of children and adults with cancer undergoing HSCT ^{6,7}. Although the evidence is limited, especially in pediatric populations, the results are promising and no significant adverse events due to PA have been reported to date ⁷⁻¹¹. To successfully and safely prescribe or



engage in PA with children undergoing HSCT, it is important to understand the basics of the disease processes and the complications frequently encountered.

Common Phases and Types of Hematopoietic Stem Cell Transplantation

Phases of hematopoietic stem cell transplantation

The HSCT procedure is composed of 5 different phases (refer to *Figure 8.1*) ¹². These phases include: 1) conditioning; 2) infusion; 3) neutropenic; 4) engraftment; and 5) post-engraftment.



Figure 8.1. Phases of hematopoietic stem cell transplant

Note. Data taken from ¹³.

1) The **conditioning phase** lasts approximately one week. Chemotherapy and/or radiotherapy are administered to eliminate any existing disease, prevent graft rejection, and create space for the HSCs. In order to achieve this, the bone marrow of the patient is partially or totally destroyed. Consequently, patients may develop pancytopenia and fatigue.

2) During the **infusion phase** (also known as "Day Zero"), the new HSCs (from a donor or own patient) are infused into the patient through a central venous catheter. In order to eliminate all the cytotoxic agents from the patient's body, a day of rest is given between conditioning and infusion. Typically, stem cell infusions are rather uncomplicated ¹².

3) **Neutropenia** phase is characterized because the patients present an abnormally low count of neutrophils, a type of white blood cell that helps fight off infections. The **neutropenia phase** typically lasts 2-4 weeks and it is at this point that the patient's immune function is significantly reduced (Refer to *Chapter 5*). The threshold for defining neutropenia in children



varies with age. Severe neutropenia occurs when the **absolute neuthrophil count (ANC)** drops below 0.5×10^{9} /L. Moreover, due to the toxicity of the conditioning regimen, in the neutropenia phase the patient's normal mucosal and the skin barriers are disrupted, which allows for the invasion of endogenous bacteria. As a result, patients are at a high risk of acquiring an infection during this phase of treatment. Thus, in this phase of treatment, the patient is usually isolated in their hospital room and any health care professionals or allied health care professionals entering their rooms must follow special precautions. During this phase, medication will be given to prevent infection and GVHD. Special consideration must also be taken when exercising. See *Chapter 5* for special consideration in patients with pancytopenia.

4) Engraftment occurs after several weeks when the new blood-forming cells (i.e., HSCs) begin to grow and make sufficient number of healthy blood stem cells to normalize the patient's blood cell counts (neutrophils, platelets, and erythrocytes). This typically occurs 14-20 days post HSCs infusion. It is an important milestone in the transplant recovery and marks the end of the need for isolation. Neutrophil engraftment is defined as the first day of three consecutive days where the neutrophil count (absolute neutrophil count) is 500 cells/mm³ (0.5 x 109/L) or greater ¹³. A platelet count of 20,000 to 50,000/microliter for three days without blood transfusion is sign of platelet engraftment ¹³. At this time, the patient may begin to experience healing of the damaged mucosa, resolution of bacterial infections, and the development of acute GVHD. The lymphocyte function (e.g., T cells and B cells) remains compromised due to immunosuppressive medications and the delayed process of immune reconstitution. Thus, patients are at an increased risk for viral infections, such as cytomegalovirus, varicella zoster, and others. In addition, opportunistic protozoal and fungal infections may occur. Prophylactic strategies must be implemented to try to prevent morbidity from these infections. If no other complications are present after engraftments occur, the patient will be discharged.

5) The **post-engraftment** period is where immunological recovery and immune reconstitution tolerance will occur. As immune system reconstitution is slow, the post-engraftment phase is the longest phase and can take up to 1 to 2 years in the allogenic transplant ¹⁴. Natural killer cells are part of the innate immune system and are one of the first cells that regenerate. However, lymphocyte function (lymphocytes T and B) remains poor until 8-10 months post transplantation. This may be further delayed by the presence of chronic GVHD, in which case it may never fully reconstitute. Autologous HSCT immune reconstitution is faster than in the allogeneic HSCT reducing the incidence of infections ¹⁴.



Sources of hematopoietic stem cells

HSCs can be found in different sources such as bone marrow, peripheral blood and cord blood (3). Refer to *Table 8.1.*

HSC sources	Known as	Procedure	Observations
Cord blood	HSC transplantation	Collect HSCs from the cord blood at birth.	Cord blood has relatively low numbers of cells and is associated with delayed immune recovery and a high risk of viral infection.
Peripheral blood	Peripheral stem cell transplantation	The HSCs are obtained from the peripheral blood by leukapheresis following mobilization with granulocyte colony stimulating factors HSCs.	Most common source used to obtain HSCs. The procedure to obtain engraftment and immune reconstitution are faster with peripheral blood.
Bone marrow	Bone marrow transplantation	Bone marrow aspirated from the iliac crest has traditionally been the primary source of HSCT.	This was the first type of transplant that was performed in 1960. Sometimes this term is used interchangeably with HSCT.

Table 8.1. Sources of hematopoietic stem cells

Note. Compiled from ¹⁵⁻¹⁷. HSCT: Hematopoietic stem cell transplantation; HSCs: Hematopoietic stem cells

Types of conditioning regimens

There are two types of conditioning regimens: **Myeloablative** (classical) and **nonmyeloablative (mini or reduced intensity)** transplant ^{18,19}. In the myeloablative conditioning regimen, the goals are to ablate cancer cells, create space within the bone for new marrow



elements and to suppress the immune system of the patient to allow the donor cells to grow and avoid rejection. Bone marrow ablation promotes pancytopenia resulting in an increased risk of hemorrhage, fatigue and infection ^{18,20}. The non-myeloablative transplant aims to suppress the

patient's immune system sufficiently to allow engraftment of the donor cells. The non myeloablative conditioning regimen was created due to the understanding that there is an immunological response from the donor cells against the patient's cancer cells named **graft versus tumor effect (GvT).** Total or partial eradication of cancer

Chimerism analysis is the study of the genotype origin of post-transplant hematopoiesis. If after transplant the patients present all hematopoietic cells from the donor origin, the patient is called "complete chimera". However, if the patient has their own hematopoietic cell coexisting with their donor hematopietic cell, the patient is called "mixed chimera". The evolution of post –transplant chimerism most often is a dynamic process in which chimera can change from full to mixed and vice versa.

cells occurs due to GvT, in other words the capacity of the new HSCs (from the donor) to eradicate the cancer cells ¹. Because the recipient hematopoietic tissues are not destroyed by the non-myeloablative conditioning regimen, mixed hematopoietic chimerisms can last after transplantation ²¹. These non-myeloablative regimens are less toxic and very well-tolerated ²².

Immune Cell Alloreactivity as a Basis of Allogenic Hematopoietic Stem Cell Transplantation

Alloreactivity only occurs in the setting of allogeneic HSCT. This process is initiated

because differences in the **human leukocyte antigen (HLA)** between donor and recipient exist. The host, or patient HLAs, interact with the antibodies or T-cell receptors of the donor. The T cells only respond to foreign peptides, so differences in the HLA between donor and recipient will make T cells respond. This interaction might lead to three different results ²³:

Human leukocyte antigen (HLA): any of a complex of genetically determined antigens, occurring on the surface of almost every human cell, by which one person's cells can be distinguished from another's and histocompatibility established

- 1- GVHD: alloreactivity induces damage in recipient tissues, which is the major drawback of HSCT. See HSCT complication in this chapter for more information.
- 2- Graft rejection: the patient immune system recognizes the HSCs of the donor as foreign and destroys them. The more similar the antigens are between the donor and recipient, the less likely that the HSCs will be rejected. In myeloablative transplants, the bone marrow is destroyed; therefore patients who experience graft rejection can become quite ill and, in some instances, die of complications from the treatment.



3- Graft versus leukemia (GvL) or GvT: the donor's immune cells may recognize residual leukemia, lymphoma or cancer cells as being different and destroy them. Retrospective studies have demonstrated that patients with prior malignant disease who develop acute or chronic GVHD have lower disease recurrence rates than patients who do not ²⁴.

Hematopoietic Stem Cell Complications and Their Implication for Physical Activity

Complications after HSCT are quite common and many of them are life-threatening. We will describe those that might affect the child's participation in PA.

i) Conditioning regimen-related

Conditioning regimen, specifically myeloablative, is associated with damage of epithelial and endothelial cells that can cause symptoms such as nausea, vomiting, **mucositis, diarrhea** and pain. This can impair the ability of a child to be involved in PA. Mucositis also might impair the ability of a child to eat and therefore contribute to inadequate nutrition and low energy, further decreasing the ability of a child to do PA³. If poor nutrition is a problem, prioritize flexibility, strength training and functional mobility in order to maintain muscle mass and functional mobility. Minimize aerobic training in order to decrease energy consumption. Also, prolonged bed rest during the HSCT is a common problem. Specifically, children undergoing HSCT may be hospitalized for approximately 30 days or more spending most of the time in bed. This prolonged time of inactivity might lead to decreased muscle mass and cardiorespiratory fitness³. Pain is also common at this time. Pain should never be ignored. A pain rating scale (refer to *Appendix E*) should be used to monitor pain during PA. If pain increases during PA, immediately stop and consult with the oncologist.

ii) Alloreactivity-related

GVHD is a major complication of allo-HSCT following myeloablative and nonmyeloablative conditioning regimens. Prevalence of acute GVHD is directly related to the degree of mismatch between HLA proteins. The newly transplanted cells regard the recipient's body as foreign and attack it. GVHD is the consequence of the alloreactive response and reflect an inflammatory state.

There are two types of GVHD: acute and chronic ²⁵. In children, the incidence is lower than adults and chronic GVHD ranges between 25-50% ²⁶. Symptoms in both acute and chronic



GVHD range from mild to severe ²⁵ (refer to *Table 8.2*). Acute GVHD typically occurs within 100 days from transplant and chronic GVHD usually occurs after this time point. **Acute GVHD** has been associated with increased toxicity-related mortality and decreased disease free survival. The clinical spectrum of chronic GVHD is wider than acute GVHD and has significant impact on **quality of life (QOL)** and mortality. Strategies to decrease GVHD include pharmacological immunosuppressive drugs (cyclosporine, methotrexate, corticoids, mycophenolate mofetil), as well as ex-vivo and in-vivo T cell depletion ^{27,28}.

	Acute GVHD	Chronic GVHD
	Addie Offic	
Time	More common between 0-100 days	More common from 3 months ongoing, but could appear at any time.
Causes	Donor T cell induced	T cells chronically stimulated by the presence of minor histocompatibility antigens. B cells may be implicated.
Risk factors	HLA mismatch transplants	Acute GVHD
Symptoms	Skin (rash), gastrointestinal tract (vomiting, diarrhea) and liver (jaundice).	Lichen-type features, dryness, sclerosis of the several organs including: skin (sclerosis), mouth (xerostomia), eyes (xerophthalmia), vagina, esophagus, liver,lung (bronchiolitis obliterans), fasciitis, serositis (including pericardial or pleural effusions) and rarely kidneys (nephrotic syndrome).
Treatment	Corticosteroids. Supportive care, steroid-refractory setting: anti-thymocyte globulin (ATG), cyclosporine, ECP, daclizumab, etanercept, sirolimus, tacrolimus, mycophenolate mofetil, pentostatin, denileukin diftitox mesenchymal stem cells.	The general approach to treatment is immediate initiation of therapy, typically high dose steroids (1-2 mg/kg/day) with calcineurin inhibitor, with steady weaning of steroid until the lowest allowable. The mean duration of the therapy is three years after that around 50 % are able to stop therapy 5 years post HSCT.

Table 8.2. Acute and chronic GVHD.

Note. Compiled from ^{26,29}.

No studies have been conducted in children examining the effect of PA in patients with GVHD. However, in a recent review that examined the exercise intolerance of children undergoing HSCT, the authors postulated that children affected by GVHD have a greater loss of muscle mass and performed worse on tests of neuromuscular function, compared to children and



survivors without GVHD. Because GVHD is an inflammatory effect, children with GVHD present an increased systematic inflammation that may reduce their ability of skeletal muscle to produce energy ³. This might contribute to decreased PA and therefore contribute to a poor fitness condition.

iii) Immune recovery delayed (Infections)

Infections remain a main cause of morbidity and mortality in patients undergoing HSCT ^{30,31}. The principal risk factors for infections after HSCT are the status of the hematological disease, comorbidities, degree of neutropenia, disruption of anatomical barriers, depressed immune function and immunosuppressive therapy. Immune recovery depends on the type of transplantation, progenitor source, conditioning regimen, alloreactivity, immunosuppression and the presence of GVHD ³². From conditioning to engraftment, neutropenia and disruption of anatomical barriers are the most important risk factors ³². In autologous HSCT, the risk of infection decreases significantly after neutrophil engraftment ¹⁴. Refer to *Chapter 5* for recommendations and precautions for PA in immunocompromised patients.

iv) Cardiac and pulmonary damage

Cardiotoxicity is common side effect of the administration of anthracyclines, a common chemotherapeutic agent administer as part of the conditioning regimen that impairs the ability of the heart to pump oxygenated blood and therefore decreases the ability to do PA. Cardiotoxicity usually is a long-term effect, however sometimes might lead to early myocardial damage in children ³.

Pulmonary toxicity is common in children after HSCT and usually present as increased lung fibrosis, bronchitis and exercise-induced shortness of breath. This may decrease the ability of the lungs to sustain oxygen exchange during exercise, contributing to exercise intolerance ³. Refer to *Chapter 5* and *6* for more information.

v) Anemia

Anemia is a decrease in the red blood cells that thereby impacts the ability to transport oxygen and leads to subsequent fatigue. This is common after HSCT and must be taken into account when prescribing exercise. Refer to *Chapter 5* for more about PA prescription for patients with anemia.



Hematopoietic Stem Cell Transplantation Research Summary

Physical activity and graft versus host disease prevention and treatment: the anti-inflammatory role

In acute GVHD, exacerbated inflammation leads to lesions in the skin, lung and the gastrointestinal tract. In the chronic form, all organs are vulnerable to damage ³³. GVHD can be extremely debilitating and lead to a poor health state, impairing QOL and physical functioning ³³. It is widely accepted that regular PA at a moderate intensity may decrease systematic inflammation and improve immune function ³⁴. Although no studies to date have examined the impact of PA in humans with GVHD, preliminary data gathered from animal models appears promising. For example, an 11-week study exploring moderate aerobic training in a group of mice with chronic GVHD undergoing daily cyclosporine showed that PA increased survival rate, diminished total clinical severity scores, improved physical fitness and reduced the production of two cytokines strongly related to the severity of chronic GVHD: tumor necrosis factor alpha (TNF α) and interleukin-4 (IL-4) ³³. TNF α inhibition has been used as a therapeutic strategy in experimental therapies against GVHD. IL-4 was also linked to the severity of the chronic GVHD. These results must be carefully interpreted, as it was performed in a mice model and there was a small sample by the end of the study. However, this data suggests that PA may be an important non-pharmacological adjuvant therapy to improve the disease course and QOL in these patients without altering an already depressed immune system ³³.

Physical activity and infections: the antiviral effect and safety of physical activity interventions

The recovery of the immune system plays a key role in the risk of infection after HSCT. Moderate PA improves antigen-specific T-cell function, cytokine production and innate immune response, which may translate into better protection from infectious agents ³⁵. An adequate immune response plays a critical role in the clearance of viral infections in the post-transplant period. Therefore, it is likely that PA would be beneficial in this population. Until recently, PA was not recommended in the neutropenic phase of treatment due to concerns about the possible detrimental impact on the immune system. However, PA is recognized as being beneficial during treatment as it has been well-established that prolonged bed rest leads to



muscle atrophy and aggravates the already low functional capacity induced by the immunosuppressive therapy given to children receiving HSCT ³⁶.

Performing mild to moderate PA from the conditioning to engraftment phase has been hypothesized to be beneficial. For example, Chamorro et al. performed a study during the conditioning and neutropenic phase of HSCT in children ⁸. This study showed that a moderate and individualized PA program was feasible, safe and did not alter immunological recovery. The authors also found that the intervention group was able to increase the time spent in aerobic training and increase the amount of resistance training by the end of the 10-week intervention. Rosenhagen et al. conducted a similar study and corroborated this finding ¹⁰. Refer to *Table 8.2* for a summary of the interventions. Therefore, there is a hypothesis that PA-mediated changes in immunity may contribute to improved immune recovery and function after HSCT ^{37,38}.

Also, some studies performed in adult populations show an increase in NK cell function after a moderate PA intervention ^{37,39}. NK cells are very important in the control of tumor growth and also are the first line of cells that regenerate after HSCT ⁴⁰. Following exercise, increases were seen also in lymphocyte proliferation and the number of granulocytes. However, the research in this are is scarce and more research is needed to understand why these changes occur and the link between clinical outcomes and changes in the immune system due to PA ⁴¹.

Physical activity improves fitness, fatigue and quality of life

To our knowledge, only three PA interventions have been performed in pediatric patients undergoing HSCT. Two were performed in the neutropenic phase ^{8,10} and one was performed in the post-engraftment phase ⁹. Taken together, the three interventions show promising results reporting increased aerobic capacity and increased or maintained strength. In addition, San Juan et al., ⁹ and Rosenhagen et al.,¹⁰ have both shown increased QOL in the patients after the PA intervention. Chamorro et al. has also shown that the training induced gains in body mass and **body mass index (BMI)** over the hospitalization period. During the neutropenic phase, a decrease in BMI is a common side effect and is associated with a negative HSCT outcome ⁴². Maintenance of skeletal muscle proteins is crucial in immunocompromised children ⁴³. Avoiding decreases in body mass during pediatric HSCT is important, as children undergoing this treatment are at a risk of malnutrition ⁴⁴. This evidence, with the extrapolated results from the adult population studies, suggest that recipients of HSCT may benefit from PA ¹¹. No harmful effects were reported from the PA interventions ^{6,11,45,46}. However, far more research is needed to generalize the benefits of PA in pediatric HSCT patients.

Author/Stu dv Design	Population	Intervention	Result
San Juan et al. 2008	HSCT post- transplant	 - Duration: 8 wk. Supervised in-hospital intervention - Frequency: 90 min/ 3/wk - BDT: 1 set of 8.15 repotitions of 11 types of evercise encoding the major muscle 	- Aerobic capacity was lower in - HSCT patients than in CG.
Quasi-	treatment	groups (bench press, shoulder press, leg extension, leg press, leg curl, abdominal	totation the strength (p<0.05).
experimen	(IG:8±4 yr,	črunch, low back extension, arm curl, arm extension, seated row and lateral pull down).	;
tal	CG: 7±3 yr)	1-2 minute rest period between exercises with stretching of the muscles involved in the	
	N= 15 IG= 8 HSCT	last exercise. - Aerobic training: the intensity and duration gradually increase during the program	
	CG= 7	from 10 min at 50% of age predicted maximal heart rate (HRmax) to 30 min at 270 %	
	healthy	HRmax.	
	children		
Chamorro-	HSCT in	- Duration: from the beginning of conditioning regimen until neutrophil engraftment (~30	- IG: ↑ BMI and weight
Viña et al.	neutropenic	days). Supervised in-hospital intervention	(p<0.001).
2010	phase (4-16	- Frequency: 50 min 5/wk (5/wk aerobic training + 2/wk strength training)	-↑ Aerobic fitness and strength.
	yr)	- PRT:1 set of 8-15 repetitions of 6-10 types of exercise engaging the major muscle	 CG: ↔ BMI, body fat and
Quasi-	N= 20	groups (bench press, shoulder press, leg extension, leg press, leg curl, abdominal	weight with a trend to decrease.
experimen	IG= 7	crunch, low back extension, arm curl, arm extension, seated row and lateral pull down).	
tal	CG= 13	1-2 min rest period between exercises with stretching of the muscles involved in the last	
(historical		exercise.	
controls)		- Aerobic training: range from 10 to 40 min depends of child status. Intensity controlled	
		by heart rate monitor between 50%- 70% of age predicted HRmax.	
Rosenhag	HSCT in	- Duration: approximately 34 days supervised intervention during the isolation phase of	I.G. 10 % ↑in the time spent on
en et al.	neutropenic	HSCT. In -hospital intervention.	the bicycle ergometer.
2011	phase of	- Frequency: approximately 50 min 3/wk.	- ↔ Strength assessed by hand
	treatment	- PRT/coordination training: This was individualized for each participant and included	held dynamometer.
Quasi-	(15.3 ± 3.7	working the main muscles groups. Barbells, balls, bar and body weight was used to	- CG: non reported
experimen	yr)	prescribe exercises.	- Regular PA during isolation
tal		- Aerobic training: Stationary bicycle ergometer with a minimal resistance of 6 watt for a	phase of HSCT is feasible, safe
	N=23	minimum of 10 min. The resistance of the bicycle was increased in the next class only if	and counteracts the side effect
	IG: 13	participant reach 10 min. Intensity of training: Heart rate should not exceed [180- patient	of immobilization like muscular
		age] and breathing frequency has to be below 35 per minute. Participant train for a	atrophy.
		median of 18 minutes	
Note. PRT: Pi	rogressive resis	tance training; N: number of participant; IG: intervention group; CG: control group;BMI: body	mass index; HSCT:
hematopoietic	c stem cell trans	plantation; yr: year(s); wk: week(s); min: minute(s); ↔: maintain/ no change; ↓ : decrease; 1	: increase/improve

Table 8.2. Physical activity interventions performed in children undergoing hematopoietic stem cell transplantation



Physical Activity Recommendations

To date, three interventions have been performed.

Table 8.2 summarizes the interventions performed in pediatric HSCT. All three included aerobic, strength and flexibility exercises. The three authors highlight the importance of tailoring



PEER program/balance training

the intervention to each participant's need due to a myriad of complicated side effects. In general, mild to moderate aerobic training is recommended in order to avoid an increased risk of infection and to avoid extreme fatigue ²⁰. Wearing a heart rate (HR) monitor or using rating perceived exertion scale (RPE) scales (refer to Appendix F) may help allied health care professionals control the intensity of aerobic training better. Avoiding contact sports and mitigating the risk of falling is highly recommended, due to thrombocytopenia and osteoporosis risk in order to avoid hemorrhage and fractures respectively ²⁰. *Table 8.3* shows PA recommendations for children undergoing HSCT based on the three interventions performed ⁸⁻¹⁰ and the authors' own experience.



Table 8.3. Physical activity recommendation for children undergoing HSCT

	Recommendations
Objectives of PA	Conditioning, neutropenic or early post-transplant phase : maintain the patient's capacity to perform ADLs. Later post-transplant phase: enhance the patient's health-related fitness capabling bim/bor to angege in DA with big/bor bootthy page without undue
	fatigue.
Aerobic capacity	 Frequency: at least 3 days/wk. Preferably most days of the wk. Intensity: ✓ Conditioning and neutropenic phase: Low to moderate in order to avoid fatigue and not compromise the immune system. If using HR to control intensity, be between 50-70% of age predicted HR max. RPE scales between 1-4. ✓ Post-transplant phase: start with low to moderate intensity. If patient is not immunocompromised, he/she can slowly progress to vigorous intensity. Time: 10-40 min as tolerable without fatigue Type: any activity that the child enjoys (e.g., dancing, riding a bike, playing sports, playing active video games etc.) If a child is immunocompromised, some activities might be discouraged by a physician, such as swimming or sports in groups. However this is variable and consultation with the physician at your centre should occur. Precautions should be taken if the child has other comorbid conditions, such as GVHD, anemia, thrombocytopenia, osteoporosis or at risk of cardiotoxicity (refer to <i>Chapter 5</i>).
PRT	 Frequency: at least 2 days a week Intensity: 1-2 sets of 8-15 repetitions. In conditioning and neutropenic phase, 1 set is enough. 1-2 min rest between exercises while stretching the muscles worked. Type: performe 6-10 exercises engaging the major muscle groups. Alternate upper body muscles groups with core and lower body muscle mass. Do it as tolerable. In conditioning and neutropenic phase, weight-bearing exercises, or just the exercise without or at very low loads, might be enough to challenge a patient (i.e., bed strength exercise such as bridges and knee extensions).
Fundamental skills	Is important to work fundamental skills (e.g, running, jumping, balance, and coordination) in the pediatric cancer population. Improvements in these fundamental skills will allow them to improve their self-confidence and facilitate the reinsertion of these children in PA with their healthy peers.
Consideration	 Due to the large variability of comorbid conditions associated with HSCT, PA has to be individualized for each child. A PA plan for children undergoing HSCT should consider i) phase of treatment, ii) treatment and side effects, iii) comorbid conditions, iv) fatigue levels, v) immune system status, and vi) child preferences.



 Physician clearance is always needed.
 If you are working with a child during conditioning regimen, infusion
or neutropenic phase, check on the child's status from their
physician or primary nurse before engaging them in exercise.
These phases of treatment are very challenging and the health
status of the child may quickly change
\checkmark A supervised PA program is preferable at the initiation of exercise.
\checkmark If the child is in the conditioning regimen or in the isolation phase
they may be tired, have nausea, nain or/and diarrhea. Adjust the PA
to the child's specific needs and symptoms. Some days they may
able to only do a few passive flexibility exercises in bed. Something
is better than nothing
$\sqrt{-}$ During the conditioning infusion, neutropenic and early post
transplant stages, the shildren undergoing HSCT will have a control
line in their chest. Do sure that the control line is high and protected
hate in their criest. Be sure that the central line is high and protected
before the exercise session. Avoid heat and pressure on the central
ine. Avoid a exercises in which resistance is put in the chest, such
as those in which the child lies on his/her tummy.
 Know the child's preferences to create and tailor their PA.
✓ FUN is a key factor!
✓ Corticosteroids are widely used to treat and prevent GVHD.
Complications might after the child's ability to engage in PA,
atrophy Also mood changes may occur therefore be prepared to
be patient

Note. PRT: Progressive resistance training; PA: Physical activity; ADLs: Activities of daily living; min: minutes; wk: week/s. Compiled from ⁴⁶⁻⁵⁰.

In summary although research in this field is scarce, it has been demonstrated that PA is both safe and feasible in immunocompromised patients. Due to the uniqueness of this population, PA interventions have to be tailored and heath care professionals and allied health care professionals should be aware of the risks and precautions in this population. All patients should receive physician permission and clearance prior to participation.

Future Research

Due to the rarity of this procedure in pediatric populations, multisite interventions to recruit a large number of participants are highly needed. Studying the role of PA in the recovery of the immune system and the effect on the GVHD are encouraged.



Take Home Message

Research studying the effect of physical activity in children undergoing hematopoietic stem cell transplantation is scarce, however preliminary results indicate it is feasible and safe. Improvements in aerobic capacity, strength and quality of life have been reported. Physical activity in this special population must be adapted to each participant's condition, phase of treatment and co-morbidities. It is necessary to maintain open communication with the transplant physician.



7 years old cancer survivors working coordination and balance

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Chapter 9

Physical Activity and Solid Tumors

Corinna C. Winter, PhD

Learning Objectives:

After completing this chapter you will know:

- ...common types and treatment of solid tumors in children.
- ...potential side effects of cancer and its treatment and implications for physical activity.
- ...that physical activity is almost always possible; however modifications and creativity are necessary.

Introduction

Solid tumors are compact, beginning as localized tumors that derive from different cellular origins, and are classified into benign and malignant tumors. Among the malignant tumors, those of the **central nervous system (CNS)** are most common and account for 23% of malignant pediatric tumors in children up to the age of 15. Neuroblastomas follow with 7%, then nephroblastomas with 6%, soft tissue sarcomas with 6% and bone tumors with 5% ¹. *Table 9.1* lists the major characteristics of the diseases ¹.

Central nervous system tumor

Also referred to as brain tumors. See *Chapter 10* for more information.

Neuroblastoma

Neuroblastomas derive from immature cells of the sympathetic nervous tissue and are mainly located in the abdomen, the adrenal medulla or the sympathetic ganglia ².



Nephroblastoma

Nephroblastomas are also called Wilms tumor and are located in the kidneys. They originate from embryonic primitive tissue ³.

Table 9.1. Disease characteristics.

Tumor Entity	Symptoms	Median Age at Diagnosis	5-year Survival	Sex Ratio (Male:Female)
Neuroblastoma	Non-specific, weight loss, fever, abdominal disturbances	1yr 3m	59-66%	1:2
Nephroblastoma	Palpable abdominal mass Fever, vomiting, hematuria	3yr 2m	84-90%	0:9
Soft Tissue Sarcoma	Vary according to tumor site	6yr 5m	65-73%	1:2
Bone Sarcomas	Swelling and pain in the tumor region Loss of function Pathologic fractures can occur	11yr 6m	61-66%	1:1
Osteosarcoma	Major location lower extremity (knee region)	12yr 0m		1:0
Ewings Sarcoma	Typical tumor sites: Lower extremity and pelvis	10yr 10m		1:3

Note. yr: years; m: months. Compiled from ¹⁻⁶.

Soft tissue sarcoma

Soft tissue sarcomas are a heterogeneous group of malignant tumors stemming from muscles, vessels and nerves. For example, rhabdomyosarcoma arises from striated muscle and is the most common soft tissue sarcoma in childhood ⁵.



Malignant bone tumors

Osteosarcoma and Ewing's sarcoma are the 2 main types of bone cancers in the pediatric population.

Osteosarcoma

Osteosarcomas are the most common malignant bone tumors and derive directly from the bone-tissue. Osteosarcomas can originate in any bone, however they mainly occur in regions with great growth rates (such as the methaphysis of the distal femur and the proximal tibia). Therefore, approximately 50% are located around the knee. The upper limb is affected in approximately 10% and the pelvis in 5-10% 4,6 .

Ewings sarcoma

Ewing's sarcomas: originate from mesenchymal stem cells. They very often affect bones; 22% of tumors are located in the long bones of the lower extremity, 28% in the pelvis, 26% around the spine and the trunk and 11% at the upper extremity ^{6,7}.

Common Treatments

Most pediatric cancer survivors are treated according to international treatment protocols, which place survivors in specific treatment groups. Three primary treatment options exist for children with cancer, including solid tumors (chemotherapy, surgery, and radiation). Often these options are combined to ensure the best possible response to treatment ^{4,6,7}.

Following the diagnosis of a malignant bone or soft tissue tumor, which includes a minor surgery to take a **biopsy** to confirm the diagnosis, treatment begins with 3 months of **neo-adjuvant chemotherapy**. This is followed by major surgery for tumor removal. Depending on the tumor site and size, several surgical options exist and are individually tailored to the patient. The goal of all surgeries is to completely remove the tumor while preserving the best function possible. For tumors located in the lower limb, the affected bone is removed and replaced by an **endoprosthesis** in 85% of cases ⁸. In some cases, **amputation** is necessary and a **rotationplasty** can be performed. For tumors located in the pelvis, hip transposition is most frequently performed. In the upper limb, **biological reconstructions** and endoprosthetic replacements are most common ^{8,9}. Surgery is followed by another 6 months of chemotherapy and where indicated (e.g., Ewing's sarcoma), additional radiation is often given ⁷.



Potential Treatment Side Effects and Implications for Physical Activity

Apart from side effects resulting from chemotherapy and irradiation, late effects of surgeries have to be considered in survivors with a solid tumor. Compared to other cancer entities such as leukemia or lymphomas, surgical intervention is an additional factor that may further influence **physical activity (PA)** performance and functional mobility. Specifically, those survivors with a malignant bone tumor have demonstrated significant restrictions with respect to



Cruz, 5 years old. Cancer patient's sibling

being physically active and may struggle to reach highly intense activity levels ¹⁰. This is likely due to substantial surgical intervention, off-loading instructions and long periods needed for recovery. Improvements in both the amount and the intensity of PA could still be observed 18 months post-surgery, indicating that it takes long periods of time to recover from treatment ¹¹.

Survivors after surgery for a

malignant bone or soft tissue tumor have to be looked after with special attention and patience. In most cases, muscle tissue has to be resected and in some cases, nerves may be disturbed or removed. These side effects of treatment result in several limitations including loss of muscle strength, impaired range of motion, lack in coordination, and gait asymmetries ¹²⁻¹⁵. Most PA will be more exhausting for survivors than for a normal population. For example, walking with a prosthesis requires greater exertion ¹⁶. Immediately after surgery, survivors might have **non-weight bearing** instructions and will likely need to use aids like crutches or a wheelchair for several weeks. This obviously limits the options they have to participate in PA, and adaption of equipment might be necessary. In general, additional creativity is needed to involve survivors in PA and being familiar with the surgical treatment of the individual patient can help the professional tailor the intervention to the patients' needs. Moreover, given the risk of injury, the risk of falls should be reduced as much as possible. Finally, in some cases, biomechanical investigations might add valuable information about joint forces and gait patterns that would help to develop a suitable intervention program ¹².



Physical Activity and Bone Tumor Research Summary

Survivors with a solid tumor have been subject to some interventional studies, however studies investigating mixed tumor entities were primarily identified ¹⁷⁻¹⁹. In all the studies, interventions were feasible ^{20,21}. Different interventional approaches were performed including supervised PA programs as well as home-based and educational programs ²⁰. While supervised interventions appeared to have more effect than non-supervised programs ²⁰, benefits have been observed for both ¹⁷.

Overall, positive effects have been observed for the outcomes of sleep efficiency, upper body muscle strength and flexibility ¹⁸⁻²². Moreover, preliminary results have been found suggesting the benefits of PA on the cardiovascular system, physical functioning, **quality of life (QOL)**, and fatigue reduction ^{17,19,22,23}.

To date, one study has been identified that investigated only malignant bone tumor survivors ²⁴. This study examined survivors that participated in a supervised training program during hospital stays of acute treatment in comparison to a group without the intervention. Patients' PA was improved by the intervention at several time points during therapy as compared to the control group. However, differences were not significant and decreased with time from the end of intervention.

Physical Activity Recommendations

In general, PA is possible for every survivor with a solid tumor during almost every stage of treatment. The **Center of Disease Control (CDC)** recommends 60 minutes or more of PA every day, including aerobics as a major part but also muscle and bone-strengthening (CDC recommendations: http://www.cdc.gov/HealthyYouth/physicalactivity/guidelines.htm)²⁵.

Interventions should be individually tailored to the survivor's recent well-being and possible restrictions including those imposed by surgery. Therefore, especially in the initial phase, personalized training sessions supervised by an exercise or rehabilitation specialist may be the best option. Later on, parental supervision or a supervised group-based community PA program are additional options. Checking in with the medical team, physiotherapist, exercise or rehabilitation specialist (in person, over the phone or online) to ensure the program is safe and beneficial for the participant is very important to consider for home-based options. See *Appendix 9.A* for an example of an exercise plan.



Warm-up

Every PA session should start with 10-15 minutes of warm up. Walking or using a crosstrainer is possible for most survivors. Cycling might be restricted due to little range of motion in the knee joint (for patients and survivors with lower-extremity osteosarcoma). A shorter crank could potentially help. If no force can be put on the lower extremity, hand-crank ergometers can be used. Rowing is limited for most patients as they are either restricted in moving their arm/shoulder in the position needed or cannot bend their knee far enough.

Aerobic training

Depending on what worked best during warm-up; the same mode of exercise can be



Progressive resistance training at the PEER program

also used for the aerobic training. Starting with 10 to 15 minutes of aerobic training at the beginning, a constant increase should be achieved to reach the ultimate training goal. As patients transition to survivors, it may not be possible to make extra appointments and come to the hospital or gym to gain the recommended daily amount of PA. Here flexible home-based exercises like walking or cycling can be used to achieve PA goals and might even be included into everyday routines.

For survivors with a bone tumor water activities are a good option as the body weight is reduced and limbs can be moved more easily. However, appropriate precautions such as infection risk (e.g., immune status and wound integrity) should be acknowledged.

Progressive resistance training

Building up muscle strength is of major importance, especially in survivors with a bone tumor in the rehabilitation process, as it assists the survivor in regaining muscle size, strength, function, joint range of motion, as well as bone mass ^{26,27}. Sufficient gains in strength can further improve gait, physiological joint loading including the spine and help with reducing the risk and consequences of falls. Independent of tumor site, a whole body program including 8 to 10



different exercises should be performed regularly, at least twice a weak. Generally, intensities should be adapted to the individual capabilities and be chosen according to the survivor's needs and aims. If maximum muscle strength is of major interest, intensities should be rather high at a smaller number of 5-8 repetitions ^{26,27}. However, precaution should be taken with any maximal intensity activities, such as performing them under the supervision of an exercise or rehab specialist. Muscular endurance training is ideal to promote capillarisation and improve range of motion. For muscular endurance training, less intensity (e.g., light loads) and more repetitions (e.g., 15 -30 repetitions) is suitable ²⁸.

After hip-transposition, leg length discrepancies can be found in most survivors ²⁹. This can lead to the development of a scoliosis of the spine. Special attention should thus be drawn to exercising the back muscles as well as the abdominals. In survivors affected in the upper limb, a reduced range of motion can be improved by suitable resistance PA such as rowing exercises, shoulder rotation exercises, and latisimmus dorsi training. PA can either be performed on resistance machines or with dumbbells, elastic bands or the body weight itself, depending on what is available and feasible for the survivor.

Coordination training

Coordination is a skill that is related to the ability to use the senses (such as sight and hearing) together with muscles and joints to perform motor tasks smoothly and accurately. Therefore, coordination exercises should be an inherent part of any training program ³⁰. Survivors have to gain trust in their limbs again which might feel completely different from before surgery and treatment. Besides equipment like wobble boards, active computer games including balance activities are of good use, as from our experience, survivors are distracted from the feeling of putting too much load on the limb.

Flexibility training and cool down

Each training session should end with some stretches and relaxation. Some joints, such as the ankle joint, might be restricted in motion due to the therapy or offloading periods ³¹. These restrictions should be identified and addressed. An individually adapted active dynamic or passive way of stretching may help to reduce these limitations ³². For some patients **Proprioceptive Neuromuscular Facilitation (PNF)** can be helpful, as this method is highly functional and mobilizes patients' untapped potential ³³. Stretching in PNF is used as a stimulus in order to facilitate muscle activity, and must be taught by an experience therapist ³⁴. For cool



down, different options can and should be explored so that survivors can discover what works best for them. Some children like to play a game (e.g., table soccer or seated badminton). Others prefer rather quiet options like progressive muscle relaxation or being read a story.

Future Research

In patients with solid tumors, very little research has been conducted within the field of PA interventions. The recommendations so far rely on some smaller studies, general recommendations and expert opinion. Future research should investigate dose-response relationships, underlying mechanisms and effects on different organ systems as well as mental health. The influence of tumor site and surgical procedures should be investigated in more detail as they play an important role in planning and conducting PA interventions. Much is left to be understood about what works best for which patient group and what works best at which stage of recovery.

Take Home Message

Patients and survivors with malignant solid tumors are a population with unique needs. They have to be looked after with special attention and patience. However, some form of physical activity will almost always be possible in this group. The greatest limitations result from the effects of surgery. We would encourage anyone working with these patients/survivors to speak to the surgeons and physiotherapist who care for the patient/survivor and adapt physical activity interventions accordingly. Improvements might appear small in the beginning, but it is worth the effort as patients' report improving many months after surgery.



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Appendix 9.A

A Practical Example: Case Report

Characteristics of the Patient:

- ✓ Age/Sex: 13 year old female
- ✓ Diagnosis: Osteosarcoma of the left distal femur
- ✓ Stage of treatment: Adjuvant chemotherapy, 4 weeks post surgery
- ✓ Anthropometrics:
 - ✓ Endoprosthetic replacement of the knee joint
 - ✓ Knee flexion: 65°
 - ✓ Partial off-loading instruction

Characteristics of the Program:

- ✓ Individualized program
- ✓ Performed daily during in-patient stays

	Objective	Example
Warm-Up		Cycling with a shortened crank (as the patient had limited knee flexion) or hand
Duration: ~10 min		crank ergometer.
Intensity: RPE 3-4		
Resistance Training	Improving strength and bone density.	Crunches 2-3 sets of 10 Back Extensions
		2-3 sets of 10 Variations: Standing position, bent forward
Duration: ~ 25 min		2-3 sets of 10 Bicep curls
Intensity: RPE 6-7		2-3 sets of 10 Triceps extensions
		2-3 sets of 10 Leg press
		2-3 sets of 5-8
		Affected limb: unloaded knee-bents



		Hip Adduction 2-3 sets of 5-8 Variations: cushions proximal to the prosthesis
Aerobic Training Duration: ~15-30 min	Improving endurance. Increase heart rate above resting. Ensure the child is able to maintain conversation (able to talk) while exercising.	Hand-crank ergometer.
Intensity: RPE 5		
Flexibility Training	Improving range of motion	Unloaded and assisted knee bends, Ankle dorsiflexion stretches, Sit and reach.
Duration: ~5 min		
Intensity: RPE 2		
Cool down	Preparing to cool-down and return to quiet activities.	Table Football or seated table tennis/badminton.
Duration: ~5 min	Return the heart rate to baseline/resting.	
Intensity: RPE 1		

Note. min: minutes; RPE: Rating Perceived Exertion Scale, Intensity according to the RPE Scale (Scale from 1-10). See *Appendix F* for RPE Scale.



Chapter 10

Physical Activity and Late Effects of Treatment for Childhood

Brain Tumors

Iman Sahnoune, BSc & J. Leigh Leasure, PhD

Learning Objectives:

After completing this chapter you will know:

- ...the current literature in pediatric brain tumors and the long-term, detrimental effects of common treatments.
- ...neurocognitive and quality of life outcomes in the pediatric brain tumor survivor population.

• ...physical activity may be a potential treatment as it relates to brain health after a malignancy.

Introduction

Cancers of the brain and spinal cord are the most common solid tumors in children, accounting for almost 30% of all childhood cancers ^{1, 2}. In recent years, the proportion of cancer deaths due to brain and other **central nervous system (CNS) tumors** has increased from approximately 18% to 26% from 1975 to 2006 ³. Fortunately, with the advent of novel

Brain Tumor

A brain tumor begins when normal cells in the brain change and grow uncontrollably, forming a mass. A brain tumor can be low grade (generally not cancerous and slower growing) or high grade (more likely to grow and spread quickly). The level of impact of a tumor is commonly evaluated through its type, location in the brain, size, and stage of development. In general, primary brain tumors, meaning those that start in the brain, do not spread outside of the CNS. technologies and treatment methods, survival rates exceed 70% across children and young adult age groups ^{1, 4}.

Although survival rates are increasing, **quality of life** (QOL) in survivors is not. An estimated 40-100% of pediatric



brain tumor survivors experience deficits in **cognitive function**¹. Frequently, these cognitive late effects emerge months or years after treatment, and lead to profound cognitive, social and physical impairments ^{1, 5}.

Many factors influence neurocognitive functioning in children with brain tumors. Because of the vulnerability of the developing brain, age of diagnosis and treatment heavily influences the severity of future neurocognitive dysfunction - the younger the child, the greater the dysfunction ^{1, 5, 6}. Gender is also an important determinant of future neurocognitive impairment, with girls being more affected than boys ^{7, 8}. Tumor size and location are major factors in neurocognitive outcome. **Cortical tumors** tend to result in more cognitive late-effects

than, for example, 3rd or 4th ventricle tumors, ² while left hemisphere malignancies have the largest prevalence of cognitive impairment due to the relationship to language and

Central Nervous System Tumor

A **CNS** tumor begins when normal cells in the brain or the spinal cord change and grow uncontrollably, forming a mass. A tumor can be benign (noncancerous) or malignant (cancerous, meaning it can spread to other parts of the body).

complex processing ⁹. Finally, the size of the area of affected tissue and dose of radiation also play integral roles in cognitive outcome (refer to *Figure 10.1* for a visual representation of the lobes of the brain) ⁵.

Figure 10.1. Lobes of the human brain and their functions.





Effects of Common Treatments

The most common treatments for brain tumors are surgery, **cranial radiotherapy** (**CRT**), chemotherapy, and combination therapy. Because of its devastating long-term consequences, CRT is used for tumors that are not surgically accessible or which constitute too great a surgical risk. CRT works by killing dividing cells, which effectively eradicates tumors. **Neurons** do not divide, and so are not directly impacted by CRT. However, CRT does destroy the brain's actively dividing stem cells. Since these stem cells ultimately become glia and blood vessels ¹⁰, which collectively form a network that supports neuronal health and function ^{11, 12}, CRT indirectly impacts established neurons. Moreover, in the hippocampus (a brain region important for learning and memory) neural stem cells are able to develop into neurons ¹⁰, a process called hippocampal neurogenesis. Analysis of post-mortem tissue following cancer treatment shows almost complete ablation of hippocampal neurogenesis ¹³, which likely contributes to the cognitive impairments observed in survivors ¹⁴. Refer to *Figure 10.2*.

Figure 10.2. Brain irradiation in rats leads to nearly complete ablation of cell proliferation.



Note. Panel A shows a brain section from a normal rat hippocampus. The small black cells are positive for Ki67, a protein expressed during cell division.

Note. Panel B is a section of hippocampus from a rat treated with 20 Gy of radiation. There is no evidence of cell proliferation.

A wide range of cognitive functions are impacted by brain tumors and treatment, including **executive function**, **working memory**, **visuo-spatial abilities**, **processing speed**, language, and **attention**^{9, 10}, all of which may contribute to the well-established finding of reduced **intellectual quotient** (**IQ**) score ¹¹⁻¹⁵. For example, survivors treated with either a combination of radiation therapy and surgery, or the same plus chemotherapy, were found to have deficits in visuo-spatial capabilities, processing speed, and attention and most of these



effects did not manifest until 3-5 years after treatment ⁶. The significant decline in attention renders pediatric brain tumor survivors less able to make age appropriate developmental gains ⁶. It is important to note that cognitive decline in children recovering from brain tumors is not necessarily due to a loss of knowledge, but rather to a decreased rate of learning ⁸. This distinguishes the cognitive late effects of pediatric radiotherapy from conditions such as dementia, in which there is diminished function. This decreased rate of learning suggests that more time may be required for children recovering from brain tumors to catch up to their peers ¹⁰.

In addition to these cognitive effects, survivors of pediatric brain tumors often suffer personal outcomes that can further lower QOL. One study reported that only 30% of 10-year survivors of medulloblastoma were able to drive, live independently, or find employment ¹⁶, while another found that 78% of brain tumor survivors had never married, with women at a particular risk for lower rates of marriage than men ¹⁷. These after-effects of pediatric brain tumors are long lasting and can severely impact the QOL of survivors years to decades after diagnosis. This necessitates an intervention that can combat these detrimental neurocognitive deficits and enhance outcomes in all domains over time.

To summarize, although pediatric brain tumor survival rates are increasing due to efficacy of treatments, it is important to remember that these treatments are not without their drawbacks. Whether it is cranial radiation therapy, chemotherapy, or a combination, there are always a number of variables at play, and no two survivors will have the same outcome. This makes finding an effective intervention absolutely essential. We focus on the potential of **physical activity** (**PA**) as a strategy to combat the cognitive late effects of pediatric brain cancer treatment.

Treatment effects and their implications for physical activity

PA has arisen in recent times as a potential therapy to mitigate the deleterious effects of brain tumors in pediatric populations. Survivors of pediatric cancer have been found to be at a higher risk of developing sedentary lifestyles, due to treatment-induced fatigue, cardiorespiratory problems and muscular deconditioning, and inactive children are likely to become inactive adults ¹⁸⁻²⁰. Through its effects on neurogenesis and **cognition**, there is evidence for the use of PA to remediate and possibly reverse deficits sustained from pediatric brain cancer treatment.



PA increases proliferation of neural stem cells, an effect that would directly counteract the suppressive effect of cancer treatment. In a number of studies, it has been evidenced that PA increases hippocampal neurogenesis and enhances the microvascular environment ²¹⁻²⁵. Additionally, it has been found that PA up-regulates brain processes associated with neuroplasticity, promotes synaptic plasticity, and increases gray matter in frontal regions and the **hippocampus** ^{26, 27}.

PA has been shown to enhance a variety of cognitive functions, including those most impacted by cancer treatment, such as executive function ^{28, 29}. This is important to pediatric brain tumor populations, since attention is one of the most common neurocognitive deficits that occurs after treatment, with the potential to detrimentally affect academic achievement ¹. Meta-analytic evidence indicates that PA in children yields a significantly positive impact on academic achievement and cognitive outcomes, and that aerobic activities provide the largest impact ³⁰. Importantly, it was found that elementary-age children were found to have the largest cognitive benefit from PA, with the effect decreasing as the age group advanced. This is a relevant finding, as PA can potentially be introduced to school-age children diagnosed with brain tumors as a therapy, and the regimen modulated as age increases for enhanced benefit. Another finding in the meta-analysis supports that children who were cognitively impaired or physically disabled profited more from PA than children without impairments. This coincides with findings that suggest that young adults lowest in working memory may have the most to gain via PA manipulations and that PA may be most beneficial for healthy adults in whom cognitive performance is lowest ³¹.

In addition to providing neural benefits, PA could counteract chronic conditions that arise from cancer treatment, such as impaired pulmonary and cardiac function ³² (refer to *Chapter 5 and 6*). PA may also ameliorate depression, anxiety and other emotional sequelae. Unfortunately, treatment-induced fatigue, cardiorespiratory problems and muscular deconditioning tend to promote sedentary habits during treatment that linger into adulthood, with the result that childhood cancer survivors are much less physically active than their healthy peers ^{20, 33, 34}. Recent studies suggest that physical fitness is an achievable goal for childhood cancer survivors ^{32, 35}, and adds to the wealth of evidence substantiating the potential of PA to greatly benefit them.



Physical Activity Research

Animal-model research: Key points

- ✓ Animal models provide a useful means by which to assess the efficacy of intervention therapies on the cognitive effects of cancer treatment (see ³⁶ for review).
- ✓ In human populations, deficits in executive functioning and attention are commonly reported in survivors of pediatric brain cancer.

Thus, our group has been focusing on a rodent model of attention deficits following cranial radiation ^{36, 37}. The 5-choice serial reaction time task assesses visual attention and other frontal lobe-mediated processes in the rodent, including processing speed and impulsivity ³⁸. Refer to *Figure 10.3*.

We have found that young animals that underwent cranial radiation (a fractionated dose of 20 Gy) require significantly more trials to reach criterion in more difficult stages of training, compared to non-irradiated controls. This acquisition deficit is seen 3 months post-radiation (comparable to several years for a human), and thus mimics late-appearing cognitive effect seen in children treated for pediatric brain cancer ³⁶. Refer to *Figure 10.4*.

Figure 10.3. Diagram of the testing chamber and measures obtained for the 5 Choice Serial Reaction Time Task.



Note. The animal must monitor the 5 apertures for the presentation of a light stimulus and then nose-poke into the hole in which the stimulus was presented. Correct responses are rewarded by a food pellet dispensed into the magazine at the rear of the chamber.



Figure 10.4. 5 Choice Serial Reaction Time Task training phase: trials per stage.



Note. Radiated animals take longer to learn the 5 Choice Serial Reaction Time task (N=21, RT=10, SHAM=11). In later (more difficult) stages of training, radiated animals require significantly more trials per stage, compared to controls.

Future Directions

The next step is to determine whether PA can ameliorate the impairments observed in frontal lobe functions. As PA has been shown to enhance plasticity in the frontal lobes ^{28, 39}, we anticipate that the executive function impairments we have observed in the 5 Choice Serial Reaction Time Task will be ameliorated by PA. It is necessary to determine whether PA has an adequate neural substrate on which to work. One well-established effect of PA is its ability to induce the formation of new blood vessels ^{24, 25}, a result that depends upon the brain's capacity to produce new endothelial cells. As cancer treatment decreases the brain's pool of stem cells, the ability of PA to create new vessels may be limited. It is possible that the effects of PA would be dampened in brains that have been treated with CRT or chemotherapy, and that PA would therefore have limited value as a stand-alone treatment. PA may be a particularly useful combination therapy. For instance, stem cell replacement shows promise in the irradiated rodent brain ⁴⁰, and may eventually be possible in humans. PA could help to enhance the proliferation and survival of implanted stem cells.



Take Home Message

The long-term effects of treatment for pediatric brain tumors can be devastating. At present, there is no effective therapy to alleviate these long-standing impairments and lowered quality of life. Physical activity represents a promising, inexpensive, and easily accessible way to promote brain health, and may prove an effective means, alone or in combination, by which to ameliorate the cognitive late effects of pediatric brain tumor treatment.



Camryn, 7 years old.



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Chapter 11

Physical Activity and the Palliative Stage of Treatment

Melanie Keats, PhD & Hillary Woodside, MSc

Learning Objectives:

After completing this chapter you will know:

- ...various terminologies used in addressing non-curative cancer care.
- ...the physical and psychosocial benefits of physical activity for the non-curative cancer patient.
- ...the specific considerations when designing a physical activity program for pediatric, adolescent, and young adult non-curative cancer patients.

Introduction

With advancing research and ever-changing methods of therapy, an array of vague and often overlapping post-diagnostic terms has emerged. To better understand the current gaps in non-curative cancer care, we must first clarify what is meant when we talk about non-curative, palliative, advanced, terminal, and end-of-life cancer. By recognizing the distinct characteristics of the above phases of cancer care, we will be better able to tailor treatment plans for these specific and critical times in the patients' cancer journey.

Patients who have been diagnosed with a **non-curative cancer** have a form of cancer where a procedural cure has yet to be identified ¹. Individuals who fit this category are typically referred to palliative care. Although their cancer cannot be cured, palliative care teams work to assist in pain and symptom management. **Palliative cancer care** as defined by the World Health Organization, involves an approach "that improves the **quality of life (QOL)** of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" ¹.

The remaining terms are used to characterize the stage of the patients' cancer, typically referring to their estimated **survival length** (e.g., time of diagnosis until death). The use of the term, "**advanced cancer**", identifies those individuals who typically have an incurable cancer ².



Advanced cancer may also be referred to as **terminal cancer**, which too identifies that the patient has a cancer that is unlikely to be cured. The last and final stage of the cancer continuum is **end-of-life (EOL)**. EOL care is a part of palliative care that involves providing comfort care to individuals who are facing immanent death ^{3, 4}. Throughout the remainder of this chapter, the all-encompassing term **non-curative** will be used when presenting the different **physical activity (PA)** options for individuals who have been confronted with a non-curative diagnosis.

Rationale for Physical Activity and Non-Curative Cancer Care

Medical and technological advancements have been able to improve the survival length of individuals diagnosed with a non-curative cancer ⁵. With an increased survival length, maintaining the functional fitness of the pediatric, **adolescent and young adult (AYA)** cancer patient should be top priority. With this approach in mind, we can assist in helping to optimize QOL of those with a non-curative diagnosis.

PA is an increasingly popular adjunct therapy that is enabling adult non-curative cancer patients to continue their activities of daily living. The inclusion of PA into the overall supportive care plan for non-curative cancer patients maintains or enhances QOL because it lessens the physical and psychological symptoms related to the disease (e.g., nausea, fatigue, shortness of breath, muscle wasting)^{6,7}. With these symptoms reduced, non-curative cancer patients are able to maintain their independence and autonomy for a longer period of time.

Quick Facts

- Cancer is the second leading cause of death in pediatrics ⁸ and the number one cause of disease-related death in AYAs ⁸.
- ✓ In Canada, 18% of children and 15% of AYAs will not survive 5 years after their cancer diagnosis ^{9, 10}.
- ✓ Although medical advancements have improved survival length, QOL of the AYA has not improved relative to the pediatric and adult populations ⁴.

Regrettably, no empirical studies to date have explored the role of PA for the pediatric and AYA non-curative cancer patient. With a lack of data in younger populations, we look instead to the PA recommendations emerging from the adult non-curative cancer literature. The following sections of this chapter will highlight the benefits of PA for non-curative cancer



patients; what types of PAs are useful for non-curative cancer patients; and will conclude with suggestions as to how the PA programs can be delivered.

Benefits of Physical Activity for Non-Curative Cancers

Understanding the benefits of PA for the adult non-curative cancer patient is challenging due to uncertain disease trajectory and high rates of attrition. Nonetheless, studies report that PA for non-curative cancer patients is safe, feasible, and demonstrates QOL benefits ^{6, 7, 11-13}. Lowe et al. ¹² examined PA for the adult non-curative cancer patient and found that 92% of patients would be interested in and felt able to participate in a PA program. Even with a 3-12 month life expectancy, non-curative cancer patients who participated in a PA program reported positive results on fatigue and emotional well-being ^{14.} *Table 11.1* highlights the physical and psychosocial benefits of including a PA into the overall treatment plan for the adult non-curative cancer patient. These benefits have been reported from time of diagnosis up until EOL.

Table 11.1. Physical and psychosocial benefits of adult non-curative cancer patients' participation in PA programs.

Physical Benefits	Psychosocial Benefits
 ✓ Reduces nausea ✓ Improves sleep ✓ Reduces perception of dyspnea ✓ Reduces cancer-related fatigue ✓ Reduces pain ✓ Maintains muscle strength and endurance ✓ Maintains range of motion ✓ Maintains capacity to do activities of daily living ✓ Stimulates appetite 	 Maintains dignity and autonomy Provides sense of wellness Allows for regaining sense of control over body Provides distraction from disease Decreases sense of burden on family Maintains cognitive and social functioning Increases positive mood and higher levels of perceived self-efficacy Improves QOL

Note. Compiled from ^{5, 7, 12, 14-16}.



Types of Physical Activities for Non-Curative Cancer

Pediatric and AYA patients represent a demographic that have unique developmental needs. For example, AYA cancer survivors have expressed PA preferences that offer an opportunity for social interaction, promote peer support, and are technology-based – permitting the activity to be accessed from a distance ¹⁷. Given the dearth of research, it has yet to be determined if those with a non-curative diagnosis will express these same preferences.



Liam, 5 years old. Cancer survivor.

However, when examining the types of activities that adult non-curative cancer patients enjoy participating in, home-based activities such as walking, cycling and yoga have been successful activities for this population ^{7, 11, 14, 18.} For example, Lowe et al. ¹¹ examined an individualized, home-based, functional walking program for patients diagnosed with an incurable cancer (e.g., gastrointestinal, lung, primary unknown, head and neck, malignant melanoma, anaplastic oligodendroglioma) receiving palliative care. Although only three of the nine



participants were able to complete pre and post assessments, trends towards improved QOL were reported ¹¹. The authors also highlighted that over time, participants' fatigue scores worsened, but it was difficult to determine whether that was due to the advancing cancer or the walking program ¹¹.

A recent study by Henke et al. ⁷ facilitated a supervised, randomized controlled trial to examine whether an individual strength and endurance training program on 29 palliative lung cancer patients (18 received intervention, 11 received standard care) receiving chemotherapy, could improve QOL and help to maintain independence. They found that palliative lung cancer patients who participated in endurance and breathing exercises 5 days per week, and strength training every other day, were able to produce statistically significant differences in QOL, strength, and endurance maintenance when compared with the control group ⁷. Most notably, the walking, stair climbing, and elastic band strength exercises used in this study, were able to minimize muscle atrophy, and allow the palliative lung cancer patient to maintain their functional capacity.

Similarly, Oldervoll et al. ¹⁴ implemented a randomized controlled trial of PA for incurable cancer patients (30-86 years of age) who were receiving palliative care. They found that upon examining 231 cancer patients with a life expectancy less than two years (121 assigned to an PA group and 110 under usual care), the PA group who completed two supervised PA sessions per week for 8 weeks (50-60 minutes in duration), were able to maintain their functional well-being, as well as decrease fatigue and sleep problems.

Lastly, Carson et al. ¹⁶ performed an 8-week, group yoga intervention (i.e., postures, breathing exercises, and meditation), for 13 women (44-75 years of age) with metastatic breast cancer (on/off treatment or cancer returned). The researchers chose yoga as their intervention as it has both a mind and body component, thus potentially contributing to longer lasting positive effects on QOL ¹⁶. Living moment-to-moment was a key focus for this intervention, highlighting that increased patient acceptance would lead to reduced stress and increased relaxation ¹⁶. With this 120-minute yoga session, participants attended on average, seven of eight sessions in the group setting and were encouraged to practice yoga for ten minutes/day at home. Participants reported feelings of invigoration, acceptance, and reduced cancer and treatment-related symptoms with longer times spent in yoga practice ¹⁶.



Physical Activity Recommendations for Pediatric, Adolescent, and Young Adult Non-Curative Cancer Patients

In order to address the unique physical and psychosocial needs of the pediatric and AYA non-curative cancer patient, PA must be age-specific ¹⁹. Offering home-based activities allows the pediatric and AYA non-curative cancer patient a familiar space where the PA can be done with friends or family. This might allow the pediatric and AYA non-curative cancer patient an opportunity to engage in more meaningful interactions with their friends and family during this challenging time. Furthermore, home-based programs decrease PA participation barriers, such as participation costs or travel time/expenses ¹¹. It also allows the pediatric and AYA non-curative cancer patient the ability to control when and how they engage in PA. By use of popular social media and regular off-site supervision of the patient's weekly PA participation, health professionals can connect with patients on a level/platform that is socially acceptable and age appropriate, thus providing the foundation for adherence to a PA program, even with a non-curative cancer diagnosis.

With regards to PA prescription, the pediatric and AYA, compared to the older noncurative cancer patients, have fewer co-morbidities ¹⁷. This suggests that the younger cohort of non-curative cancer patients may be able to engage in a wider range of PAs, potentially at higher intensities. As this area of research remains unexplored, it is recommended that all patients begin with a light PA program that fosters safe and tolerable levels of activity. Activities such as walking, yoga, and cycling are accessible and easily adaptable, and can be done anywhere, with anyone, and at a self-identified duration. The main goal of a PA program for the pediatric and AYA is not only to maintain functional fitness, but to create an atmosphere of normalcy ²⁰. With this approach in mind, we are able to attend to the holistic physical and psychosocial of the pediatric and AYA non-curative cancer patient, thus improving or maintaining QOL, despite chronic deconditioning.

Conclusion

Although there is no literature regarding PA prescription for pediatric and AYAs diagnosed with a non-curative cancer, PA has been shown to improve both physical and psychological cancer-related symptoms without any reported adverse events in the adult non-curative population ^{7, 12, 16}. It is also important to note that adult non-curative cancer patients appear both willing and able to participate in PA within a group setting or at home. While a variety of options are available, activities that have been well adhered to in the adult non-



curative population include walking, strength training, endurance training, and yoga ^{7, 12, 16}. These activities have been successful because they are low cost; they can performed anywhere, and with anyone. Although no concrete PA prescription guidelines exist for the non-curative cancer patient, it is important that the activity be tailored to the individual's interests and abilities ¹².

Take Home Message

Based on the success of physical activity in adult non-curative patients, it would seem fitting to explore the effectiveness of physical activity for pediatric and adolescent and young adult non-curative cancer patients. It may assist in maintaining their functional mobility and health-related fitness, resulting in greater autonomy and improved quality of life. Although no research has been published to confirm these benefits, related literature from the adult non-curative cancer patient population provides an encouraging foundation for future physical activity research in this population.

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Chapter 12

Assessment tools used in the physical activity and pediatric

cancer literature

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Corinna C. Winter, PhD & Fiona Schulte, PhD

Learning Objectives

After completing this chapter you will know:

- ... which measurement tools have been used in physical activity interventions with pediatric cancer populations.
- ... the administration time, important considerations, and useful links and/or resources containing additional information for each tool.

Introduction

This chapter seeks to summarize and present the tools that have been used with pediatric cancer patients in **physical activity (PA)** interventions assessing the outcomes of: i) **quality of life (QOL)**, ii) fatigue, iii) physical activity levels, iv) physical function, v) aerobic capacity, and vi) muscular strength/endurance.

The limited literature in pediatric cancer and PA, and the wide variability of the tools used to assess outcomes, makes it increasingly difficult to compare the results from different interventions. The ability to draw conclusions about the efficacy of PA in some areas is therefore hindered. The objective of this chapter is to provide health care professionals and allied health care professionals with a brief overview of the tools that have been previously used in order to assist them when selecting tools for their research or clinical practice. It is hoped this will result in more trials using similar outcome measures, so that future systematic and meta-analytic efforts may draw stronger conclusions regarding the effectiveness of PA in this population.



Methodology

This review is limited to experimental, quasi-experimental or study protocols of PA in children diagnosed with a primary pediatric cancer under the age of 18 years. The intervention studies described in this review had to include the assessment of one or more of the following: aerobic capacity, strength, motor performance, functional mobility, PA levels, QOL and fatigue after a PA intervention. Through January 2014, databases were searched by 2 independent researchers (CCH, AW): PubMed, Medline, Cochrane, SportDiscus and Embase. Search terms included a combination of population (pediatr* OR paediatr* OR child* OR adolescent OR youth) AND indication (cancer OR neoplasm OR oncology OR leukemia), intervention (physical activity OR activity OR exercise OR yoga OR walk* OR sports OR fitness OR flexibility OR strength) Additional studies identified through Google scholar and/or reference lists of selected papers were included.

A total of 21 intervention studies ¹⁻²¹ and 5 protocol studies ²²⁻²⁶ were included in this review. The inclusion criteria were: 1) > 50% of the sample between the age range: 0-<18 years, 2) human subjects, 3) participants with a diagnosis of cancer (patient or survivor), 4) full text, 5) written in English, 6) assessing one or more of the main outcome variables described above. As part of our exclusion criteria, we did not include any manuscript that did not have a PA intervention even if it met other inclusion criteria.

Results

A total of 8367 studies were identified. Based on inclusion and exclusion criteria, 26 studies with a total of 466 participants were included for review. Table 12.1 presents a synthesis of the studies. The remaining tables provide further information on the tools used to assess the outcomes of interest:

- Table 12.2 QOL
- Table 12.3 Fatigue
- Table 12.4 Physical activity levels
- Table 12.5 Functional mobility
- Table 12.6 Motor performance.
- Table 12.7 Aerobic capacity
- Table 12.8 Strength/endurance

2044-10 2044-10	Ctudy Docion	Samula Siza Diagnocia	Outcomoc	Doculto
Author	study Design	Sample Size, Diagnosis, Age, Treatment Status	Outcomes Measured	Kesults
Braam et al., ²²	- RCT	N=100	- Physical fitness	- No results - protocol
	- 12-week community-pased intervention	Ulagnosis: INIXeo-cancer Але: 8-18 vears	 Prlysical activity 	paper
	- IG: Individual 2 times/week for 45	Treatment Status: On-	- QOL	
	minutes (cardiorespiratory and	treatment and off-	- Fatigue	
	strength training) + group based	treatment (< 1 year post-		
	- CG: Care as usual	וובמווובווו <i>)</i>		
Chamorro-Vina et	- RCT	N=24	 Physical fitness 	 No results - protocol
al., ²³	 16-week in-hospital and home- 	Diagnosis: Treated with	 Physical activity 	paper
	based intervention	autologous stem cell	levels	
	 IG: 5 times/week for 20-30 	transplant	- QOL	
	minutes in patients rooms +	Age: 5-18 years	- Fatigue	
	Individualized home-based	Treatment Status: On-		
	component after discharge	treatment		
	 CG: Care as usual 			
Chamorro Vina et	 Quasi-experimental 	N= 20	 Aerobic capacity 	 Increase aerobic
al., ²⁸	 - ~30 days from the beginning of 	Diagnosis: HSCT in	- Strength	efficiency
	conditioning regimen until	neutropenic phase		 Increase strength
	neutrophil engraftment.	Age: 4-16 years		
-	 CG: Supervised in-hospital 	Treatment status: On		
	intervention. Aerobic training 50	treatment		
	min 5/week + 2/week strength			
	fraining			
	- 00. Cale as usual	9-N		
deyer et al.,	- Quasi- Expennental	Discrete: Mixed server		
	- J-ween III-IIUSpital yoga program	and hematology nationts		
-	minutes	And the fill work		
		Age. 0-13 years Treatment Status: On-		
		treatment		

Table 12.1. Summary of the studies that assessed the effect of a physical activity intervention on aerobic capacity, strength, motor performance, functional mobility, PA levels, QOL and fatigue.

 Improved QOL Improved motor 	performance	 No significant differences in ankle dorsiflexion range of motion or motor performance 	- No significant differences in fatigue	- No results - protocol paper	 Improved physical fitness during intervention but not maintained at follow-up intervention and at follow-up intervention and at follow-up intervention and at follow-up intervention and at follow-up activity levels during activity levels during
- Motor performance	- QOL	 Passive ankle dorsiflexion range of motion Motor performance 	- Fatigue	 Physical activity level Motor performance Fatigue 	 Physical fitness QOL Fatigue Physical activity levels
N= 9 Diagnosis: ALL patients	Age: 2-14 years Treatment Status: On- treatment	N= 51 Diagnosis: ALL patients Age: 5.4 years Treatment Status: On- treatment	N= 29 Diagnosis: Solid tumour and AML patients Age: 8-15 years Treatment Status: On- treatment	N= 40 Diagnosis: Mixed-cancer outside of the central nervous system and treated with vincristine Age: 3-16 years Treatment Status: On- treatment	N= 10 Age: 16.2 ±1.6 years Diagnosis: Mixed cancer sample Treatment Status: Off- treatment (5.2 years post- diagnosis)
 Quasi-Experimental 24-28 week home-based 	intervention IG: Initial physical therapy and exercise program (stretching, strengthen and aerobic exercise)	 RCT 2 year home-based and hospital- based intervention Individualized home-based exercises focused on arm and leg exercises, dorsiflexion stretches and short high-intensity exercise+ hospital-based 1 time /6 week 	 RCT 2-4 day in-hospital intervention 1G: 2 times/day for 30 minutes supervised PA on a stationary bike CG: care as usual 	 RCT 8 weeks hospital-based and home-based IG: 30 minutes/day of elective active video games 	 Quasi-Experimental 16-week community-based intervention 16-week for 90 minutes 1G: 1 time/week for 90 minutes First 8 weeks - 60 minutes PA; 45 minutes aerobic, 15 minutes core, strength and flexibility + 30 minutes informal education Second 8 weeks - 90 minutes informal non-competitive activities
Gohar et al., ²		Hartman et al., ³	Hinds et al., ⁴	Kauhenen et al., ²⁴	Keats et al., ⁵

					intervention but not at follow-up
Li et al., ⁶	, , , , , , , , , , , , , , , , , , ,	CT day integrated adventure-based aining and health education ogram over a 6-month period amponent: (e.g., wall climbing, ini Olympics etc) + education inponent 3: 4-day leisure activities over month period. Leisure activity imponent (e.g., cartoon atching, arts and crafts, chess ines) + education component	N= 71 Diagnosis: Mixed cancer Age: 9-16 years Treatment Status: Off- treatment (> 6 months post-treatment)	- QOL - Physical activity levels	- Improved QOL - Increased physical activity levels
Marchese et al., ′		CT S-week home-based and sepital-based PA intervention :: 5 times/week ankle stretches, times/week resistance ercises and 7 times/week robic training + 5 physiotherapy sistions at the hospital 3: Care as usual.	N= 28 Diagnosis: ALL during maintenance therapy Age: 4-15 years Treatment Status: On- treatment	 Aerobic capacity Muscular strength Functional mobility QOL 	 No changes in aerobic capacity Improved knee extension strength No change in functional mobility No change in QOL
Moyer-Mileur et al., 27	C G a G II 7 7	CT 2-month home-based PA tervention 1: 3 times/week, 15-20 minutes probic and resistance training + itrition program 3: Care as usual	N= 13 Diagnosis: ALL during maintenance therapy Age: 4-10 years Treatment Status: On- treatment	 Physical fitness Physical activity levels 	 Increased physical activity levels Improved physical fitness
Muller et al., ⁸	, , , , , , , , , , , , , , , , , , ,	uasi-Experimental -hospital PA intervention over ? months :: Additional exercises during in- titient rehabilitation (15-45 inutes/day) 3: Care as usual	N=21 Diagnosis: Bone tumour Age: 8-18 years Treatment Status: On- treatment	- Physical activity levels	 Improved physical activity levels
Perondi et al., ^y	 12 Q	uasi-Experimental ?-week in-hospital PA	N= 6 Diagnosis: ALL during	 Physical fitness QOL 	 Improved fitness (on specific outcomes)

	intervention	maintenance therapy			- Improved parental	
	 IG: 2 times/week for 60 minute 	ss Age: 5-16 years			perceptions of health-	_
	high intensity resistance and	Treatment Status: On-			related QOL	_
	moderate intensity aerobic	treatment				_
	training					
Rosenhagen et al.,	 Quasi-Experimental 	N= 23	- Physical	fitness	 Maintained physical 	
10	 6-week in-hospital PA interver 	Ition Diagnosis: Mixed-cancer	- QOL		fitness	
	 IG: 3 times/week for 50 minute 	ss receiving HSCT			- QOL	
	on a cycle ergometer and	Age: 15.3 ± 3.7 years				
	completing strength/coordinati	on Treatment Status: On-				
	exercises	treatment				
	 CG: Retrospective usual care 					
San Juan et al., ^{12,13}	 Quasi-Experimental 	N= 7	- Aerobic	capacity	 Improved aerobic 	
	 16-week in-hospital PA 	Diagnosis: ALL during	- Musculai	r strength	capacity	
	intervention + 20 weeks	maintenance therapy	- Function	al mobility	 Improved strength 	
	detraining	Age: 4-7 years	- QOL		 Improved functional 	
	- IG: 3 times/week for 90-120	Treatment Status: On-			mobility	
	minutes (30 minutes aerobic a	nd treatment			 No significant change in 	_
	one set 11 resistance training	5055				
	evercises (8-15 renetitions) +				. After detraining strength	_
	weeks of detraining				- And functional mobility	_
					was maintained but	
					functional capacity was	
					not	
San Juan et al., ¹¹	 Quasi-Experimental 	N=16	- Physical	fitness	 Improved physical 	
	 8-week in-hospital PA interver 	Ition Diagnosis: HSCT patients	- Function	al mobility	fitness (strength and	
	- IG: 3 times/week 90-120 minu	tes; with leukemia	- QOL	\$	functional mobility)	
	10-30 minutes aerobic exercis	e Age: 10.9 ± 2.8 vears			 Improved functional 	
	and one set of 11 resistance	Treatment Status: On-			mobility	
	exercises (8-15 reps)	treatment			 Improved QOL (select 	
	 CG: healthy controls 				outcomes)	
Sharkey et al., ¹⁴	- Quasi-Experimental	N= 10	- Aerobic	capacity	 No significant changes 	
,	 12-week in-hospital and home 	 Diagnosis: Mixed cancer 	- Physical	activity	in functional capacity	
	based PA intervention	Age: 16-22 years	level		 Increased physical 	_
	 IG: 2 times/week; 45-60 minut 	es Treatment Status: Off-			activity level	
	aerobic (at 7-weeks, 1 time/we	ek treatment			•	
	home-based PA program					
	supplemented)					
Soares-Miranda et	- RCT	N= 60	- Aerobic	capacity	 No results - protocol 	
al., ²⁵	 Duration of neoadjuvant 	Diagnosis: Extracranial	- Muscle s	strength	paper	_
				,	-	1

	chemotherapy in-patient PA	solid tumours	,	Functional mobility	
	intervention	Age: 4-18 years	ı	Physical activity	
	 IG: 3 times/week for 60-70 	Treatment Status: On-		levels	
	minutes individualized aerobic	treatment	ı	QOL	
	and strength program				
Spever et al ¹⁵	- RCT	N= 30	,	OOL	- Improved QOL
	- Duration of hosnitalization in-	Diagnosis: Mixed oncology		1)	1
	hospital PA intervention	and hematology			
	 IG: 3 times/week for 30 minutes 	Age: 9-18 years			
	 CG: Care as usual 	Treatment Status: On-			
		treatment			
Takken et al., ^{т6}	 Quasi-Experimental 	N=4	ı	Aerobic capacity	 No significant
	 12-month community-based and 	Diagnosis: ALL	ī	Muscular strength	differences on any
	home-based PA intervention	Age: 9.3 ± 3.2 years	ı	Functional mobility	outcomes
	 IG: 2 times/week community- 	Treatment Status: Off-	ı	Fatigue	
	based for 45 minutes strength	treatment			
	and endurance based exercises				
	changing focus every 4 weeks +	2			
e e	times/week home-based				
Tanir et al., ^{1/}	- RCT	N= 41	ı	Aerobic capacity	 Improved aerobic
	 3-month home-based PA progra 	m Diagnosis: ALL in	ı	Muscular strength	capacity
	 IG: 5 times/week for 3 times/day 	remission	ı	Functional mobility	 Improved strength
	flexibility exercises	Age: 8-12 years	ı	QOL	 No change functional
	 3 times/week for 3 times/day 	Treatment Status: On-			mobility
	strengthening exercises	treatment			 Improved QOL
	 3 times/week, 1 time/day for 30 				
	minutes aerobic activity				
	 CG: Care as usual 				
Thorsteinsson et al.,	- Quasi-Experimental	N= 120	ı	Aerobic capacity	 No results - protocol
07	- Duration of treatment supervised	Diagnosis: Mixed-cancer	ī	QOL	paper
	in-hospital physical, social and	and non-malignant			
	educational intervention	hematological diseases			
	 IG: Physical, social and 	(new diagnose)			
	educational intervention	Age: 6-18 years			
	 1 time education of the cancer 	Treatment Status: Off-			
	patient's mate at school and	treatment (< 1 year)			
	recruitment of two ambassadors				
	which visit the child with cancer	<u> </u>			
	the hospital.				

		3 times/week individual training from 5-120 minutes depending on the type of training and the general condition of the child 2 times/week group physical activity/social intervention 3 days/week for 4 hours/day CG 1: Care as usual at another hospital CG: Healthy siblings			
		CG 3: Healthy class mates CG 4: Historical control			
Winter et al., ¹⁸	ı	Quasi-Experimental	N= 31	 Physical activity 	- No significant
	ı	6-montns in-nospital PA	Diagnosis: Malignant bone	Ieveis	differences in PA levels
	ı	IG: 7 times/week for 30-60	Age: 10-17 years		
		minutes combined aerobic,	Treatment Status: On-		
	1	resistance and flexibility training	treatment		
		OO. Oare as usual Oundi Eventimental	0		
עעמוב פו מו.,		12-week community-based voga	Diagnosis: Mixed-cancer	- CUL - Functional mobility	- Improved functional
		intervention	patients	 Physical activity 	mobility
	ı	IG: 2 times/week for 60 minute	Age: 8-17 years	levels	 Improved physical
		yoga class	Treatment Status: On-		activity levels
			treatment		
Yeh et al., ¹⁹	ı	Quasi-Experimental	N= 22	- Fatigue	 Improved symptoms of
	ı	6-week home-based PA	Diagnosis: ALL during		general fatigue
		intervention	maintenance therapy		
	ı	IG: 3 times/week for 30 minutes	Age: 7-15 years		
		aerobic exercises with a PA video	Treatment Status: On-		
	ı	CG: Care as usual	treatment		
Note PCT. Pandomiz	c pa	control trial: IC: intervention aroun: CC		f narticinants: ALL - actite I	wmphoblastic laukamia:

AME: ROL: Rendomized comploting the intervention group, OG. comploting group, N. number of participants, ALL: acute tymphoblastic reukerina, AML: acute tymphoblastic leukemia; PA: physical activity; QOL: quality of life; HSCT: hematopoietic stem cell transplant; BMI: Body mass index.

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Table

Additional Comments	 Child report and parent proxy report Translated to more than 20 languages High test-retest validity with small effect sizes may limit its efficacy for use in intervention studies For more information see: 	www.healthactchg.com.	 Child report and parent proxy report Translated into several languages Age range: 2-18 years Used commonly in pediatric cancer For more information see: http://www.pedsql.org/ 	 Child report and parent proxy report Multiple translations Age range: 2-18 years For more information see: http://www.pedsal.org/ 	 Parent and proxy versions Different forms for children and adolescents 	- Lengthy - Available in various landuades	 Age range: 6-17 years For more information see: 	http://www.childhealthprofile.org/index.asp?p ageid=48
Time to Administer and Score	Not reported in the intervention paper; the website states it takes 16-25 minutes Scoring software required.		4 minutes to complete and 4-5 minutes to score	4 minutes to complete and 4 minutes to score	Takes 20 minutes to complete	Scoring software required		
Pediatric -Specific	Yes		Yes	Yes	^o N			
Cancer- specific	°Z		°Z	Yes	Yes			
Studies Used in	Speyer et al., ¹⁵		Thorsteinsson et al., ²⁶ Tanir et al., ¹⁷ Braam et al., ¹⁷ Geyer et al., ⁵ Gohar et al., ⁵ Keats et al., ⁵ Li et al ⁶ Marchese et al., ⁷ Chamorro et al., ⁹ Perondi et al., ⁹ Wurz et al., ⁹	Tanir et al., ¹⁷ Braam et al., ²² Marchese et al., ⁷ Perondi et al., ⁹	San Juan et al.,	San Juan et al.,		
Assessment Tool	Child Health Questionnaire (CHQ)		Pediatric quality of Life (PedsQL) 4.0	PedsQL Cancer 3.0	Child Health and Illness	Profile (CHIP- CF and CHIP-	AE)	

Available in various languages Are range 3-17 years	Can be use for free. Download in the	webpage.	For more information see:	http://www.kindl.org/english/information/		
	ı		ı			
Takes 20-25 minutes to complete	Scoring software required					
There is a general	module	and also	has an	oncology	specific	module.
Yes						
Rosenhagen et al ¹⁰						
KINDL						

Assessment Tool	Studies Used in	Cancer- specific	Pediatric -Specific	Time to Administer and Score	Additional Comments
PedsQL Multidimensional Fatigue Scale	Yeh et al., ¹⁹ Kauhanen et al., ²⁴ Chamorro- Vina et al., ²³ al., ⁵ Braam et al., ²² Perondi et al., ⁹	oz	Yes	Less than 5 minutes for each	 Acute version: measures fatigue over past 7 days Standard version: measures fatigue over past 1 month Age range: 2-18 years For more information see: <u>http://www.pedsql.org/</u>
CIS (Checklist Individual Strength	Takken et al., ¹⁶	Yes	oZ	4-5 minutes to complete and 4-5 minutes to score	 Measures fatigue over the past 2 weeks For more information see: <u>http://www.psychischenwerk.nl/pw/subarticle.ph</u> p?id=133&aid=2382
The Fatigue Scale – children (FS-C)	Hinds et al., ⁴	No	No	Takes 5-7 for child, 4-5 for adolescent and 6-8 for parents to complete	 Measures fatigue over past 24 hours (can be daily or weekly) For more information see ²⁹

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Table12.3.

Assessment	Studies	Cancer-	Pediatric	Time to Administer and Score	Additional Comments
Tool	Used in	specific	-Specific		
Leisure score	Keats et al., ⁵	No	No	<5 minutes	- Subjective
index (LSI),	Wurz et al.,				 Measures PA over the past 7 days
questionnaire	20				 Type of instrument: questionnaire
					 See questionnaire at:
					http://www.godin.fsi.ulaval.ca/Fichiers/Quest/Godi
					n%20leisure-time.pdf
UCHK-PARCY,	Li et al., ⁶	No	Yes	< 5 minutes	- Subjective
questionnaire					 Measures PA over the past 12 months
					 Type of instrument: questionnaire
					 See a copy of the questionnaire at
					http://www.biomedcentral.com/1471-2458/10/303
Uniaxial	Winter et al.,	No	No	2 minutes plus interpretation of	 Objective measure
accelerometer	¹⁸ (step			results	 Measures PA for up to 2 months
	watch 3)				 Type of instrument: uniaxial accelerometer that
					assess vertical accelerations
					 For more information regarding MTI actigraph
					see: http://www.actigraphcorp.com/
					 For more information regarding step watch 3 see:
					http://modushealth.com/
					 For an additional resource see:
					http://trace.tennessee.edu/cgi/viewcontent.cgi?art
					icle=2027&context=utk graddiss

Table 12.4. Assessment tools used to asses physical activity levels.

Note. UCHK-PARCY: The Chinese University of Hong Kong: Physical Activity Rating for Children and Youth).

Additional Comments	 Familiarization sessions are required For safety reasons, children are allowed to hold on to a hand rail The number of stairs reported varies between 11 stairs 12 stairs and 14 stairs Easy to do For more information see ³⁰ 	 TUG scores should be adjusted for height Test is quick, requires no special equipment or training and is easily included as part of the routine medical examination If the subject runs during the test, the test has to be repeated For more information see: http://www.cdc.gov/homeandrecreationalsafety/pd f/steadi/timed_up_and_go_test.pdf and ³¹
Administer and Score	utes	utes
Time to	3-5 minu	3-5 minu
Pediatric -Specific	°Z	°Z
Cancer- specific	oz	°Z
Studies Used in	Marchese et al., ⁷ San Juan et al., ^{12,13} San Juan et al., ¹¹ Takken et al., ¹⁶ Tanir et al.,	San Juan et al., ^{12,13} San Juan et al., ¹¹ Takken et al., ¹⁶ Tanir et al., ¹⁷ Thorsteinsso n et al., ²⁸ Chamorro vina et al., ²³ Vina et al., ²³
Assessment Tool	TUDS (timed up and down stairs test)	TUG 3m TUG 10m (timed up and go test)

Table 12.5. Assessment tools used to assess functional mobility.

Note. TUG: timed up and go test; TUDS: timed up and down stairs test.

		-	
Additional Comments	 Assesses gross motor function rather than quality of motor performance. Age range: 5 month to 16 years S-year old child should be able to successfully complete all skills For more information see: <u>http://canchild.ca/en/measures/gmfm.asp</u> 	 Assesses developmental functioning of infants and toddlers Age range: 16 days to 42 months and 15 days Last revision 2006: BSID-III Normative data is available Examiners should be familiar with and have training in developmental assessment and interpretation For more information see: <u>http://www.tandfonline.com/doi/pdf/10.1080/17405629.</u> 	 Aims to identify children with motor difficulties Not appropriate for children with severe disability, very limited use of extremities, in a wheelchair Age range: 3-16 years Age-related norms to transform results into percentile scores For more information see: http://www.ncbi.nlm.nih.gov/pubmed/19197761
Time to Administer and Score	GMFM: 45-60min	50-90 min for entire BSID- III	20-40min
Pediatric- Specific	Yes	Yes	Yes
Cancer- specific	Dimensions 4 and 5 have been adapted for children with ALL	°Z	°Z
Studies Used in	Gohar et al., ²	Hartman et al., ³	Hartman et al., ³ Kauhanen et al., ²⁴
Assessment Tool	GMFM (Gross motor function measure)	BSID (Dutch Bayley Scales of Infant Development)	Movement-ABC (Movement Assessment Battery for Children)

Table 12.6. Assessment tools used to assess motor performance.
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Additional Comments	 Seat height adjusted to patient's leg W_{peak} is recorded VO_{2peak} is recorded: average value over the last 30s before subjective exhaustion Prediction of VO_{2max} with Steep Ramp Test. VO_{2max}: = 6.7Watt Steep Ramp Test +356.71³² 	 Submaximal test Requires no material other than a distance measured accurately for length and a stopwatch Distance of at least 30m Walking and running is permitted 	 10 subjects can be tested simultaneously in an ordinary gym No special equipment 10 min warm-up No verbal encouragement Prediction of VO_{2max} VO_{2max} = 18.38 + (0.033*distance) – (5.92*sex) (with boys =0 and girls =1) ³³ For more information see: http://www.holdspil.ku.dk/publikationer/baggrundslitteratur/Th e use of Yo-Yo IR1 and Andersen testing for fitne.pdf
Time to Administer and Score	Godfrey: 4-10 minutes	20 minutes	20- 25 minutes
Pediatric- Specific	Steep Ramp Godfrey: Yes	°N N	8
Cancer- specific	°Z	NO	°Z
Studies Used in	Steep Ramp Test: Braam et al., ²² Godfrey Protocol: Braam et al., ¹⁶ al., ¹⁶ specified): Sharkey et al., ¹⁴	Marchese et al., ⁷ Tanir et al., 17	Thorsteinss on et al., ²⁶
Assessment Tool	Bicycle Ergometry	9-min run-walk- test	Andersen Test

Moyer- No No 15 minutes - For more information see: re Mileur et - for more all, 27 - for more all, 27 all, 27 all, 27 - for more all, 27	Maximal Yes 20- 30 minutes - Important to perform the test under similar environmental conditions and at the same time of day within and between test: stan Juan test: conditions and at the same time of day within and between subjects stan Juan test: conditions and at the same time of day within and between subjects San Juan test: conditions and at the same time of day within and between subjects San Juan et al., ¹¹ At least one familiarization session on the treadmill is necessary San Juan et al., ¹¹ At least one familiarization session on the treadmill is necessary San Juan et al., ¹¹ At least one familiarization session on the treadmill is necessary Sources- Maximal - At least one familiarization session on the treadmill is necessary Niranda et al., ¹¹ Evonoti et al., ¹² - At least one familiarization session on the treadmill is necessary Sources- No - At least and HRpeak are recorded as the highest value of al., ¹³ Miranda et al., ³² - Test ends at 80% of age-predicted max heart rate (208- (0.7*age)) Maximal - For more information see ¹³ Minance - For more information see ¹³	etry Soares- Yes Yes 20-30 minutes - A crank arm-ergometer (Monark Rehab Trainer model 881E, Miranda et - Starting at 5 W, the load will be increased in a ramp-like fashion, i.e. by 5 watt every 20 s, while cadence is kept constant at 50 rpm - This protocol was used only in those participants with a solid
Moyer- Mileur e al., ²⁷	Maxim endura test: San Ju; San Ju; San Ju; et al., 25 al., 26 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 5 al., 26 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 27 al., 20 al., 27 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 al., 20 27 al., 20 20 20 20 20 20 20 20 20 20 20 20 20	Soares Mirand: al., ²⁵
PACER (Progressive Aerobic Cardiovascular Endurance Run)	Graded exercise test on treadmill	Arm ergometry

Table 12.8. Assessment tools used to assess strength.

Additional Comments	 Muscle strength of the proximal and distal muscles in the upper and lower extremities at the right and left side of the body is measured by hand held dynamometer (Citec http://www.citec.nu/frm/uk.htm) In the break method the examiner gradually overcomes the muscle force and stop at the moment the extremity gives away The examiner has to be experienced in order to obtain reliability in the measures The same assessor with the same dynamometer has to do all the assessments in order to avoid interinstrument and inter-observer bias. For more information see: Backman ³⁴ 	 Assesses knee extension strength and ankle dorsiflexon strength In the Knee extension test, the child was in a prone position with the knee flexed to 90° and thigh stabilized In the ankle dorsiflexion test the child was sitting with the knee flexed 90° and the foot in a neutral alignment. Nicholas Model 01160- Lafayette instrument was used see Effgen et al ³⁵ for a full description of the methodology 	 The measurement is carried out with back and leg dynamometry The child's feet are arranged on the dynamometer bench while he is on his feet with legs bent. The arms are taut, the back straight and the body slightly leaning forward. In this position, the child grips the dynamometer bar vertically and uses the legs at a maximum, pulling the bar up. This is the point where the measurement is taken This is repeated three times and the best value in kg is recorded
Time to Administer and Score	5- 10 minutes each muscle group	5- 10 minutes each muscle group	5-10 minutes
Pediatric- Specific	°Z	oz	° N
Cancer- specific	°Z	°Z	°Z
Studies Used in	Braam et al., ²²	Marchese et al., ⁷	Tanir & Kuguoglu ¹⁷
Assessment Tool	Dynamometer- break method	Hand-held dynamometery	Back and leg dynamometry

		1		
- For more information see ¹⁷	 The grip strength techniques used were not reported by Rosenhagen¹⁰ For the technique used by Thorsteinsson²⁶, see Abizanda³⁶ 	 Authors defined gains of strength comparing the final loads of each exercise at the beginning of the training period with the loads at the end of the training periods. This is not the most accurate way to assess increases in strength however the results from the study do give an idea of the muscular adaptation that happened over the course of a training period 	 Keats et al. ⁵ assessed push-ups and sit-ups. They used the Fitnessgram protocol created by the Cooper institute Easy to administer Some equipment is required For more information see: <u>http://www.fitnessgram.net/</u> Moyer Mileur study the authors assessed push-up only and did not describe the protocol 	Details of the protocol were not described
	5-10 minutes		5- 6 minutes each assessment of the battery	8-15 minutes the entire assessment
	٥N	0 Z	Yes	0 Z
	oN	oz	oz	oz
	Rosenhag en et al., ¹⁰ Thorstein sson et al., ²⁶	Chamorro et al., ²⁸	Keats et al., ⁵ Moyer Mileur et al., ²⁷	Takken et al., ¹⁶
	Grip strength- Hand-held dynamometer	Registered training loads during training and compared post value training loads versus values of pre -training loads.	Registered number of sit- ups, push- ups,	30 –seconds repetition maximum for sit-ups, push- ups and head and leg raises 60 seconds repetition maximum for squats

Seat height has to be adjusted to each child's height See protocol at Bohannon ³⁷	 Dynamic upper- and lower-body muscle strength were measured using 6 maximal repetition of the following exercises: seated bench, seated lateral row, and seated leg-press machine Pediatric strength machines are required Familiarization period is required before the initial assessment. For complete protocol see ¹³ 	 Prior to the test, a familiarization period is required. After a warm up 3 to 5 separate single attempts were performed until the 10-repitition maximum was attained. The interval between each unsuccessful attempt was 4 min 4 exercises were performed: leg press, bench press, leg extension and lateral pull down For complete protocol see⁹
3-5 minutes	10 -15 minutes each muscle group.	14-20 minutes each muscle group
°Z	°Z	°Z
°Z	Yes	0 N
Thiorstein sson et al., ²⁶ and Chamorro -Vina et al., ²³	San Juan et al., ^{12,13} San Juan et al., Soares- Miranda et al., ²⁵	Perondi et al.,
Sit-to stand-test	6 maximal repetitions test	Dynamic upper and lower extremity 10 maximum repetitions test



Conclusion

The effect of PA interventions on the recovery of children affected by cancer is an emerging field of research. As described in this chapter, a wide variety of assessment tools have been used to describe the outcomes of PA interventions in pediatric oncology. Because of the inherent difficulties conducting research in this field (e.g., small population, difficulties with recruitment), it is recommended that researchers strive to use similar assessment tools in order to facilitate the comparison and interpretation of data across PA interventions in an effort to better ascertain the effectiveness of PA in this population. That being said, we recognize that the use of the same assessment tools is not always feasible, and that the selection is associated with a myriad of variables (e.g., budget availability, researchers previous experiences and beliefs, time to conduct the assessment, equipment available, age of participants, language, etc.). It is hoped that this chapter provides useful information and helps future researchers when making their tool selection.

Take Home Message

The variability of measurement tools used in physical activity interventions with pediatric cancer populations makes it difficult to compare results across studies. We have provided a brief overview of the assessment tools used to date. Further we outline the administration time, important considerations, and useful links and/or resources containing additional information for each tool. We hope that this summary will aid researchers and professionals when choosing their assessment tools for future clinical and research work.



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Chapter 13

Prototype of Sustainable Community-Based Physical Activity

Programs

- i) Carolina Chamorro-Viña, PhD; Lauren Capozzi, MD/PhD Candidate & S.
 Nicole Culos-Reed, PhD: Pediatric cancer patients and survivors Engaging in Exercise for Recovery
- ii) Travis Gallagher, Athletic Trainer & Anastasia Fischer, MD: Play Strong
- iii) Carmel Nottle, Accredited Exercise Physiologist

Learning Objectives:

After completing this chapter you will know:

- ... the required and desired qualifications for fitness professionals to run a community based-exercise program for childhood cancer patients and survivors.
- ... the importance of knowing the participant's current medical health status and history.
- ... the importance of communicating with participant's physician.
- ... the importance of involving the parents in the rehabilitation process.
- ... that enjoyment and confidence when performing physical activity are important outcome measures, in addition to fitness gains, for children in relation to long-term participation in physical activity.
- ... the need for individually designed physical activity programs, even for programs delivered in a community based group setting, to ensure maximal participant satisfaction and fitness related outcomes.



Introduction

The expanding body of evidence supporting **physical activity (PA)** for pediatric cancer survivors warrants the development of both clinic and community-based PA programs specifically designed for this population. As indicated in *Chapter 2*, PA plays an important role in patients and long-term survivors, encompassing both physical and psychosocial rehabilitation goals. It is evident that PA can potentially positively impact the functional, psychosocial, and disease-related outcomes of the cancer experience ¹⁻³. Thus, it is necessary to highlight the importance of translating this existing PA and cancer knowledge into sustainable and accessible community-supported patient programs ^{3,4}.

Unfortunately, there remains a gap between our current level of PA evidence and what is put into practice. Despite these challenges, clinic and community-based PA programs are actively running around the globe. By offering PA programming on a consistent basis, it may addresses this current gap in knowledge translation and has the potential to contribute to improved PA adoption and adherence rates among pediatric cancer survivors ^{4,5}.

Three leaders in pediatric oncology PA programming are highlighted in this chapter. Each section will review the specifics of program development, facilitation and coordination of program delivery, participant characteristics, and overall sustainability, including ongoing barriers, program limitation, lessons learned, and future steps. The three programs to be examined are: 1) Pediatric cancer patients and survivors Engaging in Exercise for Recovery (PEER), 2) Play Strong and the 3) University of South Australia and Little Heroes Physical Activity Program.



Pediatric cancer patients and survivors Engaging in Exercise for

Recovery



Program Development

Utilizing the existing four key pillars of the Thrive Centre model (a free fitness facility center for adults cancer patients and their support people) (see *Figure 15.1*), including 1) evidence-informed, 2) volunteer-run, 3) community-based, and 4) sustainability, the PEER program for pediatric cancer patients and survivors was developed in May 2012 in the Health and Wellness Lab, University of Calgary, Canada. This program was developed by a multidisciplinary team of cancer and exercise specialists, certified exercise physiologists, oncologists, psychologists and physiotherapists from the Health and Wellness Lab in the Faculty of Kinesiology and the Alberta Children's Hospital, based on the best research evidence available. PEER is an innovative fitness program that aims to empower and improve the **quality of life (QOL)** for children affected by cancer. The program provides a safe and supportive exercise environment for pediatric cancer patients, survivors and their siblings.

The Health and Wellness Lab partnered with the Kids Cancer Care in April 2013. To our knowledge, this community-based exercise program is the first exercise program developed in Canada for children with cancer.

Running and Supervision of the PEER Program

The PEER program runs a group exercise session for 60 minutes once a week, that is tailored to the special needs of each participant. Kinesiology student volunteers are responsible for facilitating the sessions, based on a predetermined curriculum (see *Appendix 13.A* for curriculum and a session example). The design of each program for the cancer patients/survivors is approved by a pediatric cancer and exercise specialist or a **certified exercise physiologist (CEP)** prior to the session. While the volunteers lead the session, a CEP or a pediatric cancer and exercise specialist is also in attendance to ensure the safety of all



participants. All participants are required to receive physician clearance before participating (see *Appendix H*). Furthermore, parents are required to complete a detailed medical history form for their child (see *Appendix G*). The medical history form asks about: cancer type, disease status, treatment (received/ongoing) and side effects. Communication with the participants' physicians and physiotherapists is a key factor in PEER and is fundamental to ensure the safety and individualization of the program.





Volunteer training requirements

The PEER volunteers must meet the following criteria:

- ✓ Be a Thrive Centre volunteer for a minimum of one semester (four months) prior to applying.
- ✓ Have completed the Thrive Center General volunteer training. The Thrive Centre training is designed to prepare volunteers with the necessary background knowledge to be comfortable and competent in their responsibilities. Volunteers are educated on cancer and related treatments, common side effects experienced by cancer survivors, and the latest cancer and exercise



researching findings. They are then exposed to a practical learning session outlining their specific Thrive Centre gym supervision roles, responsibilities, and their scope of practice. Volunteers are provided with a cancer and exercise training manual and are required to pass a short exam before volunteering in the Thrive Centre. Each year, volunteers are required to attend a three-hour refresher training.

✓ Have Thrive Center Pediatric-Oncology specialization training. The pediatric oncology specialization training is a nine-hour training delivered by a multidisciplinary team comprised of oncologists, psychologists, physiotherapists, CEPs and cancer and exercise specialists. This training provides the volunteers with the tools necessary to tailor exercise sessions (dependent on age, cancer diagnosis, treatment stage, comorbid conditions, psycho-social variables). The POEM manual and handout materials have been developed for this training. A refresher training session is also offered to these volunteers each year.

 \checkmark Have rubella and chickenpox immunization records.

✓ Have a criminal record check.

The two last additional criteria are in place at the ACH. We chose to implement these criteria to ensure our PEER volunteer requirements aligned with current safety protocols of the hospital.

Program Description

PEER program goals are to:

- ✓ Improve physical literacy in children affected by cancer and their families.
- Promote an active lifestyle in order to decrease the risk of acquiring other chronic diseases resulting from the perpetuation of a sedentary lifestyle, promoted by cancer and its treatment.
- Restore healthy levels of muscular strength, muscular endurance, aerobic capacity and flexibility.
- \checkmark Improve QOL, body image and self-confidence and decrease levels of fatigue.

We are in the process of redesigning the PEER program based on what we have learned over the past 2 years. One of our main limitations in running the program has been the wide range of ages. Thus, we now split the PEER program into two groups: (a) 5-13 years and (b) 14-18 years. Even though both groups share the same space, they perform different



activities. Occasionally they participate in some activities together such as warm up, cool down or games.

Because teenagers are affected mainly by bone tumors and they all have different expectations, preferences, barriers and motivational factors, we have developed specific PA programs for each teenager. This tailored approach allows each teenager to reach their goals, meet their needs and overcome their barriers to being active. At the same time, the PEER program offers the opportunity to socialize with other adolescents undergoing a similar experience. The CEP or cancer and exercise specialist conducts an initial interview with each teenager and their parents where they review, exercise preferences, barriers, motivational factors, treatment received and related side effects, disease status, and fatigue. After the interview, the CEP or cancer and exercise specialist designs a unique PA program for each teenager. The volunteers are then able to deliver a tailored PA program for the teenagers in each PEER session. The PA program is adjusted when needed in order to maintain high motivation and health-related fitness improvements.

Physical Literacy

Individuals who are physically literate move with competence in a wide variety of physical activities that benefit the development of the whole person. Physically literate individuals consistently develop the motivation and ability to understand, communicate, apply, and analyze different forms of movement. They are able to demonstrate a variety of movements confidently, competently, creatively and strategically across a wide range of health-related physical activities. These skills enable individuals to make healthy, active choices throughout their life span that are both beneficial to and respectful of themselves, others, and their environment.

Physical and Health Education Canada, Position Paper 2009

For the age group between 5-13 years old, we are in the process of completing the development of a full curriculum that will have three modules (fall, winter and spring). Each module will contain 12-14 sessions. The development of the curriculum is based on the Ontario PA curriculum ⁶, Canadian Sport for Life Physical Literacy ⁷ and fundamental movement skills developed by

Physical Health and Education Canada⁸. Also, the curriculum takes into account PA research performed in pediatric cancer populations as well as suggested adaptations of PA guidelines to guarantee safety when side effects related to treatment are present (e.g., cardiotoxicity, peripheral neuropathy). The ratio of volunteers running the program to participants has been set at a minimum of one volunteer to four participants. Additionally, we have set the maximum at 12 participants.



PEER curriculum

The rationale for creating a curriculum for the PEER program is:

- \checkmark To give the program continuity and progression.
- ✓ To give the volunteers additional guidelines and instruction.
- To motivate parents to bring their children to the PEER program regularly in order to achieve the benefits of the program.
- \checkmark To better inform parents and physicians about the PEER program.

The curriculum has three main objectives:

- 1. Movement competence
- 2. Active living
- 3. Healthy living

1) Movement competence

This objective focuses on the development and improvement of fundamental skills such as balance, coordination, running, jumping, and dribbling. As the literature highlights, one of the barriers children with cancer face is missing the stage where most children start to develop fundamental skills, preparing them for success in different sports/PAs. As a result of missing this developmental stage, they feel as though they do not fit in when they want to return to practice PA/sports with their peers. The PEER program provides children with the opportunity to increase their self-confidence by developing and improving their mastery of fundamental skills within three different levels of difficulty (easy, moderate and advanced) for each fundamental skill. All children engaging in the PEER program are able to work on the same fundamental skills at a level of difficulty that is specifically adapted to each child's development and health status.

2) Active living

The active living objective aids in fostering skills and knowledge that are frequently required to safely participate in PA, providing a platform where participants enjoy being physically active and teaching children how to develop and enhance their own health-related fitness. Encouraging children to engage in daily PA is an important component of this objective. Participating in moderate to vigorous PA on a daily basis, outside the PEER program, will help participants restore their healthy levels of fitness and enhance their understanding of the importance of PA as part of a healthy lifestyle.

3) Healthy living

The healthy living objective helps participants develop an understanding of factors that contribute to their healthy development such as being sufficiently active, making healthy eating



and drinking choices, a sense of personal responsibility for lifelong health and a respect for their own health in relation to others and the world around them. Participants will acquire the knowledge and skills needed to develop, maintain and enjoy a healthy lifestyle, as well as to problem solve, make decisions, and set goals that are directly related to their personal health and well-being. The key part of this objective is learning how to establish, monitor and maintain healthy habits.

Each objective addressed at the PEER sessions is developed and reinforced by encouraging PA participation outside of the PEER program and by completing the activities and worksheets in the logbooks provided during the program.

To ensure that parental support is provided for the child, educational sessions are offered monthly. These sessions are designed to share tools that will aid in the development of a healthy lifestyle for their child.

Finally, assessments at the beginning and at the end of each curriculum module will be provided in upcoming PEER sessions (see text box below for assessment outline). The child's parents and physician will receive a report containing assessment results and suggested guidelines to improve health-related outcomes.

Participants

Participants are pediatric cancer patients (on and off treatment), 5 to 18 years old. All participants receive clearance from their physician to participate in the PEER Program. The



participants between 15 and 18 years complete the PARmed-X clearance form. Participants between 5 and 15 years complete our own clearance form based on the PARmed-X (refer to *Appendix H*). In addition, parents are asked to provide information regarding their child's disease, treatment and side effects, allowing the facilitators to effectively adapt the PA program (refer to *Appendix G*). Participants are mainly recruited through the ACH and the Kids Cancer Care Foundation. Parents are also asked to authorize the exchange of information pertinent to their child's health between ACH and the PEER program in order to ensure their child's safety.

Ensuring Sustainability

Student run

Both the Thrive Centre and PEER model operate by utilizing student volunteers. This is advantageous for 2 reasons: 1) due to the economic burden that cancer survivors and their families endure, it is important that we offer this program without any cost; 2) the volunteers gain invaluable clinical and practical experience with this unique population.

Engaging community organizations

The PEER program operates in partnership with Kids Cancer Care. This partnership has



PEER participant doing core training

funds a CEP or cancer and exercise specialist to ensure the safety of the program. In addition, the program runs out of the Gordon Townsend School located in the ACH. This strengthens the program's credibility, as patients and parents are able to see firsthand our connection with the hospital. This partnership has also increased accessibility for those children that are hospitalized. Future directions aim to expand the program to be available at other locations in Calgary.

Research indicates that cancer survivors are more likely to engage in PA if recommended by their physician. As such, it is crucial that primary nurses, child life specialists and physicians/oncologists are aware of the positive impact of PA on the childhood cancer patients' well-being, as their recommendations are directly linked to recruitment and



participation in PA programming. In our experiences, the relationship created with the hospital from the beginning has facilitated fluent communication with health care providers and also helped participant's parents to feel confident in the program and the potential benefits for their child.

Main Barriers and Limitations of the Program

Many parents are reluctant to have their children join the program if they report being tired, therefore children tend to miss many sessions. For this reason, early education surrounding the importance, benefit and safety of PA throughout the cancer journey is required for parents and caregivers. Another limitation is managing a group session with a wide variety of ages, capabilities and limitations. Ideally, we would have a program exclusively for teenagers. However, due to a low number of potential participants, we have been unable to facilitate such a program.

Lesson Learned

Education of parents that PA is safe, beneficial, and strongly encouraged throughout the cancer journey is absolutely essential for the success of PEER. Parents also need to be aware that PA should be fun and enjoyable for their child. These are two key factors that need to be promoted in any PA program designed for kids in order for PA to be adopted as a lifelong practice.

Future Directions

Kids Cancer Care is supporting PEER in its growth as a program. As the class attendance continues to grow, there is potential for multiple classes a week and/or multiple locations around Calgary for different age ranges. With hopes of expansion, we are creating a manual of the PEER program to enhance consistency across sites, and promote PEER within other organizations that may wish to reproduce this program.



Play Strong

Program Development

Play Strong was developed by athletic trainers and physicians at Nationwide Children's Hospital, Department of Sports Medicine (Columbus, Ohio, USA). The current program was developed in 2011 and the first patient was seen in early 2012. Play Strong does not require any outside funding because our services are billable to insurance. The department's administration made a commitment to devote staff time for the development and implementation of the program.

Running and Supervision of Play Strong

Participants in the Play Strong program are led and supervised by licensed **athletic trainers** (**ATs**) under the direction of physicians. ATs must graduate with a bachelor's or master's degree from an accredited athletic training education program that encompasses the prevention, diagnosis, and intervention of emergency, acute and chronic medical conditions involving impairment, functional limitations, and disabilities. ATs must become both nationally certified and licensed by the states in which they practice. ATs are similar to **Accredited Exercise Physiologists (AEPs)** and **Certified Exercise Physiologists (CEPs)**.

In addition to this general skill set, the Play Strong ATs have specific experience in Functional Rehabilitation: returning athletes back to sport. This return-to-sport progression framework allows the ATs to break down a movement to its simplest form and assist the patient in developing the strength, balance, and control necessary to perform that skill. Over time, they combine skills until the final movement is reached. The development team has also completed the American College of Sports Medicine's Cancer Exercise Trainer six-week webinar series (AACSM/ACS Cancer Exercise Trainer. http://certification.acsm.org/cet-webinar)⁹.

Program Description

Play Strong aims to guide pediatric, adolescent, and young adult cancer survivors in a safe transition back to PA, whether the goal is simple play or return-to-sport. Along the way, improvements in functional movement skills, muscle strength and power, balance and coordination, and confidence are addressed. Confidence is gained not only by the participants, but also by the parents as they are witnesses to their child's progressing ability to execute the



PA skills listed above. By bearing witness to their child's improved functional movement, parents are granted peace-of-mind knowing that their child is on a path of physical literacy. With the new or re-established confidence in the child and consistent parental support, patients and survivors have the fundamental tools to be active throughout their lives.

The participants' progress is monitored using discrete, quantifiable measurements. Participants are examined on a series of tests that measure functional movement skills, balance, flexibility, agility, core strength, upper/lower extremity power, and cardiovascular endurance. We also have the participants complete a survey at the beginning and end of the program to assess their thoughts and attitudes towards physical activity (see text box for testing protocol).

An important component in Play Strong is the inclusion of game play and fun in each class. This is done both to create an atmosphere in which the participants want to be involved, but also as a way to obtain compliance to their home PA program. What is more likely to happen at home? (1) child performs squat exercises or (2) child, who loves

Assessment

- ✓ Resting Heart Rate / Blood Pressure
- ✓ Height/Weight
- ✓ Balance Error Scoring System (BESS)
- ✓ Sit-up Screen
- Squat Screen
- ✓ Edgren Side Step Test (modified)
- ✓ Sit & Reach Flexibility Test
- ✓ Chest Pass (seated)
- Vertical Jump
- ✓ PACER Test

football pretends to be a quarterback taking a snap from center? Both accomplish the same task, but are thought of very differently by the participant. Although many of these participants are motivated to return to play, the training can be difficult, both physically and mentally. Doing something because it is fun does not require any extrinsic motivations. The participants are not doing it because they want to achieve a specific outcome but instead because it is enjoyable. That is the key to Play Strong. They are simply playing and when they improve their measurable deficits, everyone wins.

Play Strong meets twice weekly with participants entering on a rolling admission via an 8week referral. Many participants continue on for a second or third 8-week referral depending on participant needs and insurance coverage. Play Strong is conducted in a small group setting whenever possible; after all, game play is better when you have more kids with whom to play. However, at times the physical deficits and individual needs of a participant require 1:1 attention.



Participants

Participants need to be referred into the Play Strong program by their oncologist. Included in the referral is a clearance for PA and any restrictions they have. Physicians are asked to include the specific cancer type and any pertinent treatment history that may affect



Cancer survivor in a Play Strong session

participation status. In some cases, the oncologist has also obtained clearance from another physician, e.g. a cardiologist or orthopedist, depending on the participant's treatment history. Finally, Play Strong asks for any other diagnoses that are a result of the cancer and/or its treatments, such as abnormal weight gain or physical deconditioning. A few other criteria for entry have to be met. Play Strong participants must be able to work independently and also socially in a group setting. Participants also have to be mentally ready to change and increase their current physical activities. If the participant is not ready, they may not be successful. The participants are grouped based on their skill levels and age. The youngest participants that the program had were six years of age. They were grouped together with other 6 to 8year-olds and the class format was vastly different than if the participant who was returning to his varsity

high school soccer team.

The participation in the Play Strong program does not affect their involvement in the Oncology Survivorship Clinics that occur at various times post-treatment. As part of the program, summary notes to the oncology clinic team updating the caregivers of the progress the participants have accomplished.

Sustainability of the Program

As mentioned previously, the program is billable to the participant's insurance. Therefore, outside funding is not required. There is simply a commitment from our department and hospital administration to keep this program ongoing. As with other therapies within the hospital, as long as the Play Strong program can demonstrate existing deficits and work



towards the improvement and eventual elimination of these deficits, the cost of the program is cover by the patient's insurance.

Main Barriers and Limitations of the Program

The main limitation to the Play Strong program is the referral source. Play Strong is located in the the only hospital in the country with two sports medicine buildings for kids with dedicated gym space for programming. The program is geographically limited to the numbers of cancer survivors who are (1) in the easily traveled distance from our locations, (2) ready to change their behaviors of physical activity, and (3) willing to attend more hospital visits related to their cancer after the hundreds they have already completed.

In addition, Play Strong has had to educate the oncology providers that ATs are different from personal trainers. ATs are healthcare providers and are well-versed in the cancer-care setting. This is especially important in the pediatric oncology population, when it can be critical to recognize the warning signs of recurrence, when it is appropriate to progress or halt a progression, and when a referral back to their oncologist is needed.

Lessons Learned

The biggest lesson learned was how to include the parents of the participants. In every case thus far, the parent has been extremely enthusiastic about this program. While that is a great thing, it can sometimes be counter-productive to the progress of the participant. In order for Play Strong to be successful and in order for the participants to begin changing their activity habits at home, the participants need autonomy. They need to be the ones making the choices for change. They need to initiate when their screen time ends and what PA is performed. If the inclusion of increased PA becomes a battle between parent and child, then PA can be thought of as a punishment. It has been our stance to instruct the parents to be supportive of every effort the participant is making in changing their habits, but not in a controlling manner. It can be difficult for many, if not all, the parents not to push the participants, but it is needed.

Future Directions

While it is important to increase PA after treatment has concluded, having participants as active as possible during treatments is important too. The next step is to expand to the Inpatient population. The idea of play will again be vital, but the intensity levels and expected limitations will obviously be much different.



University of South Australia and Little Heroes Physical Activity

Program

Program Development

In 2009, the Little Heroes Foundation (formerly the McGuiness-McDermott Foundation) sought expressions of interest for the provision of a PA-based program for childhood cancer survivors within their Survivorship Services program.

The Little Heroes Foundation is a charity organization that supports children with serious illness by raising funds for essential equipment and services for the children and their families. The proposal put forward by the School of Health Sciences from the University of South Australia was the successful applicant due to the evidence based nature of the program and the individualized services proposed. An element which also appealed to the Foundation was that the program would not be hospital based or supervised by doctors in a clinical setting, yet would still be safe for participants and specific to their needs. Based on a collaborative approach, the Little Heroes Foundation provided funding for development and delivery of individual PA

programs by an **Accredited Exercise Physiologist (AEP)** for the participants including pre and post testing, ten weeks of supervised PA sessions, plus program evaluation and reporting.

The School of Health Sciences from the University of South Australia provided in-kind

What is an Accredited Exercise Physiologist?

Exercise physiologists hold a four-year equivalent university degree and are allied health professionals who specialize in the delivery of exercise, lifestyle and behavior modification programs for the prevention and management of chronic diseases and injuries. Exercise and Sports Science Australia is the regulatory body responsible for accreditation of Exercise Physiologists (http://www.essa.org.au/). AEP's are equivalent to **Certified Exercise Physiologists (CEPs)** in Canada.

funding through the use of private consulting rooms, fully equipped gymnasiums, basketball courts, ovals and other multipurpose rooms plus equipment and the services of their Clinical exercise physiology staff. A unique element of this program was also the involvement of students within the Graduate Diploma in Clinical Exercise Science, and the Human Movement and Health Studies programs, who assisted in the delivery of the AEP-supervised PA sessions. The initial program proposed by the School of Health Sciences was developed by PhD qualified academic staff, AEP's working within the School of Health Sciences Exercise Physiology Clinic, and students completing practicum placements within the Exercise Physiology Clinic as part of



their Graduate Diploma studies. The proposed program ran for the first time in 2010 on the City East Campus of the University of South Australia. In 2011, 2012 and 2013, the program extended and was offered at a range of different locations across the Adelaide metropolitan region, with the program concluding in April 2013.

Running and Supervision of University of South Australia and Little Heroes Physical Activity Program

The PA programs were prescribed for the specific needs of each participant by an AEP, and delivered with support and assistance provided by students from both the Graduate Diploma in Clinical Exercise Science and Human Movement and Health Studies programs. In delivering the service the AEP's worked closely with other medical and allied health professionals who were involved with the management of the participant as required. Within the Australian Health Care System an AEP is a recognized and qualified allied health professional trained in clinical PA interventions for individuals with, or at risk of developing, chronic and complex medical conditions and injuries. All AEP's involved in the delivery of the Little Heroes project were University trained AEP's with prior experience in clinical PA delivery, although not all had extensive experience with cancer clients.

Program Description

The objective of the program was to provide a 12-week individualized evidence based PA program under the direction of an AEP for children within the Little Heroes Foundation Survivorship Services Program (children aged 5-18 years). The program also included clinical outcome measures for all participants taken pre and post participation. In its first year, only a single 12-week block was delivered and over the subsequent years, delivery was adjusted to 10-weeks (8 weeks PA with 1 week pre and post testing) to coincide with the South Australian School term. Additionally, in 2011 and 2012, multiple 10-week blocks were offered although each block was considered to be a stand-alone, with pre and post measures taken for each block. Providing participants still meet the age criteria, they were able to participate in multiple blocks throughout the year. The following briefly outlines the methodology used for each of the 10-week blocks.



- ✓ Week 1
 - Initial Consultation: Participant attended a 60-minute individual initial consultation with an AEP following recruitment into the program including the assessment of the outcome measures.
- ✓ Week 2
 - PA Prescription: Delivery of an individual PA program supervised by a PA Physiologist with assistance from students. Each session was 60 minutes in duration.
 - Home-based PA Prescription: Provision of a home-based program to support the supervised sessions
- ✓ Weeks 3 9
 - PA Delivery: Ongoing monitoring of program by the AEP on a weekly basis (up to 2 sessions per week per participant).
- ✓ Week 10
 - Review Consultation and Report: Outcome measures were reassessed, participant satisfaction was evaluated, and reporting performed.

While the PA programs developed were individualized for each of the participants, the younger children between 5 and 10 years of age typically performed activities with a focus on motor skill development, movement coordination, endurance and fitness. These were performed in large open rooms, on basketball courts and on ovals (note: when possible children with similar physical capabilities attended in small groups (2 to 3 children) which allowed the sessions to include game play and socialization). The older children in the 10 – 18 year age group typically performed their sessions in a gym-based setting with more of a focus on strength, endurance and PA self-efficacy. As with the younger children, individuals were typically paired with others of similar ability for the session (maximum of 2 individuals) although they still performed their own programs. For some individuals with complex presentations (e.g., blindness), sessions were always conducted as one-on-one supervised sessions. While the description provided here does separate the participants into two age groupings (5-10 and 10-18 years), these groupings were only used as a guide for PA assessment and were not strictly enforced due to the individual nature of the PA prescription.

Individual goals were developed for each participant during the initial consultation and therefore the specific objectives for each individual varied. However, the overall objective for the program was to provide a safe structured PA program for pediatric cancer survivors. As many of the participants had been inactive during their developmental years due to their illness, the



program aimed to allow the participants to regain function and restore their fitness to a level that would allow them to participate in main-stream sporting activities with their peers. For many of the participants, this included restoring their enjoyment and confidence in performing PA. As mentioned previously, for younger participants the program aimed at assisting in gross motor skill development, which was commonly delayed due to the period of inactivity during the child's illness. This focus on restoring the participants' enjoyment of PA and confidence in their own abilities was a key component of the program and one of the reasons it was so successful.

In the first year of the program, pre and post measures included the anthropometric measures of height and weight, motor skills assessment (McCarron Assessment of Neuromuscular Development), self-reported physical activity levels and self-reported enjoyment of physical activity. In the second and subsequent years this was revised to standardized testing protocols to ensure reliability (see text box) ¹⁰⁻¹².



In instances where the participants could not complete all testing due to physical limitations, other testing such as balance testing was included to ensure a clinical outcome for that individual pre and post PA intervention. As with the above testing, any additional testing was performed using validated and reliable measure to ensure accuracy in detecting changes in the measure. In addition, the participants (10-18 years), or their parent/guardian (5 -10 years) were asked to complete a questionnaire about the child's physical activity levels which included questions relating to their willingness to perform PA, how well they typically performed in sports related activities, and how they felt they performed compared to their peers (refer to *Appendix 13.B*).



Participants

The participants, who were all aged 5 to 18 years, were recruited by the Little Heroes Foundation through their survivorship service, with all interested participants contacted by the programs senior AEP to book an appointment for an individual initial consultation. Written



consent was obtained from the parent/guardian of all participants, and a medical clearance sought from the participant's general practitioner/oncologist as needed. To be suitable for inclusion into the program, participants were required to be "off-treatment" as stated by their Oncologist, and therefore would not be undergoing any active treatment. Some individuals however, were still receiving on going treatment for conditions

Jacey, 5

related to their cancer but were considered to be 'off treatment'. Some individuals had been off treatment and considered cancer free (or in remission) for several years while other were still receiving regular monitoring having only recently completed treatment. Additional information was sought from other members of the individual's medical team such as oncologists, physiotherapists and occupational therapists as needed following the initial assessment to guide PA prescription. Additionally, the parents/guardians of all participants were asked if they would like post program reporting to be made to any member of the child's health care team, with a number opting for this to occur. While Acute Lymphoblastic Leukemia was the most common diagnosis of participants, inclusion or exclusion was not based on a specific cancer diagnosis for participation in the program.

Sustainability of the Program

The sustainability of the program that was developed means that it does require an ongoing funding commitment, with the funding primarily for the cost of the time of the AEP's involved. The amount of funding required is therefore directly related to the number of participants involved in the program at any given time. For the program described above,



services were offered at cost, as it was not developed as a program that would be offered as an income generator but rather a collaborative project. An alternative to this would be for the program fee to be paid by the participants. Although a number of the parents/guardians were interested in this option when the program was finished in 2013, it was not pursued. Another option would therefore be to look at a mixed payment option where some of the program is funded and then the gap in funding is met by the participants. This would most likely represent the best option for long-term sustainability of a program if it were to be offered on a large community scale.

If the funding source for this program however were changed, additional avenues for recruitment would need to be explored. The program explained here was specifically for individuals within the Little Heroes Survivorship Program and this was the referral avenue. More advertising and promotion of the program would also be required if participation was open to other individuals who had previously had cancer and were now off treatment.

Main Barriers and Limitations of the Program

One of the main barriers to the program was finding a location and time that was suitable for a majority of the participants and their parents/guardians. While a variety of times were offered earlier, times were reported as being difficult due to travel immediately after school, while later times interfered with family dinner preparations or sporting commitments of older siblings. Many parents/guardians were also reluctant to let children attend if they had been unwell, meaning that sessions were frequently missed due to illness.

Lessons Learned

Over the duration that the Little Heroes program was offered, one of the biggest lessons learned by the AEP's offering the program was the importance of education for the parents/guardians with regards to PA and their child. Due to their child's previous illness, a number of the parents/guardians were unsure of their child's capacity for PA and often showed caution when allowing their child to participant in activities due to concerns of illness or injury. For some participants, this 'protective' instinct meant that inactivity was contributing negatively to their child's health with high levels of sedentary behaviors, obesity, poor cardiovascular fitness and a dislike of PA seen in many participants. While the PA program was targeted at the child participant during the initial consultation, time was needed to be spent outlining to both the child and the parent/guardian how PA would benefit the participant, the evidence for PA in



relation to cancer survivors and also how a safe prescription would be implemented. Explaining how the prescribed PA would meet the specific goals of the participant was also important from a long-term behavior change perspective.

Future Directions

In 2013, restructuring of the Little Heroes Foundation changed the funding available for ongoing projects and as such the program described above ceased to be offered. The design and overall concept of the program however demonstrated strong clinical outcomes for the participants involved during the time that it was offered. A strength of the program was the individualized evidence-based nature of the PA prescription. This means that the program as a concept could easily be offered to other client groups and would not be exclusive to an oncology group or a pediatric group. Using students from a University setting in assisting in delivery of programs such as this not only enriches the experience of the participant, but also provides much needed clinical experiences for students.

Take Home Message

As evidenced by the three programs highlighted in this chapter, communitybased physical activity programs for pediatric cancer survivors are feasible, beneficial and potentially sustainable through various funding models. These three programs emphasize the need for well-trained staff to facilitate exercise sessions, as well as strong communication between the staff members, clinicians and family members. Also, it was consistently noted that the design of the program should facilitate a fun environment that supports the growth of confidence among participants and also includes parent participation and support. Offering programs with an individualized approach, while still capitalizing on peer social support through fun and interactive activities, is ideal.

Significant future research is warranted to examine the effective methods of PA program development in pediatric oncology. Studies examining factors associated with external validity, using frameworks such as RE-AIM, as well as economic evaluation, will further bolster the ongoing development and sustainability of these programs.



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	PEER Curriculum
	Overall Expectations
Fund •	<i>Idmental Movement Skills:</i> The overall objective of the PEER Curriculum is to introduce and teach fundamental movement skills to allow our participants to gain better competency, knowledge and understanding fundamental movements in sport and activity and therefore become physically literacy. With this understanding we hope that our participants will have smooth transitions engaging in
Activ •	prysical activity in their communities. e Living: PEER participant will be able to understand the benefits of participating in physical activity, the guidelines and challenges associated with physical activity, as well as ways to maximize safety for themselves and others. Health-Related Fitness: Restore healthy levels of fitness in order to diminish fatigue, increase confidence and improve quality of life.
Heali •	<i>thy Living:</i> The healthy living component is aimed to teach participants about their bodies and give them tools to actively participate in healthy living practices throughout their lives. These skills include basic nutrition knowledge in conjunction with Canada's Food Guide, Rate of Perceived Exertion and Pain scales, relaxation and recovery techniques, Heart Rate ranges, hand washing practices, and more!

ate Hard Active living Healthy living cion Application objective objective	Use of the logbook Safety. Understand the common terminology used in class as well as behavioral expectations and class rules.	 Running Review and understand the backwards guidelines and important Learn and practice of physical activity proper hand washing techniques and importance of washing hands in prevention of illness
Moderate pplication of skill		printing
Easy I application A of skill		- Breaking - S down movement - Running on the spot -Slow run or jog
Fundamental Movement Skill	Baseline test	Run
Week	1	5

ţ in January, 2014. In order to offer a safe and fun physical activity program for this specific population we based the development of this curriculum in the following resources:

- The Ontario Curriculum http://www.edu.gov.on.ca/eng/curriculum/elementary/healthcurr18.pdf •
- Physical literacy concept paper http://www.physicalliteracy.ca/sites/default/files/Physical Literacy Concept Paper.pdf
- CS4L Physical Literacy http://www.physicalliteracy.ca/sites/default/files/imce/Physical%20Literacy%20Movement%20Preparation%20Guide Web.pdf
- Fundamental Movement Skills I and II (PHE Canada).
- Scientific review about unmet needs of children and youth with cancer.

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Acknowledge: Ashley Fox, BKin, CSEP-CEP, NCCP. Be Fit For Life Centre University of Calgary - Active Living



WEEK 2- RUN (example session)

Objectives:

- Movement Competence objective (Skills & Concepts):
 - o Fundamental skill: RUN
 - Body awareness: body mechanics, moving legs and arms, keeping head up bending knees and arms at 90 degrees
 - Spatial awareness concept: being aware of who is around you and what is around you, awareness of pathway to movement.
 - Effort awareness concept: understanding difference in effort (sprinting, jogging and distance)
 - Relationship concept: relationship with others playing with you and the surroundings. Focus on sportsmanship and respect
- Active living: overview of Physical Activity Guidelines
- Healthy living objective: hygiene

Healthy Living Instructions – 15 minutes

At the beginning of class, talk about the importance of washing hands with all the participants. First ask them what they think, and then explain to them that washing your hands is one of the best ways to prevent the spread of illness and disease! It helps protect YOU and helps protect OTHERS from getting sick.

Go over the following guidelines and then practice washing hands in the bathrooms (split girls and boys). Use the neon gel and see if they can wash it all off!

Use warm, running water Use soap and rub hands together vigorously for 15-20 seconds (DON'T forget under your nails and fingertips!) Rinse thoroughly and dry off hands

1) Dynamic warm up - 5 minutes

Active Living	During the warm up volunteers are to mention what the physical activity
Instructions	guidelines are for children (60mins of moderate to vigorous physical
	activity 5 days a week, strength training two days of the week, and
	flexibility training most days of the week).
Side Scuttle	Participants begin perpendicular to the start line. Lowering themselves
	into a squat position, they will take a large step with the leading foot,
	making sure to keep toes pointed forward. Maintain a steady pace and
	change lead legs once halfway line has been reached.
	*Head should maintain a constant level throughout.
Horse Trot	In short, quick steps, drive the knee upward as close to chest as possible.



	Important that contralateral forearm drives up with knee.
Butt kicks	In short, quick steps, bring the heel as close to the bum as possible. Keep toes dorsiflexed. Make sure that upper leg stays perpendicular to the floor during the movement. Important that contralateral forearm drives up with heel
One foot	Participants will hop three times, for distance, on one foot. After the
hops	third hop, switch legs and repeat.
Twisty turkey	Participants will begin parallel to the start line. With a two-footed jump, participants will spin 180 degrees in the air and land on two feet. Jumping again, they will return to the original position and jog to the centerline. They will repeat, the two jumps and jog to the finish. Over the course of the semester, the number of jumps can increase.
Alternating Banana	Begin by standing with your arms straight above you and raise a one leg while fully extended and bring the opposite arm down into a banana shape. Switch legs and repeat

2) Circuit strength training- 7 minutes

We will do 30 seconds in each station and then they will go to the other station using if possible the fundamental skills

- 1. Throw medicine balls in pairs
- 2. Jump rope in pairs
- 3. Rowing with elastic bands in pairs
- 4. Squat with medicine balls in pairs
- 5. 30 degrees sit up in pairs while they pass a ball
- 6. Jump in the trampoline
- 7. Scooter race with belly in the scooter using their arms

3) **Description of Skill/ Movement Concept – 15 minutes**

- ✓ Run: "Move fast by using one's feet, with one foot off the ground at any given time"
- ✓ Ask the participants to show you the skill... Should give you base line of there knowledge
- ✓ Want to break down the movement from head to toe.
- ✓ Focus on keeping head up with straight spine
- ✓ Ask participants to try and run without moving their arms. Have them see the difference when they move their arms.
- ✓ Reminder to keep arms bent at 90 degrees and move opposite arm to opposite leg.
- ✓ For legs want to practice track A's and B's
 - ✓ A's: have the participants do high knees up to 90 degrees and alternate arms with legs.



B's: bring legs up to 90 degrees and then extend from the knee and then bringing foot down.

- ✓ Show difference between running with flat feet, on the balls of your feet and on heels (balls for your feet should be fastest when sprinting)
- ✓ Have kids try different speeds for running while maintain correct form
- ✓ If they are ready have them try to run backwards
- ✓ Relay race putting all the components of the run together, arms, legs and feet

4) Games – 15- 20 minutes (suggestions only pick two or three)

- ✓ Red light, green light (focus on different speeds and form)
 - Have participants line up on the back line
 - A volunteer will either yell "red, green or yellow light"
 - Participants move depending on what light it is
 - Red light is stop, green light is sprinting, yellow is walk
 - Have kids focus on proper mechanics of running
 - Yell Autoban if your want them to sprint.
- ✓ Variety of tag games: freeze tag, toilet tag, revenge tag, etc...

- Freeze tag: once you get tagged you need to freeze in that position and someone needs to run around to for you to be "free"

- Toilet tag: once you get tagged you need to get on one knee and someone sits on your knee and flushes you.

- Revenge tag: Everyone is it. If you get tagged you sit down until the person who tags you gets tagged

Want to keep the participants running and moving in a variety of different directions
 ✓ Capture the Flag:

- Split the group into two teams
- Have beanbags behind the back lines use that as flags or treasure
- Split the gym into the two halves each team get a half
- Team can tag other team once they are on there half
- People are safe behind the back lines
- if you get tagged you sit down or go back to your half
- you can only get one treasure or save one person
- Cannot throw the treasure
- remind about sportsmanship and respect
- ✓ Relay races (focus on form and speed)

5) Cool down and static stretch – 5 minutes

Routine 1 of the yoga handout.

We can also ask questions for the fundamental skill worked and the active and healthy objectives.

Make sure that parent handout is passed out.


Appendix 13.B







Child Physical Activity Attitudes Questionnaire

Date of assessment: / / Pre / P	ost assessmen	t A	Assessor:		
	Not at all	A little bit	Some- what	Quite a bit	Very Much
I can be physically active on most days of the week?	0	1	2	3	4
Do you like playing games?	0	1	2	3	4
I can participate in activity when others make fun of me?	0	1	2	3	4
I could participate in activity even if I was not good at it?	0	1	2	3	4
Do your friends do physical activities or play sports with you?	0	1	2	3	4
I am self-conscious about my looks and ability when I exercise or play sports?	0	1	2	3	4
My health means I'm not good enough to participate in activity with my friends	0	1	2	3	4

Note. Adapted from: Ward DS, Saunders RP and Pate RR 2007, *Physical activity interventions in children and adolescents*, Human Kinetics, Champaign, Illinois.



Chapter 14

Yoga in Pediatric Oncology

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Learning Objectives

After completing this chapter you will know:

- ... the existing literature on yoga for childhood cancer patients and survivors.
- ...the potential benefits of yoga for this population.
- ...key considerations in developing a yoga program for this population.
- ...future research directions in yoga and pediatric oncology.

Introduction

Yoga is increasingly recognized as an important addition to cancer care programs for adult patients and survivors ^{1-4.} Yoga employed in clinical contexts is commonly defined as a gentle **physical activity** (**PA**) that combines physical postures (*asana*), breathing exercises (*pranayama*), and meditation (*dhyana*) ^{4, 5}. Yoga offers the potential for both psychological and physiological benefits. The evidence gathered from adult cancer populations ^{1, 2} and reviews by Galantino et al., ⁶ and Birdee et al., ⁷ highlight the psychosocial and physical benefits of yoga for pediatric populations. Although the evidence is preliminary, research suggests that yoga may be a promising form of alternative PA for childhood cancer patients and survivors.

Yoga Benefits: Research Findings

Table 14.1 provides an overview of the four research studies that have been performed exploring yoga and pediatric oncology/hematology. Research by Geyer et al.,⁸ investigated the feasibility of a therapeutic yoga program on the **quality of life** (**QOL**) in children hospitalized with oncological/hematological diagnoses. The authors designed a yoga protocol, **Bendy Kids**



Yoga (BKY), with the help of trained physical and occupational therapists and rehabilitation aides, that incorporated stretching, strengthening, balance, breathing techniques, relaxation, and body awareness ⁸. The authors found statistically significant differences in children's self-perceived physical function. Specifically, children reported positive changes in walking, running, participating in play, sports and exercise, lifting heaving objects, bathing, need for help with chores, and levels of aches, pains, and energy. There were also trends toward significance on children's rating of their emotional and social function.

Authors	Sample	Intervention	Findings/Conclusions
Geyer et al. ⁸	N=6 MOD	1 (BKY) session/week for 5 weeks; (60 minutes/session)	Improved child perception of physical function
Moody et al. ¹¹	N=20 MHOD	1-3 individualized yoga sessions (duration not specified)	Improved pain and anxiety scores Patient quotes suggest yoga was beneficial (relaxation)
Thygeson et al. ⁹	N=16 MHOD	1 group yoga session (45 minutes/session)	Improved anxiety Improved general well-being
Wurz et al. ¹⁰	N=8 MOD	12 week program; 2 group yoga sessions/week (60 minutes/session)	Feasible (based on recruitment, retention, attendance, and reporting of adverse events) Improved patient and parent
			reported QOL Improved hamstring flexibility Improved functional mobility Improved PA levels

Table 14.1. Summary of yoga research in pediatric oncology.

Note. BKY: Bendy Kids Yoga; MOD: mixed oncology diagnoses; MHOD: mixed hematology and oncology diagnoses; ROM: range of motion; PA: physical activity; QOL: quality of life.

Another study by Moody et al., ¹¹ found reductions in pain and anxiety scores in their 20 pediatric oncology/hematology patients, suggesting that yoga was beneficial especially for relaxation. Similarly, Thygeson et al., ⁹ concluded that yoga was a feasible intervention for their 16 children and adolescents affected by cancer and blood-disorders. Finally, Wurz et al., ¹⁰ found their 12-week community-based yoga program was feasible based on recruitment,



participation, and the lack of adverse effects. Moreover, participants reported improved QOL, functional mobility, hamstring flexibility, and PA levels over the course of the intervention.

To our knowledge, there are only four studies investigating the benefits of yoga with pediatric oncology patients and survivors. Although these studies show preliminary benefits, the field is still limited and it is difficult to generalize results. However, a much larger body of evidence shows that yoga in adult oncology ^{4, 1,} as well as in other clinical pediatric groups, is associated with a range of psychological, social, neuromuscular, cardiopulmonary, and musculoskeletal benefits ^{6, 7}.

Yoga: Practical Recommendations

There are no existing guidelines for the adaptation of yoga to the needs of pediatric oncology patients and survivors. However, based on our experience with a 12-week community based yoga program ¹⁰, basic therapeutic modifications and considerations can be made based on the cancer diagnosis and associated treatment-related side effects.

Therapeutic modifications

Below is a list of modifications that the authors found to be beneficial when teaching yoga to pediatric oncology patients and survivors through their research projects and evidenceinformed Yoga Thrive for Youth community program (refer to *Appendix 14.A* for website for more information). An example of their general class plan can be seen in *Appendix 14.B*, and images of the poses described below can be seen in *Appendix 14.C*. Prior to participating in yoga, the child should be cleared for PA by their physician, and any concerns that may limit activity should be clearly communicated to the yoga instructor.

- Balance: Pediatric oncology patients may experience dizziness, peripheral neuropathy, or a general decreased sense of balance as a result of cancer and its treatments. The use of a wall, chair, or floor to modify poses can address this consideration. For example, if a participant is experiencing balance issues, they may do Tree Pose/*Vrksasana* (standing on one leg with the opposite leg lifted, externally rotated and the foot propped against the inside of the calf or thigh) while holding on to the back of a chair or placing one hand against a wall (refer to *Appendix 14.C* for image).
- Weight-bearing: Children with bone tumors (pre and post-surgery) may not be able to bear weight on one or both legs for extended periods of time. Similarly, children who are experiencing dorsiflexion-range of motion issues may have difficulty rooting down



through both of their feet. In these cases, the use of a wall, chair, or floor to modify poses is important. For example, if a participant is experiencing weight-bearing issues, they may do Tree Pose/ *Vrksasana* while fully reclined on the floor. Or they may perform a variation of a pose such as Crescent Moon/*Alanasana* with the thigh of the affected limb placed on the seat of a chair for support (refer to *Appendix 14.C* for images).

- *Fatigue:* There are several adaptations to account for fatigue. Some examples include: starting with shorter yoga sessions (e.g., 10 or 20 minutes) and progressively increasing the duration; holding yoga poses for shorter amounts of time and progressively increasing the duration; and offering props to modify poses and account for differing energy levels among participants. Instructors can also offer chairs to modify standing poses so participants use less muscular strength, which may enable them to hold a pose for a longer period. For example, as with the weight bearing example above, a participant may use a chair for Crescent Moon/*Alanasana*, or perform Tree Pose/*Vrksasana* lying down. It is also important to offer participants rest throughout the yoga class. For example, invite students to take Relaxation Pose/*Savasana* (lying flat on the ground with arms and legs extended) or any other resting seated/reclined pose when needed (refer to *Appendix 14.C* for images). Another possibility is to start and end class with restorative poses and breath work, which will allow participants to conserve and build their energy appropriately.
- Range of motion (ROM): In instances when ROM of any joint is affected by peripheral neuropathy or surgery, the instructor should offer modifications and cue participants to move within the current ROM without pain.
- Pain: Do poses slowly with the breath, and/or hold the poses for a shorter period of time.
 It is important that any activity not be associated with pain. The participant should stop yoga if they experience pain, and it may be appropriate to consult with a physician.
- *Props:* In addition to chairs and walls, props such as yoga blocks, blankets, and bolsters may be important in a therapeutic setting. For example,
 - ✓ In Standing Forward Bend/Uttanasana (refer to Appendix 14.C for image), participants can rest their hands on blocks, the back of a chair, or a short table if they are unable to reach the ground comfortably.
 - ✓ In Seated Forward Bend/Paschimottanasana, sitting on a blanket or bolster elevates the hips above the knees, which can help increase comfort in the pose and a participant's ability to lengthen their spine.



✓ Placing a bolster under the knees in Relaxation Pose/Savasana may help alleviate discomfort in the lower back.

Areas of emphasis

As noted above, yoga offers participants potential psychosocial as well as physical benefits, which can be encouraged through a number of group or individual activities. These are a few examples taken from the authors' experience in their yoga research ¹⁰ and the Yoga Thrive for Youth community program.

✓ *Breathing:* A focus on breathing during yoga poses can strengthen children's attention and energy during class. Specific breathing exercises (pranayama) may also be used to help participants learn relaxation techniques. For example, in the authors' 12week yoga intervention several breathing exercises were found to be useful, including Balanced Breath, Elongated Exhalation, Bharmari Breath, Chandra Bhedana, and Peace Breath. As for all PA, breath work needs to

Sample Breathing Exercises

- Balanced Breath: Inhale and exhale equal counts. Focus on the belly expanding on inhale, and falling back on exhale. Can be performed sitting, lying, or standing.
- Élongated Exhalation: Inhale focusing on the belly expanding and exhale longer (than the inhale) with belly contracting. Can be performed sitting, lying, or standing.
- Bhramari/Bee Breath: Inhale through nostrils, and exhale making a buzzing sound at the back of the throat (lips gently touching). Should be performed seated.
- Chandra Bhedana/Moon Piercing: Block the right nostril with right hand and inhale through the left nostril, then switch and block the left nostril and exhale through right nostril. Repeat this same cycle a few times. Should be performed seated.
- Peace Breath: Inhale through both nostrils and exhale saying peace (or any other word). Should be performed seated.

be individualized. Each participant should be taught to monitor his or her efforts so as to maintain a smooth, rhythmical, tension free, and regulated breath.

- Mindfulness/focus: Yoga offers participants an opportunity to focus on the present, which can be beneficial as they may experience distress as a result of the cancer and related treatments. Ways to cultivate mindfulness among participants include the use of:
 1) breathing exercises; 2) guided visualizations; 3) affirmation meditations; and 4) challenging, yet safe, yoga poses (e.g., standing balances).
- ✓ Deep relaxation: Providing participants with 10 to 15 minutes of relaxation at the end of class is important for helping them to slow down their heart rate and breathing, as well as absorb the benefits of their practice. Participants should lie in a supine posture, such



as Relaxation Pose/*Savasana*, and be guided into relaxation, meditation, and/or visualization by the instructor. Using props to ensure comfort (e.g., bolsters under the knees) may aid the relaxation process. Providing participants with blankets will help keep them warm and increase relaxation. The use of gentle music and/or a focus on the breath during relaxation can also help participants maintain focus.

✓ Fun: As with all PA, children are more likely to participate in yoga if they find it fun. In a group setting, partner yoga poses or doing poses in a group circle can contribute to a playful environment. Children also enjoy making up their own names for yoga poses and incorporating those names promotes a sense of community in the class.

Areas of caution

In addition to the PA precautions specific to patients and survivors experiencing side effects (refer to *Chapter 5*), there are a few additional considerations for yoga practice.

- ✓ Inversions: Instructors should use caution with inversions, especially those that may put excessive pressure on the head. Therapeutic modifications and restorative poses, such as Legs Up the Wall/Viparita Karani variation (lying with legs up the wall), are more appropriate for this population because they are less physically demanding than traditional inversions.
- ✓ Weight-bearing: Participants at risk of fractures or who have recently completed surgery for a bone tumor diagnosis should not perform any weight bearing activity that has not been approved by their treating physician. Therefore, all poses should be modified, such as by performing poses reclined or by using props such as chairs.
- ✓ Balancing poses: Participants at increased risk of fractures (e.g., in the case of children with bone tumors or osteoporosis) should be encouraged to place their hands against a wall or on a chair for support to increase stability and reduce the likelihood of a fall.
- ✓ Forward bending: Avoid deep forward bends or moving up and down too quickly (with the head dropping below the heart) since this may affect balance/dizziness. To lessen the bend, participants can bring their hands to blocks or a chair instead of the ground.
- Pain: Participants who are experiencing acute pain should not be advised to do yoga, similar to general PA guidelines.
- ✓ Group size: When working with a group of patients and survivors, classes should be kept small (e.g., no more than 6 to 8 participants) depending on the physical limitations, immune system conditions, and needs of the group.



What to Look for in a Yoga Instructor

As with fitness instructors leading PA programs for pediatric oncology patients and survivors, a yoga instructor works as part of a team with the participant, their parents, and their health care providers. It is important to identify a yoga instructor with appropriate teaching credentials. There are no governing bodies for the certification of yoga instructors broadly, or in the fields of yoga for children or yoga for cancer survivors specifically. However, there are key qualifications to look for when interviewing potential yoga instructors. At a minimum, the instructor should have: 1) a 200-hour yoga teaching certificate; 2) certification and/or experience teaching children; and 3) certification and/or experience in teaching yoga for cancer patients or survivors.



While certifying programs in yoga for cancer survivors are limited, a yoga instructor may have related qualifications working in similar therapeutic environments or with other clinical populations (e.g., children with disabilities or other chronic illnesses). The Health and Wellness Lab at the University of Calgary has developed the Yoga Thrive Teacher Training Program, a 32-hour course for yoga instructors to learn therapeutic adaptations for adult cancer patients and survivors (refer to *Appendix 14.A* for a website to obtain more information on the program). Yoga therapy is an emerging field and some instructors may identify themselves as yoga



therapists if they have completed advanced training (e.g., one or more programs in addition to their 200-hour teaching certificate). Yoga therapists may have more experience teaching clinical populations than yoga teachers.

Research Limitations

One of the major issues in yoga research is a lack of methodological and standardized protocols. Yoga represents a myriad of practices, and studies often lack detailed descriptions of the specific protocol, the yoga style, and the qualification of instructors. Furthermore, one of the most pressing limitations in the research is the small, mixed populations reported (refer to *Table 14.1*). There is limited research regarding the required intensity, duration, and frequency of yoga needed to facilitate optimal psychosocial and physical changes, as well as the mechanisms by which these changes are produced. Finally, to date, the interventions undertaken have been short in duration, ranging from a single session to two sessions per week for 12 weeks ⁸⁻¹¹. The short periods of these interventions offers information on the acute effects of yoga, but does not evaluate the longer-term effects associated with continued yoga practice.

Future Directions

Yoga is a therapeutic form of PA that may be a promising tool for pediatric oncology patients survivors during and after treatment because of its beneficial effects on several aspects of one's QOL, including physical strength, psychological and psychosocial wellbeing, and selfconfidence. There is limited scientific evidence outlining the mechanisms that contribute to these improvements, and thus offers an exciting area for future research in pediatric oncology. Future studies are needed to explore how yoga protocols can be tailored to the different needs of patients and survivors. This poses a challenge to researchers to develop a rigorous protocol while remaining flexible to patients' and survivors' needs and treatment priorities. For example, consideration should be given to participants' ages, and thus studies separating children from adolescents may contribute to this knowledge gap. Future research might also explore how family-centered yoga programs can improve the health of pediatric oncology patients and survivors. For example, parents could guide children through simple yoga poses and breathing exercises with the support of a printed manual, take home handouts, video, or application on their phone or tablet device. Research could also explore how yoga supports children and adolescents during cancer treatment while also building confidence and behavioral patterns that help sustain an active lifestyle throughout survivorship.



Take Home Message

Yoga is a safe and beneficial form of physical activity for children with cancer. While further research is needed, preliminary findings demonstrate that yoga may improve child perceived physical functioning, reduce pain and anxiety, and promote general wellbeing. Future research will contribute to the development of effective strategies for offering yoga to patients and survivors at all points of the cancer continuum.

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Appendix 14.A

Websites

Yoga Thrive for Youth:

http://www.ucalgary.ca/healthandwellnesslab/programs/yoga-thrive-youth

Yoga Thrive Program and Teacher Training:

http://www.ucalgary.ca/healthandwellnesslab/programs/yoga-thrive



Appendix 14.B

Yoga Thrive for Youth General Class Outline

Category of Poses	Focus of Pose/Rationale for Use
Journaling*	To promote mindfulness.
Warm-Up	To warm-up the body with gentle supine movement. To integrate breath work and continued mindfulness.
Supine/Seated/Kneeling/Prone	To start introducing more physical poses to prepare the body for the standing sequence. To continue integrating breath work and mindfulness.
Standing	To challenge the body with standing and strengthening poses: Focus on major muscle groups and joints. To continue integrating breath work and mindfulness.
Supine/Seated/Kneeling/Prone	To start moving back down to the floor. To continue integrating breath work and mindfulness.
Cool-Down	To cool-down the body with gentle supine movement To continue integrating breath work and mindfulness.
Final Resting Pose	To accrue physical and mental benefits from the class.
Journaling*	To promote mindfulness.

* Optional if time permits.



Appendix 14.C

Yoga Poses Described in the Chapter

Tree Pose/Vrksasana (variations with the lifted foot on the opposite ankle or thigh)



Modified Tree Pose/Vrksasana (holding a chair)



Modified Tree Pose/Vrksanana (against a wall)





Crescent Moon/Alanasana (variation with support under the back heel)



Modified Crescent Moon/Alanasana (on a chair)



Standing Forward Bend/Uttanasana (variations with knees bent and table for support)





Relaxation Pose/Savasana (variations without and with support under the hamstrings)







To find out more exercises visit the Health & Wellness website:

http://www.ucalgary.ca/healthandwellnesslab/yty-manual to download Yoga Thrive Youth. Practices to promote wellness during and after childhood cancer treatment. Robyn Long, S. Nicole Culos-Reed and Gregory Guilcher. The Health & Wellness Lab, Faculty of Kinesiology University of Calgary. 2014.



Chapter 15

The Power of Play: Technology Enriched Physical Activity

Melanie Keats, PhD

Learning Objectives:

After completing this chapter you will know:

- ...how to describe the role active video games play in fostering increased activity enjoyment and motivation to participate in physical activity.
- ...the role of active video game play in reducing sedentary screen time and promoting physical activity and increased energy expenditure.
- ...the benefits and limitations associated with active video game play.

Introduction

The use of **physical activity (PA)** as a feasible, safe, and supportive adjunct to promote physical functioning and enhance overall **quality of life (QOL)** in adult cancer patients and survivors, both on and off treatment, has been well established ^{1, 2}. Although there remains a lack of comprehensive, systematic study of PA interventions for children and youth with cancer, emerging evidence suggests similar benefits may be safely attained ³⁻⁵. Although greater study is needed, given the potential range of both short and long-term benefits, there is a clear need to support PA opportunities among patients and survivors of pediatric cancer. What is less well understood however, is how best to promote physically active lifestyles in a predominantly sedentary and/or insufficiently active population ⁶⁻⁸.

Getting back on track to healthy growth and development in childhood and across the lifespan requires survivors to make major changes in their routine PA patterns. Yet this is easier said than done. For example, studies with healthy youth have shown that youth frequently cite numerous barriers to being physically active, including a lack of time and preferring more appealing (e.g., fun), often sedentary, alternatives to PA (e.g., watching television, spending time on the computer, playing sedentary video games)⁹. Additional barriers to PA include social



influences, accessibility, cost, weather, safety concerns and quality of play facilities ⁹⁻¹¹. These barriers can be even greater for children from low socioeconomic households, whose parents lack the finances to enroll their children in organized sports/activities. Although PA participation is further complicated by the additional influences of the medical and therapy-related effects associated with a cancer diagnosis, research with childhood and adolescent survivors has shown that young survivors who are appropriately supported (e.g., family, friends) can overcome these medical barriers and successfully engage in PA ¹².

Power of Play

Although PA is associated with numerous health benefits, it is clear that there remain significant challenges in attracting those who have a poor attitude (e.g., fear, dislike activity) towards PA and keeping those who do begin a program motivated to achieve lasting participation and thus the associated benefits. While several factors have contributed to our increasingly sedentary lifestyles, screen-based technologies have been the source of much

AVG Practical Recommendations

- Prepare a safe space with plenty of room to move and when playing a multi-player game, ensure that there is sufficient room between players to avoid contact and potential injury.
- Select a variety of games (e.g., dance, sport, fitness, fantasy, adventure) based on the interest and ability (age-appropriate).
- Select games with multi-player options to facilitate both cooperative and competitive game play (create challenges, tournaments and leaderboards to foster motivation).
- Be a positive role model PLAY TOGETHER (create family events/challenges, challenge physicians/nurses to a game).
- ✓ AVG are NOT meant to replace traditional PA.

recent attention. Screen time has been linked to an increased risk of disease and all-cause and cardiovascular mortality ¹³, and guidelines have been presented advocating for a reduction of sedentary screen time in youth (e.g., a 2 hour daily maximum) ¹⁴. Rather than competing with these highly attractive technologies, a novel strategy gaining momentum is replacing sedentary screen time with active screen time. Specifically,

active video games (**AVG**) are well-suited for individual, group, cooperative, and competitive game play and may be a viable method to reduce sedentary screen time and promote more active lifestyles ¹⁵⁻¹⁷.

An emerging body of research suggests that AVG are the "latest tool in the arsenal to improve health outcomes" ¹⁸. AVG capitalize on the interactive and immersive qualities of traditional sedentary games, but also incorporate additional "motion capture" technology that



fosters increased movement. A recent review by Barnett and colleagues ¹⁵ noted that the growing interest in AVG as a means of promoting PA is based on at least four key reasons. First, and perhaps most importantly, recent studies have shown that *while not a replacement for vigorous PA*, AVG can increase energy expenditure to light or moderate levels (comparable to traditional activities such as brisk walking, skipping, and jogging) and can both increase PA time and decrease sedentary screen time. Second, video games are very popular and studies have shown that AVG can foster positive attitudes towards activity (e.g., greater enjoyment, "playing" rather than exercising) leading to enhanced PA adherence, greater PA volume, increased energy expenditure, and associated changes in health. Third, as many as 47% of Canadian households have at least one gaming console (e.g., XBox, PS3, etc.) and 30% report playing every day. Fourth, the presence of home-based exercise equipment can address commonly reported environmental barriers (e.g., safety, accessibility) to PA.

As today's children and youth are pervasive users of digital devices, the growing availability and popularity of AVG has the potential to have a substantial impact on the PA levels and subsequently the health of children and youth. Harnessing the fascination and wide appeal of video games, AVG has the ability to attract those children and youth who shy away from less appealing, traditional fitness activities ¹⁶. Importantly, AVGs are not confined by environmental barriers such as perceived neighbourhood safety, seasonal variations, or inclement weather ^{19, 20}. Moreover, it can give those youth with body-image concerns (e.g., overweight) and perceived

social barriers ²¹, less experience with PA, sport ability, or stamina an opportunity to practice the skill in a safe and entertaining environment – ultimately creating the confidence and efficacy ²² needed to optimize sustained behavioural change. While yet to be fully explored, this is a unique and interesting avenue of research, whereby

AVG Website Resources

Exergames Unlocked http://exergamesunlocked.org/

Exergame Fitness www.exergamefitness.com

AVG may act as a novel means of entry into organized sport and "real-world" PA. For example, there is some evidence to suggest that AVG play may foster the development of fundamental movement skills (i.e., agility, balance, coordination) essential to the pursuit and maintenance of a physically active lifestyle ²³. As children become more familiar and confident in their abilities through AVG, these qualities may be translated into improved attitudes and engagement in more structured PA ²⁴. Refer to *Table 15.1* for an overview of the benefits and limitations of AVG in pediatric oncology.



Table 15.1. Benefits and limitations of AVG in pediatric oncology.

Benefits of AVG	Limitations of AVG
 ✓ Provides an engaging and fun PA environment 	 Activity intensity is reduced for novice or inexperienced users
 May attract those survivors who are reluctant to participate in traditional sport- based or fitness activities 	 ✓ As with any PA, there is always the risk of injury ✓ Novelty appears to diminish rapidly
 ✓ Increases energy expenditure ✓ Dravidae increased into a sufference of a 	 Ability to foster sustained PA participation
 Provides immediate performance feedback 	 Is not clear ✓ Currently confined to indoor PA options
✓ Potential for motor skill development	✓ Cost of gaming systems and rapidly
 Offers a variety of activities, ranging in activity intensity (e.g., yoga, sport-based games, fitness programs) 	evolving technologies may be prohibitive for some families
 ✓ Offers a PA alternative for when inclement weather prohibits outdoor activities 	
 Provides opportunities for both individual and group play as well as cooperative and competitive play 	
 Accessible – potential for hospital, home, and school-based interventions 	
✓ Adjunct to existing PA programming	



Pediatric cancer patient exercising with AVG



Future Directions

Technology plays a large role in our everyday lives and as new technologies continue to emerge, so too will our desire to use them. While the use of technology to measure PA behaviour (e.g., pedometer, accelerometer) is not new, the use of technology in promoting PA is gaining popularity. Although many options exists AVG continue to play a predominant role in health promoting technology. In fact, Nintendo[™] recently announced their newest gaming platform will be based around developing entertaining and engaging software designed to improve health and QOL. This is not to suggest that technology will be the solution to fostering physically active lifestyles, however it appears that it may play a predominant supporting role.

Take Home Message

Given the innumerable benefits associated with PA and an increasingly sedentary population, innovative approaches to promoting PA are greatly needed. While yet to be fully explored, AVG may act as a viable means to increase PA participation and reduce sedentary behaviours



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Chapter 16

Practical Tips for Engaging in Physical Activity

S. Nicole Culos-Reed, PhD

Learning Objectives

After completing this chapter you will know:

• ... practical steps that can be taken to integrate the childhood cancer survivor back into physical activity, from both the family and health care professional perspectives.

Introduction

The benefits of **physical activity (PA)** for all children are well-known, including positive impacts on both physical and psychosocial outcomes ¹. When considering the impact of PA on children with cancer, the potential benefits are even more important to realize and have been outlined in *Chapter 2* (physical, psychosocial, fatigue and neurocognitive).

Integration of children with cancer back into PA programs within their community settings, however, requires considerations at both the medical (i.e., physician) and family levels. Specifically, at the physician level, screening, contraindications and communication should be considered. At the family level, social support, facilitating communication between the medical and fitness professional, helping a child find the benefits (including fun!) and developing strategies to deal with the potential barriers are all considerations to be addressed. This chapter is designed to provide the roadmap for navigating the transition from in-hospital or cancer-specific programming in the community back to the usual PA programming (e.g., sports, club activities or community exercise programs) in the community-setting.

Information for Physicians

Screening, and in particular noting contraindications for PA participation, is a crucial aspect of the communication to the family considering their child's involvement in a PA program.



Weiss-Kelly's article on PA prescription for childhood cancer survivors focuses on using exercise to ameliorate the long-term side effects of cancer treatment ². Guidelines for physicians suggest evaluating the survivor's risk for long-term effects and prescribing PA to manage and potentially prevent some of these problems. Thus, it is crucial that physicians be educated on the role of PA for some of the most common long-term negative effects, such as obesity, osteoporosis, cardiovascular disease, and diminished overall quality of life. Refer to *Appendix H* and *J* for an example of a physician clearance form and client intake form.



Information for Fitness and Physical Education Professionals

When working with childhood survivors of cancer, communication with families and potentially the medical team is paramount to success! This will ensure that you have the necessary and correct information to provide a safe and healthy activity environment for the child. Using an appropriate intake form to track important information is useful. Reading background information on the child's specific cancer and the long-term effects associated with their treatment can also aid you in the decision-making around what activities might be most beneficial.

While there may be some activity restrictions based on physician guidance, allowing the child to participate in all activities, as he/she is able, is important not only for physical well-being, but also for the self-esteem of the child. This may require modification of activities to include, instead of excluding the child, from his/her peers. In addition, providing positive reinforcement, encouraging the child's strengths and treating the child as normal as possible will promote self-improvement and result in a healthy sense of self-esteem and self-confidence for being active. Finally, encouraging the activities with peers will foster social support, enhance the development



of social skills, and contribute to an environment of FUN for the child. These, in turn, will be likely to enhance continued activity participation.

Information for Families

Families want to provide a healthy environment for their child. To facilitate physical activity, there are 3 key tips: Communication, Support, and Engagement.

First, communication with both health and fitness/education professionals is paramount to enhancing your child's PA participation. You are the liaison between the medical community and the fitness/sport setting your child is in. Including regular updates for any change in health status that might impact PA participation is important. A message to both the health and fitness or education professionals that you value the role of PA in your child's life will be instrumental to ensuring that these parties continue to support and promote PA for your child.

Second, support for your child for engaging in activities in their usual setting – whether it be back to sport, physical education classes at school, or engaging in another active community program – shows that you support active healthy choices.

And finally, the third component is engagement. Modeling positive PA behaviors and engaging in active healthy lifestyle choices will be beneficial not only for your health, but further supports your child.

Together, we all want to enhance the PA experience for the childhood cancer survivor. Health care, fitness and education professionals, along with the families, must communicate and collaborate to support the child in achieving healthy lifestyle behavior changes. Doing so in a supportive and fun environment will result in positive habits that enhance both the physical and psychological well-being of the child.

Take Home Message

Families, health care professionals, and fitness professionals must work together as a team to promote an active lifestyle for the childhood cancer survivor.
Education, communication, social support and engaging in active lifestyle choices themselves are all important for the family members as well as the health and fitness professionals to consider. These behaviors will aid in making the transition for the child as smooth and supported as possible



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Appendices

- Appendix A Common Medication List
- Appendix B Physical Activity Guidelines
- Appendix C Blood Pressure Measurement in Children
- Appendix D General Physical Activity Guidelines
- Appendix E Pain Scale
- **Appendix F** Rating Perceived Exertion Scale (RPE)
- Appendix G Client Intake Form
- Appendix H Physician Clearance Form
- Appendix I Infographics



Common Medication List

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Adderall	Amphetamine	ADHD	Hyper/hypotension, headache, abdominal pain, insomnia, weight loss, dry mouth, Raynaud's phenomenon mood swings, nervousness, dizziness, bruxism, diaphoresis, enuresis and incontinence	Seizures and eyesight changes
Adryamicin	Doxorubicin	Various tumors (inhibit DNA synthesis)	Nausea, vomiting, burning at site of injection, hypotension, hyperpigmentation and alopecia anemia	Hypersensitivity reactions, ulceration, heart failure, renal failure, cellulites vesication and tissue necrosis
Advair	Fluticasona + Salmeterol	Asthma	Allergic reactions, upper respiratory tract infection, throat irritation, nausea, vomiting, chills, fever and increased mucus production	Fever, hives, rash, breathing problems, chest pain, increased BP and tremors
Afinitor	Everolimus	Sub ependymal giant cell astrocytoma (Tuberous sclerosis complex)	Anemia, increased blood glucose, cholesterol and triglyceride, creatinine, mouth ulcers, infection, weakness, cough, diarrhea and constipation	Skin problems (rash, acne and dry skin), pancytopenia, nausea and vomiting, dyspnea, fever, fatigue, nosebleeds, itching, chest pain, diaphoresis, joint pain, abnormal behaviour and decreased blood phosphate level
Ambisome	Anphoterin B	Fungal infections	Nausea, vomiting, chest pain, hypocalcaemia, hypomagnesemia, confusion, headache and rash	Nephrotoxicity, anemia, leukopenia and thrombocytopenia
Amikin	Amikacin	Infections	Nausea, vomiting, arthralgia and rash	Ototoxicity, nephrotoxicity and neuromuscular block

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Anexsia	Codeine + Acetominophen	Pain Relief	Anxiety, dizziness, nausea, vomiting, headache, mood changes, blurred vision, Xerostomia and ringing in ears	Shallow breathing and slow HR, fainting, paranoia, seizures, problems with urination and jaundice
Anzemet	Dolasetron	Nausea/Vomiting (Anti-emetic)	Headache, fatigue, diarrhea/constipation, dyspepsia, chills, dizziness, fever, sweating, rash/urticarial, myalgia and arthralgia	Tachycardia, light headedness, bradycardia, hypotension, sinus arrhythmia, chest pain, urinary retention and bronchospasm
Arranon	Nelarabine	T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma	Anemia, neutropenia, thrombocytopenia, and leukopenia, cough, headache, nausea, vomiting, diarrhea/constipation, redness and pain around needle, dizziness and fatigue	Confusion or clumsiness, loss of coordination, weakness, numbness in extremities, blurred vision and seizure
Aspirin	Acetyl-salicylic acid	Pain relief (mild to moderate)	Reye's syndrome, nausea and Gl bleeding	Allergic reaction, chest pain, swelling faces/hands, dizziness, vomiting and hearing loss
Astagraft	Tacrolimus	Organ transplant – rejection reversal, graft versus host disease	Dyspnea, headache, tremors, dysesthesias, insomnia, anemia, hyperkalemia, hyperglycemia, hypertension, nausea, vomiting, diarrhea and constipation	Pleural effusion, nephrotoxicity, dizziness, seizures, neuropathy, edema, arrhythmias, anorexia, dysphagia, dyspepsia, flatulence, jaundice, pruritus and rash
Ativan	Lorazepam	Anxiety disorders, Chemotherapy- Induced Nausea/Vomiting	Clumsiness, unsteadiness, dizziness, light headedness, drowsiness, slurred speech, headache, constipation and Xerostomia	Abnormal thinking, anxiety, behavioural change, memory problems, muscle spasm, rash, trembling, unusual bleeding and yellow eyes or skin

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Avastin	Bevaxizumab	Glioblastoma, leukemia (ALL, AML)	Mild headache, back pain, diarrhea, loss of appetite, cold symptoms, dry eyes or skin, taste changes, jaw pain, swelling, numbness, fatigue, infection and hypertension	Easy bruising, numbness, severe headache, foamy urine, epistaxis, thromboembolic events, GI perforations and proteinuria
	Beta-blockers: Acebutolol, atenolol, bisoprolol, metoprolol, nebivolol, propanolol	Beta-adrenergic blocking agents	Diarrhea, stomach cramps, nausea, vomiting, rash, blurred vision, muscle cramps and fatigue	Bradycardia, hypotension, heart failure and heart attack
Bexxar	Tositumumab	Non-Hodgkin's Lymphoma	Cytopenias, infections, back pain, constipation, diarrhea, dizziness, drowsiness, headache, muscle pain, nausea, vomiting and weakness	Pneumonia, pleura effusion, severe allergic reactions, chest pain, bloody stools, fainting, pallor, shortness of breath, coffee ground vomit and myelodysplasia
Blenoxan	Bleomycin	Antitumor antibiotic (breaks DNA strands)	Hyperpigmentation, hypersensitivity reactions, hyperkeratosis, nail changes, alopecia, stomatis, fever, chills, vomiting, anorexia, weight loss, anemia, leukopenia and thrombocytopenia	Pulmonary adverse reactions, pneumonitis, pulmonary fibrosis, death, stomatitis and mucositis
Busulfex	Bussulfan (Alkyl sulfonates)	Leukemia (Bone Marrow Transplantation)	Headache, diarrhea, constipation, nausea and flushing	Pulmonary fibrosis, hyperpigmentation, seizures, and veno-occlusive disease

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
	Calcium	Hypocalcaemia	Dyspepsia, constipation, interferes with Fe and Zn intake, may increase risk of kidney stones	Milk alkali syndrome
	Calcium channel blockers: Amlodipine, diltiazem, felodipine, nicardipine, nisoldipine, verapamil	Heartburn and Pediatric High BP	Constipation, nausea, headache, rash, enema, low BP, drowsiness and dizziness	Liver dysfunction and heart failure
Celebrex	Colecoxib	Inflammation and pain	Abdominal pain, constipation, diarrhea, gas, heartburn, nausea, vomiting, dizziness	Heart attack, stroke, high BP, swelling, vomit blood, skin rashes, asthma attack, yellow skin or eyes, slurred speech
CellCept	Mycophenolate	Organ transplant – rejection prophylaxis	Diarrhea, nausea, vomiting, anemia, leucopenia, infections and tumors	Abdominal pain, thrombocytopenia, edema, hyperphosphatemia, hyponatremia, hyperglycemia, hypokalemia, skin rash and myopathy
	Cephalosporin	Infections (Antibiotic)	Hypersensitivity reactions, mild stomach cramps or upset, nausea, vomiting, diarrhea, sore tongue and sores inside mouth	Black, tarry stools, chest pain, fever, painful or difficult urination, allergic reactions, colitis, severe stomach cramps and fever
Citovene	Gancyclovir	CMV Prophylaxis	Neutropenia, thrombocytopenia, anemia, diarrhea, anorexia, hypertension	Nausea, abdominal pain, stomatitis, urinary frequency, hypersensitivity reactions, pruritus, retinal detachment, neuropathy and sweating

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Clolar	Clofarabine	Leukemia (ALL)	Nausea, vomiting, diarrhea, headache, fatigue, anxiety, mild rash and warmth/tingly skin	Myelosupression, tumor lysis syndrome, SIRS, veno-oclusive hepatic disease, hepatotoxicity and nephrotoxicity
	Codeine	Pain relief	Heartburn, nausea, upset stomach and urinary retention	Psychotic symptoms, mental and respiratory depression, stupor, delirium, somnolence, dysphoria, hypotension and dizziness
Decadron	Dexamethasone	Inflammation(anti- inflammatory)	Insomnia, irritability, increase in appetite, weight gain, hirsutism, heartburn, muscle weakness, swelling, impaired wound healing, peptic ulcer with potential perforation and hemorrhage, abdominal distention and nausea	Fever, shortness of breath, severe hot flashes, chest or jaw pain, irregular heartbeat, bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, myocardial rupture following recent myocardial infarction, edema, pulmonary edema, syncope, tachycardia, thromboenholism, thrombophlebitis and vasculitis, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic heads, pathologic fracture of long bones, tendon rupture, pancreatitis, convulsions, increased intracranial pressure with papilledema, vertigo, arthralgia and thromboembolism

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Dilantin	Phenytoin	Prevents seizures	Walking problems, slurred speech, dizziness, nervousness, insomnia, tremor, headaches, nausea, constipation, confusion, nausea, vomiting, swelling and rapid weight gain	Suicidal thoughts, swelling, trouble swallowing, skin rash, hives, fever, painful sores, unusual bruising, sever fatigue or weakness, muscle pain, upper stomach pain, loss of appetite, dark urine, jaundice, chest pain, irregular heart rhythm and feeling short of breath
Dilaudid	Hydromorphone	Pain management	Nausea, vomiting, constipation, dizziness, headache, xerostomia, sweating and itching	Seizures, confusion, weakness, fainting, hallucinations, respiratory depression, apnea, bronchospasm or laryngospasm, alterations in heart rate and blood pressure, anorexia, diarrhea, urinary retention or hesitancy and skin rashes
	Diuretics (Thiazides: chlorothiazide, hydrochlorothiazid e, indapamide metalazone. Loop Diuretics: bumetanide, ethacrynic acid, furosemide, torsemide. Potassium Sparing: Amiloride, Eplerenone, Spironolactone, triamterene	Hypertension, edema	Dizziness, light-headedness, blurred vision, loss of appetite, itching, stomach upset, headache and weakness	Rash, itching, swelling, trouble breathing, muscle cramps, pain, nausea and vomiting
Domperidone	Domperidone	Nausea and vomiting management (anti- emetic)	Allergic reactions, xerostomia, hot flashes, and uncontrolled movements	Headache, Parkinson like symptoms and anxiety

RARE SIDE-EFFECTS	Shortness of breath, faint headedness, bradycardia, seizure, tachycardia, sores in mouth, jaundice, hypocalcaemia, respiratory distress, pulmonary edema, pulmonary hypertension, and pneumonia, arrhythmia, heart failure, cardiac arrest, chest pain and neutropenia	Passing out, very thirsty/hot, unable to urinate, heavy sweating, fever, chills and bone ache.	Nausea, vomiting, diarrhea, constipation, poor appetite, headache, abdominal pain, mouth sores, insomnia, shortness of breath, wheezing and swelling of facial features.	Severe pain in upper stomach, thrombosis, hemorrhage, , fever, seizure, weakness, severe headache, pain, hyperglycemia and pancreatitis	Severe skin rash, itching, hives, difficulty breathing, wheezing, yellowing of the skin or eyes, dark urine, pale stools, fatigue, pancreatitis, arrhythmias, hepatotoxicity, hypersensitivity reactions, hepatitis and nephritis
PRIMARY SIDE-EFFECTS	Nausea, vomiting, diarrhea, headache, fatigue, anxiety, mild rash, fever and swelling in hands and feet	Nausea, vomiting, heartburn, diarrhea or constipation, loss of appetite, hiccups, hair loss, headache, dizziness, fatigue, mild rash, ringing in ears and insomnia	Rash, general weakness, fever and low magnesium levels	Mild nausea, vomiting diarrhea and mild stomach pain	Upset stomach, diarrhea, nausea, stomach pain, dry mouth, loss of appetite and constipation
TARGET	Hyperuricemia secondary to chemotherapy	Nausea/Vomiting management	Head and neck cancer	Leukemia (ALL)	Infections (Antibiotic)
ACTIVE INGREDIENT	Rasburicase	Aprepitant	Cetuximab	Asparginase	Erythromycin
DRUG NAME	Elitek	Emend	Erbitux	Erwinaze	Erythrocin
DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS	
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	Fentanyl	Pain Management (breakthrough pain)	Dry mouth, nausea, vomiting, constipation, headache, drowsiness, fatigue, sores inside mouth, pruritus and hypersensitivity reactions	Slow HR, weak or shallow breathing, severe drowsiness, confusion, extreme fear, light headedness, stupor, delirium, somnolence, dysphoria, seizures, muscle rigidity, hypotension, bradycardia, arrhythmias, urinary retention, pulmonary edema and hemolysis	
Flagyl	Metronidazol	Infections (Antibiotic)	Dizziness, headache, dizziness diarrhea, nausea, stomach pain, dry mouth, loss of appetite, constipation. Taste perversion, bacterial infection, influenza-like symptoms and moniliasis	Seizures, numbness, shortness of breath, chest pain, mood changes, encephalopathy, aseptic meningitis, optic and peripheral neuropathy, serum sickness-like reaction and thrombocvtopenia	
Fludara	Fludarabine	Leukemia, bone marrow transplantation	Myelosupression, fever, infection, fatigue nausea and vomiting	Anorexia, headache, paresthesias, stomatitis, esophagitis, mucositis, constipation, taste disturbances, abdominal pain, gastrointestinal bleeding, cough, dyspnea, diaphoresis and back pain	
Gengraf	Cyclosporine	Organ transplant – rejection prophilaxys	Infections, hyperuricemia, seizures, tremors, headache, hypertrichosi and pruritus	Renal insufficiency, leukopenia, thrombocytopenia, anemia, hyperkaliema, diahrrea, nausea and vomiting	
Genoxal	Cyclophosphamide	Leukemias, lymphomas, neuroblastoma, retinoblastoma	Nausea, vomiting, alopecia, infections, changes in nails and skin colour, leukopenia, anemia and thrombocytopenia	Anaphilatic reactions, blood in urine and stools, pallor, chest pain, intersticial pneumonitis, wheezing, extreme thirst with headache, weakness, anorexia, abdominal pain, diahrrea, skin rash and cystitis	

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
	Imatinib	Leukemia (CML, ALL)	Mild nausea, stomach pain, vomiting, diarrhea, skin rash, join pain, headache, fatigue, muscle cramps and edema	Fever, unusual bleeding, swelling, rapid weight gain, shortness of breath, nausea, bloody stool, low back pain, numbness around your mouth, dyspepsia, anorexia, constipation, brady or tachycardia, hypokalemia, neutropenia, thrombocytopenia and anemia
Imatinib	Leukemia (CML, ALL)	Mild nausea, stomach pain, vomiting, diarrhea, skin rash, join pain, headache, fatigue, muscle cramps and edema	Nausea, vomiting, diarrhea, fatigue, alopecia, leucopenia, thrombocytopenia and anemia	Wheezing, fever, pallor, petechial, painful urination, constipation, abdominal pain, anorexia, stomatitis, rash, dyspnea, cough, headache, myalgias and arthralgias
Idamycin	Idarubicin	Leukemia, Solid tumors (inhibit DNA synthesis)	Nausea, vomiting, mucositis, diarrhea, abdominal cramps, anorexia, alopecia, rash and leukopenia	Bone marrow suppression, infection or bleeding, myocardial toxicity and heart failure
Imovane	Zopiclone	Insomnia	Drowsiness, dizziness, light headedness, xerostomia, headache and upset stomach	Irregular heartbeat, rash, slurred speech, incoordination, memory loss, depression and irritability
Intron A	Interferon alfa	Angioblastoma	Headache, dizziness, muscle pain, fatigue, nausea, vomiting, diarrhea, anorexia, xerostomia, dyspnea, cough, alopecia, mild rash, burning at injection site, "influenza-like" symptoms and neutropenia	Severe depression, aggressive behaviour, fast, slow or uneven HR, fever, vision or hearing problems, unusual urination, sever stomach pain and jaundice, thrombocytopenia and anemia
Kadian	Morphine	Pain relief	Anorexia, constipation, diarrhea, nausea, vomiting, flushing, headache, memory loss and insomnia	Bradycardia, seizures, myoclonic spasms, cold skin, confusion, severe weakness, addiction and pruritus

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Keppra	Levetirecetam	Seizures (anti- epileptic)	Sleepiness, weakness, dizziness, infection, insomnia, irritability, asthenia, headache and fatigue	Depression, anxiety, suicide, cough, anorexia, nausea and pain
Kytril	Granisetron	Nausea/Vomiting management	Headache, stomach pain, nausea, vomiting, anorexia, diarrhea, dizziness and insomnia	Fast pounding heartbeats, fever, asthenia, easy bruising or bleeding, anxiety and dyspepsia
Leukine	Sargamostrim	Aplastic anemia, bone marrow transplantation, neutropenia associated with chemotherapy(Increa se WBC for Leukemia patients)	Nausea, stomach pain, vomiting, diarrhea, loss of appetite, fatigue, hair loss, weight loss, headache, mild rash, bone pain, joint or muscle pain and "flu-like" symptoms	Eosinophilia, thrombocytopenia and anemia, easy bruising, swelling, rapid weight gain, chest pain, tachycardia, weakness or fainting, coughing up blood, painful urination and problems with vision, speech, balance or memory
Lyrica	Pregabalin	Neuropathic pain	Dizziness, somnolence, ataxia, edema, weight gain, dry mouth and blurry vision	Abnormal thinking, hypoglycemia, , trouble breathing, hives, rash, suicidal thoughts and allergies
Glucophage	Metformin	Type 2 diabetes (control blood sugar)	Nausea, anorexia, diarrhea, loss of appetite, metallic taste in mouth, nausea, flatulence, stomach ache and difficulty concentrating	Weight loss, vomiting, shallow breathing, irregular heartbeat, shakiness, slurred speech, cold sweats, mood changes, pale skin and lactic acidosis
Mesnex	Mesna	Hemorrhagic cystitis prophylaxis	Disgneusia, diarrhea, nausea, vomiting, hypotension and joint/ limb pain	Mild rash and hypokalemia
Mycamine	Micafungin	Prophylaxis of candidiasis	Diarrhea, nausea, vomiting, abdominal pain, neutropenia, thrombocytopenia, headache, tachycardia, skin rash and fever	Constipation, dyspepsia, seizures, dizziness, insomnia, arrhythmia, urticarial, hypoglycemia, hypernatremia and hyperkalemia
Mycostatin	Nystatin	Candidiasis	Skin rash, pruritus and eczema	Hypersensitivity reaction

ORUG NAME Veulasta	ACTIVE INGREDIENT Pegfilgastrim	TARGET Neutropenia	PRIMARY SIDE-EFFECTS Bone pain, pain in arms or legs,	RARE SIDE-EFFECTS Severe sudden pain in left upper
		associated with chemotherapy	bruising, swelling, pain, redness, or hard lump by injection site, nausea, fatigue, alopecia, diarrhea, vomiting, constipation, fever, anorexia, skeletal pain, headache, taste perversion, dyspepsia, myalgia, insomnia, abdominal pain, arthralgia, generalized weakness, peripheral edema, stomatitis and mucositis	stomach, sever dizziness, skin rash or flushing, rapid BR and signs of infections
leumega	Oprelvekin	Thrombocytopenia Drug-induced	Edema, redness in eyes, headache, dizziness, insomnia, nausea, vomiting, diarrhea, mucositis, runny nose, cough and dyspnea	Shortness of breath, swelling, weight gain, chest pain, tachycardia, palpitations, syncope, numbness, fainting, fever, unusual urination, xerostomia and sudden vision loss
leupogen	Filgastrim	Neutropenia associated with chemotherapy	Nausea, vomiting, diarrhea, constipation, bone pain, muscle aches, hair loss, headache, fever, fatigue, mild skin rash and itching at site of injection	Sudden severe pain in left upper stomach spreading up to shoulder, dyspnea, cough, signs of infection, thrombocytopenia, anemia, myelodysplasia and hyperuricemia
lexium	Omeprazol	Gastro esophageal reflux	Headache, diarrhea, nausea, gas, stomach pain, constipation and dry mouth	Skin rash, hives, itching swelling, irregular heartbeat, muscle spasms, seizures, confusion, dizziness, hypoesthesia, insomnia, migraine aggravation, paresthesia, sleep disorder, somnolence, tremor, vertigo, conjutivitis, dyspnea, cough, muscle spasms, arthralgias and myalgias

RARE SIDE-EFFECTS	Skin rash, hives, itching swelling, irregular heartbeat, muscle spasms, seizures, confusion, dizziness, hypoesthesia, insomnia, migraine aggravation, paresthesia, sleep disorder, somnolence, tremor, vertigo, conjutivitis, dyspnea, cough, muscle spasms, arthralgias and myalgia	Black tarry stools, chest pain, fever, painful or difficult urination, allergic reactions, colitis, severe stomach cramps and fever	Vascular toxicities, anaphylactic reactions, hepatotoxicity and ocular toxicity	Insomnia, mood changes, personality changes, euphoria, psychotic behaviour and severe depression	Bone marrow toxicity, hepatotoxicity, skin rashes, alopecia, and hyperpigmentation
PRIMARY SIDE-EFFECTS	Headache, diarrhea, nausea, gas, stomach pain, constipation and dry mouth	Hypersensitivity reactions, mild stomach cramps or upset, nausea, vomiting, diarrhea, sore tongue and sores inside mouth	Severe nausea and vomiting, nephrotoxicity, ototoxicity, mild bone marrow toxicity, anaemia, hypomagnesaemia hypocalcaemia, hypokaliema, hyponatremia, hyperuricemia, muscle irritability, cramps, clonus, tremor and peripheral neuropathies	Convulsions, distended abdomen, face redness, glaucoma, headache, hives and other allergic type reactions, increased pressure inside eyes or skull, inflamed oesophagus or pancreas, bone fractures, bruising, bulging eyes, congestive heart failure, muscle weakness, osteoporosis, ulcer and sweating	Myelosupression, hyperuricemia and intestinal ulceration
TARGET	Gastro esophageal reflux	Infections (antibiotic)	Refractory solid tumors (Inhibit DNA synthesis)	Inflammation, immunosuppression	Leukemia (inhibit cell division)
ACTIVE INGREDIENT	Pantoprazol	Penicillin	Cisplatin	Prednisone	Mercaptopurine
DRUG NAME	Pantoloc		Platinol	Rayos	Purinethol

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Sancuso	Granisetron	Nausea/Vomiting management	Headache, stomach pain, nausea, vomiting, anorexia, diarrhea, dizziness and insomnia	Fast pounding heartbeats, fever, asthenia, easy bruising or bleeding, anxiety and dyspepsia
Septrin	Cotrimoxazol	Pneumocystis pneumonia prophylaxis	Nausea, vomiting, anorexia, rash, urticarial and hyperkalemia	Anorexia, stomatitis, abdominal pain, hypersensitivity reactions, anemia, leukopenia, thrombocytopenia, seizures, tremors, dizziness, lightheadness, interstitial nephritis, crystalluria, fatigue, fever, facial edema, hallucinations, confusion, insomnia and cough
	Salbutamol	asthma attacks associated with bronchitis	Nausea, vomiting, skin rash and dry mouth	Headache, tremor, tachycardia, chest pain, hypertension, anxiety, dizziness and cough
Synthroid	Levotiroxyn	Hypothyroidism	Irregular heartbeat, muscle weakness, irritability, tremors, weight loss, heat intolerance, decreased bone density, fever, sleepiness and nervousness	Chest pain, vomiting and excessive sweating
Taladine	Ranitidine	Ulcers, gastro esophageal reflux, dyspepsia	Headaches, constipation, diarrhea, nausea, vomiting and stomach pain	Hypersensitivity reaction, tachycardia/ bradycardia, myalgia, arthralgia, leukopenia, thrombocytopenia, and anemia
Taxol	Palitaxel	Will's tumor	Neutropenia mild nausea, vomiting, diarrhea, constipation, weakness, joint pain, darkening of skin or nails, temporary hair loss and hypersensitivity reactions	Fever, chills and body aches, easy bruising, unusual bleeding, bradycardia, light headedness seizure, chest pain and numbness
Taxotere	Docetaxel	Solid tumors	Fatigue, nausea, vomiting, diarrhea, constipation, muscle pain, altered sense of taste, temporary hair loss, fingernail or toenail changes, leukopenia, hypersensitivity reactions and edema	Bone marrow suppression, severe vomiting or diarrhea, fever chills body aches, pallor, light headedness, shortness of breath and hyponatremia

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Temodar	Temozolomide	Brain tumors	hair loss, fatigue, diarrhea, constipation, mild rash, dizziness, blurred vision, insomnia and cough	Seizure, numbness or tingling, signs of infection, dry cough, painful urination, white patches in mouth and black tarry stools
	Tramadol	Pain reliever	Nausea, constipation, dizziness, headache and drowsiness,	Vomiting, diarrhea, dyspepsia, pruritus, urinary retention, hyponatremia and seizures
Trexall	Methotrexate	Acute lymphoblastic leukemia, non- Hodgkin's lymphoma, meningeal leukemia, and osteosarcoma (inhibit cell division)	Nausea, vomiting, diarrhea, leukopenia, inflammation, fever stiffness and headache	Bone marrow suppressions, aplastic anemia, hepatotoxicity, mucositis, renal dysfunction, skin rash and seizures
Trisenox	Arsenic trioxide	Acute promyelocytic leukemia	Stomach pain, nausea, vomiting, constipation, diarrhea, headache, dizziness, anxiety, , joint or muscle pain, fatigue, edema, mild rash, tachycardia, QT prolongation, cough, dyspnea, dermatitis, pruritus and leukocytosis	Fever, weight gain, , light headedness, hyperglycemia, hypotension chest pain, paresthesia, anxiety, leukopenia, thrombocytopenia and anemia
Tylenol	Acetominophen	Pain reliever	Nausea, vomiting, headache, insomnia and hypersensitivity reactions	Acute renal failure, acute tubular necrosis, interstitial nephritis, thrombocytopenia, erythematous skin rash and dyspnea
Vidaza	Azacitidina	Myelodisplastic syndrome	Nausea, vomiting, diarrhea, constipation. Anorexia, anemia leukopenia, thrombocytopenia, fever, fatigue, pain, erythema, ecchymosis, petechial, pruritus, cough, dyspnea, arthralgia and headache	Stomatitis, dyspepsia, hemorrhoids, dysphagia, tongue ulceration, dizziness, insomnia, syncope, edema, tachycardia and hypotension

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Oncovin	Vincristine	Various tumors	Neuropathy, temporary alopecia, decreased weight, jaw pain, bone pain, nausea, vomiting, constipation, diarrhea, fatigue and weakness	Pallor, easy bruising, numbness, burning, pain and tenderness in stomach, spinning sensation, seizure, leukopenia, thrombocytopenia and anemia
Zofran	Ondansetron	Nausea and vomiting management	Headache, stomach pain, nausea, vomiting, anorexia, diarrhea, dizziness and insomnia	Fast pounding heartbeats, fever, asthenia, easy bruising or bleeding, anxiety and dyspepsia
Zovirax	Acyclovir	Infection – Varicella and Herpes Virus (Antiviral)	Dizziness, headache, fatigue, diarrhoea, abdominal pain, skin rashes, pruritus, tiredness and photosensitivity	Renal dysfunction, drowsiness, confusion, hallucinations, seizures, anxiety, tremors, erythema multiform, and Stevens Johnson syndrome toxic epidermal necrosis

Appendix B

Physical Activity Guidelines

In this appendix a summary of the physical activity guidelines promoted by three recognize organizations are presented.

Physica	I Activity Guidelines for Children 5-17 years old				
"Children and adolescents show this 60 minutes will have to be	uld do 60 minutes (1 hour) or more of physical activity each day" split in three different types of activities explain below.				
Aerobic Activity	Aerobic activity should make up most of your child's 60 or more minutes of physical activity each day. This can be moderate or vigorous intensity. Be sure to include vigorous intensity aerobic activity on at least 3 days per week.				
Muscle Strengthening Include muscle strengthening activities at least 3 days per week as part of your child's 60 or more minutes. Examples, gymnastic, push up, climbing.					
Bone Strengthening Include bone strengthening activities at least 3 days per week as part of your child's 60 or more minutes. Example: jump a rope, in the trampoline, run.					
For children and young people, chores, recreation, physical edu community activities. This table Center for Disease Control au Physiology(CSEP). See links	physical activity includes play, games, sports, transportation, ucation, or planned exercise, in the context of family, school, and was created based on the World Health Organization (WHO) , nd Prevention (CDC) and Canadian Society for Exercise to the website of each institution below.				

Institution	Link
WHO	http://www.who.int/dietphysicalactivity/factsheet_young_people/en/
CDC	http://www.cdc.gov/physicalactivity/everyone/guidelines/children.html
CSEP	http://www.csep.ca/english/view.asp?x=804



Blood Pressure Measurement in Children

A Pocket Guide to Blood Pressure Measurement in Children

From the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.



U.S. Department of Health and Human Services National Institutes of Health National Heart, Lung, and Blood Institute

Girls SBP by Age and Height (Normal SBP is less than the prehypertensive result.)

Age į	BP Classification			Syst	olic BP (m	mHg)		
3	Height (cm)	91	92	95	98	100	103	105
	Prehypertension	100	100	102	103	104	106	106
	Stage 1 HTN	104	104	105	107	108	109	110
	Stage 2 HTN	116	116	118	119	120	121	122
4	Height (cm)	97	99	101	104	108	110	112
	Prehypertension	101	102	103	104	106	107	108
	Stage 1 HIN	105	106	107	108	110	111	112
-	Stage 2 mil	117	110	115	120	122	125	124
5	Height (cm)	104	105	108	111	107	118 100	120
	Stage 1 HTN	105	103	105	110	111	112	113
	Stage 2 HTN	119	119	121	122	123	125	125
6	Height (cm)	110	112	115	118	122	126	128
	Prehypertension	104	105	106	108	109	110	111
	Stage 1 HTN	108	109	110	111	113	114	115
	Stage 2 HTN	120	121	122	124	125	126	127
7	Height (cm)	116	118	121	125	129	132	135
	Prehypertension	106	107	108	109	111	112	113
	Stage 1 HTN	110	111	112	113	115	116	116
	Stage 2 HIN	122	123	124	125	127	128	129
8	Height (cm)	121	123	127	131	135	139	141
	Prehypertension	108	109	110	111	113	114	114
	Stage 7 HTN	174	12	114	127	178	118	130
	Unight (are)	125	120	124	120	140	144	147
9	Prehypertension	125	110	112	113	140	116	116
	Stage 1 HTN	114	114	115	117	118	119	120
	Stage 2 HTN	126	126	128	129	130	132	132
10	Height (cm)	130	132	136	141	146	150	153
	Prehypertension	112	112	114	115	116	118	118
	Stage 1 HTN	116	116	117	119	120	121	122
	Stage 2 HTN	128	128	130	131	132	134	134
11	Height (cm)	136	138	143	148	153	157	160
	Prehypertension	114	114	116	11/	118	119	120
	Stage 2 HTN	130	130	131	133	134	135	124
12	Linkt (am)	142	140	150	455	100	104	100
12	Prehypertension	143 116	140	117	119	120	120	120
	Stage 1 HTN	119	120	121	123	124	125	126
	Stage 2 HTN	132	132	133	135	136	137	138
13	Height (cm)	148	151	155	159	164	168	170
	Prehypertension	117	118	119	120	120	120	120
	Stage 1 HTN	121	122	123	124	126	127	128
	Stage 2 HTN	133	134	135	137	138	139	140
14	Height (cm)	151	153	157	161	166	170	172
	Store 1 HTN	119	120	120	120	120	120	120
	Stage 2 HTN	135	136	123	138	140	141	141
15	Height (cm)	152	15/	158	162	167	171	173
'	Prehypertension	120	120	120	120	120	120	120
	Stage 1 HTN	124	125	126	127	129	130	131
	Stage 2 HTN	136	137	138	139	141	142	143
16	Height (cm)	152	154	158	163	167	171	173
	Prehypertension	120	120	120	120	120	120	120
	Stage 1 HIN	125	126	12/	128	130	131	132
47		1.57	455	155	1-10	172	1-15	
	Prehypertension	152	120	120	163	16/	1/1	174
	Stage 1 HTN	125	126	127	129	130	131	132
	Stage 2 HTN	138	138	139	141	142	143	144

Boys SBP by Age and Height (Normal SBP is less than the prehypertensive result.)

Age į	BP Classification			Syst	olic BP (m	mHg)		
3	Height (cm)	92	94	96	99	102	104	106
	Prehypertension	100	101	103	105	107	108	109
	Stage 1 HTN	104	105	107	109	110	112	113
	Stage 2 HTN	116	117	119	121	123	124	125
4	Height (cm)	99	100	103	106	109	112	113
	Prehypertension	102	103	105	107	109	110	111
	Stage 1 HIN	106	107	109	111	112	114	115
	Stage 2 min	110	115	121	125	125	120	127
5	Height (cm)	104	106	109	112	116	119	120
	Stage 1 HTN	104	105	106	108	11/	115	112
	Stage 2 HTN	120	121	123	125	126	128	128
6	Hoight (cm)	110	112	115	110	122	176	127
	Prehypertension	105	106	108	110	111	113	113
	Stage 1 HTN	109	110	112	114	115	117	117
	Stage 2 HTN	121	122	124	126	128	129	130
7	Height (cm)	116	118	121	125	129	132	134
	Prehypertension	106	107	109	111	113	114	115
	Stage 1 HTN	110	111	113	115	117	118	119
	Stage 2 HTN	122	123	125	127	129	130	131
8	Height (cm)	121	123	127	131	135	139	141
	Prehypertension	107	109	110	112	114	115	116
	Stage 1 HTN	111	112	114	116	118	119	120
<u> </u>	Stage 2 HTN	124	125	127	128	130	132	132
9	Height (cm)	126	128	132	136	141	145	147
	Prehypertension	109	110	112	114	115	11/	118
	Stage 2 HTN	125	114	128	130	132	133	134
10		120	120	127	1.00	140	150	452
10	Prehypertension	111	133	114	141	140	119	119
	Stage 1 HTN	115	116	117	119	121	122	123
	Stage 2 HTN	127	128	130	132	133	135	135
11	Height (cm)	135	137	142	146	151	156	159
	Prehypertension	113	114	115	117	119	120	120
	Stage 1 HTN	117	118	119	121	123	124	125
	Stage 2 HTN	129	130	132	134	135	137	137
12	Height (cm)	140	143	148	153	158	163	166
	Prehypertension	115	116	118	120	120	120	120
	Stage 7 HTN	131	120	122	123	125	127	127
12	the induction (and	447	450	455	150	150	474	472
13	Prehypertension	147	118	120	120	120	120	120
	Stage 1 HTN	121	122	124	126	128	129	130
	Stage 2 HTN	133	135	136	138	140	141	142
14	Height (cm)	154	157	162	167	173	177	180
	Prehypertension	120	120	120	120	120	120	120
	Stage 1 HTN	124	125	127	128	130	132	132
	Stage 2 HTN	136	137	139	141	143	144	145
15	Height (cm)	159	162	167	172	177	182	184
	Prehypertension	120	120	120	120	120	120	120
	Stage 1 HTN	126	127	129	131	133	134	135
	Stage Z HTN	139	140	141	143	145	147	147
16	Height (cm)	162	165	170	175	180	184	186
	Stage 1 HTM	120	120	120	120	120	120	120
	Stage 2 HTN	141	142	144	146	148	149	150
17	Height (cm)	164	166	171	176	181	185	187
	Prehypertension	120	120	120	120	120	120	120
	Stage 1 HTN	131	132	134	136	138	139	140
	Stage 2 HTN	144	145	146	148	150	151	152





stitute

Measurement

- Begin routine blood pressure (BP) measurement at 3 years of age.
- Correct cuff size depends on arm size. Practically speaking, correct cuff size equals largest cuff that will fit on the upper arm with room below for the stethoscope head.
- BP should be measured in the right arm of a relaxed, seated child.
- BP measurement by auscultation is the Gold Standard.
- BP by automated device correlates reasonably well with auscultation, with practical advantages of rapid measurement remote from child and elimination of reader error.
- If BP is high by automated device, repeat by auscultation.

BP Classification/Interpretation

BP is classified by systolic BP (SBP) and diastolic BP (DBP) percentiles for age/sex/height. If SBP or DBP >90th percentile, repeat twice at same office visit before interpreting result.

Normal BP: SBP and DBP <90th percentile → Recheck in 1 year.

Prehypertension: SBP or DBP \ge 90th percentile to <95th percentile or BP >120/80 mmHg to <95th percentile

- \rightarrow Recheck in 6 months.
- Begin weight management (as appropriate).

Stage 1 Hypertension (HTN): SBP and/or DBP ≥95th percentile to ≤ 99th percentile plus 5 mmHg

- \rightarrow Recheck in 1 to 2 weeks.
- ➡ If BP remains at this level on recheck, begin evaluation

and treatment including weight management if appropriate.

Stage 2 HTN: SBP and/or DBP >99th percentile plus 5 mmHg → Begin evaluation and treatment within 1 week,

immediately if symptomatic.

Systolic BP Percentile Tables

Since diastolic HTN rarely occurs without systolic HTN in children, the SBP percentile tables on the next page can be used for HTN screening. If a child's SBP on screening is classified as prehypertension or HTN, then both SBP and DBP percentiles should be determined using the tables in the complete report: The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. *Pediatrics 2004 Aug;114(Suppl 2:)555-76*; or http://www.nhlbi. nih.gov/health/prof/heart/hbp/hbp_ped.htm.

Directions for Use of Tables

- 1. Heights in the table are given for age at midyear. Use closest height to interpret BP.
- 2. Prehypertension SBP ≥ value from table (90th percentile) to < Stage 1 HTN value; or SBP >120 mmHg to < Stage 1 HTN value.

Stage 1 HTNSBP \geq value from the table (95thpercentile) to \leq Stage 2 HTN.

Stage 2 HTNSBP >value from table (99th percentileplus 5 mmHg).

For more information go to: www.nhlbi.nih.gov.



General Pediatric Physical Activity Guidelines

General Guidelines for Strength Training in Children

Frequency	Intensity	Time (Duration)	Туре
2-3 times/week	Start with no resistance, until proper technique is perfected. Then progress to 1-2 set of	20-30 minutes long 10-15 minute warm- up and cool-down	Full body exercises targeting all muscle groups (including the core)
	 8-15 repetitions of 60% of 1 RM. You can increase the volume of training adding until 4 set of 8-15 repetitions. Resistance should be added slow, increments of 10% are recommended 	At least 8 weeks are needed to obtained improvement.	Should be performed through the full range of motion at each joint 8-12 exercise are recommended.

Note. Compiled from ¹⁻³. 1 RM: One-rep max

Additional Recommendations

- ✓ Obtain medical evaluation prior to beginning a formal strength-training program. This medical evaluation will identify risk factors for injury and provide an opportunity to discuss previous injury, low back pain, medical conditions, training goals etc.
 - Children with cardiac disease (cardiomyopathy, pulmonary artery hypertension) should consult with a cardiologist prior to beginning
- ✓ Strength training should only be a small part of an overall fitness or sports program
- ✓ Proper techniques and safety precautions should be followed
- \checkmark Should be coupled with aerobic conditioning
- ✓ Proper technique and strict supervision by a qualified instructor is critical
- ✓ Explosive and rapid lifting is not recommended
- ✓ Strength training in a frequency higher than 4 times/week does not have additional benefit and seems to increase risk of overuse injury.
- ✓ 8–12 exercises. These exercises can include more advanced movements such as Olympicstyle lifting, plyometrics, and balance training, which can enhance strength, power, co-ordination, and balance. Proper progression must be necessary.

Note. Compiled from 1-3

General Guidelines for Aerobic Training

Frequency	Intensity	Time (Duration)	Туре
3-7 times/week	Moderate-vigorous activity; with vigorous intensity activity at least 3 days/week	Approximately 60 minutes or more	Any tolerated physical activity (walking, biking, running, sports such as soccer, hockey, active transportation, swimming, basketball and chores)

Note. Compiled from ^{3, 4}

Assessment of Aerobic Training Intensity

	RPE Scale (1- 10)	Talk Test	Heart Rate
Low Intensity or mild	3-4	The talk test is a simple way to measure relative intensity. As a rule of thumb, if you're doing low intensity activity you will be able to sing without pausing for a breath.	A person's target heart rate should be below 50 of his or her maximum heart rate. This maximum rate is based on the person's age. See formula in text box below
Moderate Intensity	5-6	You can talk, but not sing, during the activity.	Heart rate should be 50 to 70% of his or her maximum heart rate.
Vigorous or High Intensity	7-10	You will not be able to say more than a few words without pausing for a breath.	Heart rate should be 70 to 85% of his or her maximum heart rate.

Note. Compiled from ^{5,6}

Recommended equation to calculate maximal predicted heart rate in children⁸

Predicted maximal heart rate = [208 – (0.7x age)]

Example for a 10 years old child $[208 - (0.7 \times 10)] = 201$

Definitions

Strength training: the use of resistance methods to increase one's ability to exert or resist force. The training may include use of free weights, the individuals own body weight, machines, and/or other resistance devices to attain this goal.

Set: A group of repetitions separated by scheduled rest periods.

Concentric contraction: The muscle shortens during contraction.

Eccentric contraction: The muscle lengthens during contraction.

Isometric contraction: The muscle length is unchanged during contraction.

Plyometric exercise: Repeated eccentric and concentric muscle contractions, such as jumping onto and down from a platform

Progressive resistive exercise: exercise regimen in which the individual progressively increases the amount of weight lifted and/or the number of repetitions. The more repetitions, the greater the work performed and the greater the endurance development. The more weight lifted, the greater the strength development.

Interval training: is a type of discontinuous physical training that involves a series of low- to high-intensity exercise workouts interspersed with rest or relief periods. The high-intensity periods are typically at or close to anaerobic exercise, while the recovery periods involve activity of lower intensity.

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Pain Scale

Pain Scale

Level 1-2: Pain is present but does not impede activity.
Level 3-4: Can do most activities with periods of rest.
Level 5-6: Unable to do some activities because of pain.
Level 7-8: Unable to do most activities because of pain.
Level 9-10: Unable to do any activities because of pain.



Please be sure that your child's pain never increases during physical activity. If pain increases during physical activity, **STOP** exercising and consult your physician. If your child's pain is above 4, you might want to consult his or her oncologist or primary physician to determine if he or she is able to perform physical activity. Also, check to see if there are precautions or contraindications to consider when participating in physical activity.



Rating of Perceived Exertion Scale (RPE)

Rating of Perceived Exertion Scale (RPE)

The **Rating of Perceived Exertion Scale (RPE)** is used to determine how difficult the exercise feels to you. This is a subjective rating and is designed to help you feel the sensations involved with exercising. This rating should consider both strain and how tired your muscles feel, how hard you feel you are breathing and how fast you think your heart is beating. It is important that you take all these factors into account and you do not base your rating on one factor.

The scale displayed has verbal descriptions that correspond to numbers. Read these verbal descriptions and match how you are feeling to the corresponding number.

(Cardiovascular Endurance)		
#10	I am DONE!	
#9	I am probably going to stop.	
#8	I can grunt in response to your questions and can only keep this pace for a short time period.	
#7	I can still talk but I don't really want to and I am sweating like a pig!	
#6	I can still talk but I am slightly breathless and definitely sweating.	
#5	I'm just above comfortable, I am sweating more and can talk easily.	
#4	I'm sweating a little, but I feel good and I can carry on a conversation comfortably.	
#3	I am still comfortable, but I'm breathing a bit harder.	
#2	I'm comfortable and I can maintain this pace all day long.	
#1	I'm watching TV and eating bon bons.	

Color	Intensity
	Vigorous
	Moderate
	Mild
	Resting



Client Intake Form

Client Intake Form

Please note that the document provided in this appendix is an example of the useful information that might be required by the physical activity program for children affected by cancer. This information will be helpful to program, so they can better tailor the physical activity plan for your child.

Program: Name of Program

Parents to Complete	
Participant Information	
Name of Participant:	
Date of Birth:	
Gender (select one): Male \Box	Female
Home Telephone:	
Address:	
Mother name:	
Cell phone:	
Work phone:	
Father name:	
Cell phone:	
Work phone:	
Medical Information	
Name of Family Doctor:	
	_
Name of Oncologist:	
Phone Number:	_

Name of Primary Nurse: Phone Number:	
Diagnosis:	
Date of Diagnosis (dd/mm/yy):	
Treatment status: On Treatment \Box	Off Treatment \Box
If OFF treatment, please indicate date treat If ON treatment, please indicate anticipate	tment completed (dd/mm/yy): d date treatment will end (dd/mm/yy):
Treatment protocol (current and/or comple Please specify total medication doses recei	eted): ived.
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
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Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment):	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment): 	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer
Current side/effects/symptomatology (plea metabolic, neurologic or other side effects treatment): 	ase tell us if your child has any pulmonary, cardiac, caused or not caused by cancer and/or cancer

Please list any medications your child is on:

Please list any allergies your child has:

Emergency contacts - please list 3 emergency contacts (name, relationship, contact number):

	Name	Relationship	Phone Number
1)			
2)			
3)			

Appendix H

Physician Clearance Form

Physician Clearance Form

Please note that the document provide in this Appendix is just an example of the information that a physician clearance form should contain.

Specific information about treatment and its side effects would be useful to better tailor the physical activity plan of each child impacted by cancer.

Medical Clearance Form (example)

Describe the exercise program. Describe the intensity of the exercise (i.e., sessions will be mild/moderate). If you consider that your patient is able to participate please indicate by checking: **progressive physical activity** OR **unrestricted physical activity**.

PHYSICAL ACTIVITY READINESS

Based upon a current review of the health status of <u>Name of Patient/Survivor</u> I recommend:

 \Box No physical activity

 $\hfill\square$ Only a medically-supervised exercise program until further medical clearance

□ Physical activity under the supervision of a CSEP-professional Fitness & Lifestyle Consultant or CSEP exercise therapist:

 \Box Progressive physical activity:

 \Box With avoidance of:

 $\hfill\square$ With the inclusion of:

□ Unrestricted physical activity- start slowly and build up gradually

_M.D. (printed) Date:_____

Physician Signature:

NOTE: This physical activity clearance is valid for a maximum of six months from the date it is completed and becomes invalid if the medical condition of the patient becomes worse.

Appendix I

Infographics







Abbreviation List

Abbreviation List

ACH: Alberta Children's Hospital ACL: anterior crucial ligament **ACSM:** American College of Sports Medicine **ADLs:** activities of daily living **AEP:** accredited exercise physiologist AHA: American Heart Association ALL: acute lymphoblastic leukemia AML: acute myeloid leukemia **ANC:** absolute neutrophil count **AT:** athletic trainer AVG: active video games **AYA:** adolescent and young adult **BKY:** Bendy yoga kids **BMD:** bone mineral density **BMI:** body mass index **BMT:** bone marrow transplant **BP:** Blood pressure **CDC:** Center for Disease Control **CEP:** certified exercise physiologist cGvHD: chronic graft-versus-host disease **CHF:** congestive heart failure **CIPN:** chemotherapy induced peripheral neuropathy **CNS:** central nervous system **CRF:** cancer-related fatigue CRT: cranial radiation therapy/cranial radiotherapy **CTs:** clinical trials **DF:** dorsiflexion **EF:** ejection fraction EOL: end-of-life **ESC:** European Society of Cardiology **FITT:** Frequency, intensity, time and type GVHD: graft vs host disease GvL: graft versus leukemia GvT: graft versus tumor Gy: gray HLA: Human Leukocyte Antigen **HSC:** hematopoietic stem cell **HSCT:** hematopoietic stem cell transplant HR: heart rate **HRF:** health-related fitness **IQ:** intellectual quotient **IT:** intrathecal therapy KCC: Kid's Cancer Care LV: left ventricular

MHC: major histocompatibility complex

NK: Natural Killer cells

ON: osteonecrosis

PA: physical activity

PEER: Pediatric cancer patients and survivors Engaging in Exercise for Recovery **PedsQL:** pediatric quality of life inventory

PNF: Proprioceptive Neuromuscular Facilitation

PRT: progressive resistance training

PT: physiotherapist / physical therapist

QOL: quality of life

RCTs: randomized controlled trials

RM: repetition maximum

ROM: range of motion

RPE: rated perceived exertion scale

SF: shortening fraction

SD: standard deviation

VOD: veno-occlusive disease

VO_{2peak}: peak oxygen consumption

VO_{2max}: maximal oxygen consumption
Glossary of Terms

Glossary of Terms

Absolute neutrophil count (ANC): a measure of the number of neutrophils in the blood. Neutrophils are a type of white blood cell. They help the body fight infection. An absolute neutrophil count may be used to check for infection, inflammation, leukemia, and other conditions. Cancer treatment, such as chemotherapy, may reduce the absolute neutrophil count.

Accredited exercise physiologist (AEP): synonymous with certified exercise physiologist (CEP) and athletic trainers (ATs). AEPs, CEPs and ATs are university qualified allied health professionals, who specialize in clinical exercise interventions. In addition they perform assessments, prescribe conditioning exercise, as well as exercise, counselling and healthy lifestyle education in apparently healthy individuals and/or populations with medical conditions, functional limitations or disabilities associated with musculoskeletal, cardiopulmonary, metabolic, neuromuscular, and ageing conditions.

Activities of daily living (ADLs): things done in normal living including activities performed for self-care (feeding, bathing, dressing, grooming), work, homemaking and leisure.

Active video games (AVGs): Screen-based activities that require increased physical activity to play the game compared to conventional sedentary, or passive video games.

Acute lymphoblastic leukemia (ALL): an aggressive (fast-growing) type of leukemia (blood cancer) in which too many lymphoblasts (immature white blood cells) are found in the blood and bone marrow.

Acute myeloid leukemia (AML): an aggressive (fast-growing) disease in which too many myeloblasts (immature white blood cells that are not lymphoblasts) are found in the bone marrow and blood. Also called acute myeloblastic leukemia, acute myelogenous leukemia, acute nonlymphocytic leukemia.

Advanced cancer: Cancer that has spread to other places in the body and usually cannot be cured or controlled with treatment.

Adolescent and young adult (AYA): AYA was defining in several ways. However there is agreement that AYA includes those 15+ to 29 years of age (at diagnosis) and up to 39 years of age for survivors of childhood/AYA cancers.

Aerobic training (aka endurance training): exercise training performed at submaximal intensities aimed to enhance cardiorespiratory function or the aerobic (oxidative) capacity of the exercising muscles. Typically, this type of training involves exercise activities involving large muscle masses (e.g., running, jogging, cycling, rowing, etc.). Although this type of training commonly involve continues exercise at intensities ranging from moderate to vigorous, intermittent exercise of relatively larger intensity with resting periods are also beneficial to improve oxidative capacity.

Aerobic fitness: (aka, cardiovascular fitness; cardiopulmonary fitness) is a reflection of your ability to take oxygen from the atmosphere and use it to produce energy for your muscle cells. Many factors influence aerobic fitness, including your lung efficiency, cardiac function, gender, age, training status and genetic makeup.

Aerobic capacity: (aka, maximal aerobic capacity, aka, maximal aerobic power; aka, VO2 max; maximal oxygen uptake): is the ability to transport and utilize oxygen. It is direct by measured by VO2 max that is the maximal amount of oxygen you can use during intense exercise.

Amputation: the removal by surgery of a limb (arm or leg) or other body part because of injury or disease.

Anemia: a condition in which the number of red blood cells is below normal.

Assistive device: these are tools, products or equipment that help you perform tasks and activities. They may help you move around, see, communicate, eat, or get dressed.

Athletic trainer (AT): refer to accredited exercise physiologist (AEP)

Attention: the act or faculty of attending, especially by directing the mind to an object. **Biopsy:** the removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a spiration biopsy.

Biological reconstruction: a procedure wherein limb-sparing surgery is performed using biological (usually one's own) tissue to reconstruct a limb. An example of this would be a fibular auto-graft, where one's own fibula is used to replace a portion of a removed (cancerous) femur. **Body composition:** it quantify total body fat and fat-free body mass (includes muscle, water and bone) in the body.

Body mass index (BMI): the weight in kilograms divided by the square of the height in meters. It is commonly used to identify underweight and obesity.

Bone mineral density (BMD): A measure of the amount of minerals (mostly calcium and phosphorous) contained in a certain volume of bone. Bone mineral density measurements are used to diagnose osteoporosis (a condition marked by decreased bone mass), to see how well osteoporosis treatments are working, and to predict how likely the bones are to break.

Brain tumor: a brain tumor begins when normal cells in the brain change and grow uncontrollably, forming a mass. A brain tumor can be low grade (generally not cancerous and slower growing) or high grade (more likely to grow and spread quickly). In general, primary brain tumors, meaning those that start in the brain, do not spread outside of the central nervous system.

Capillary leak syndrome: a condition in which fluid and proteins leak out of tiny blood vessels and flow into surrounding tissues, resulting in dangerously low blood pressure. Capillary leak syndrome may lead to multiple organ failure and shock.

Cardiometabolic risk: refers to an increased risk for a cluster of diseases (diabetes, heart disease or stroke).

Cardiomyopathy: Cardiomyopathy refers to diseases of the heart muscle. These diseases have many causes, signs and symptoms, and treatments. In cardiomyopathy, the heart muscle becomes enlarged, thick or rigid. In rare cases, the muscle tissue in the heart is replaced with scar tissue.

Cachexia: a state characterize for severe weight loss and tissue wasting seconday to underlying disease—e.g., terminal cancer.

Cardiorespiratory fitness: refer to maximal oxigen consumption

Cardio-Respiratory Endurance: refer to maximal oxigen consumption

Cardiovascular Fitness: refer to maximal oxigen consumption

Cancer-Related Fatigue (CRF): also referred to as fatigue. In POEM, these terms are used interchangeably. It is a condition marked by extreme tiredness and inability to function due lack of energy. Fatigue may be acute or chronic.

Central nervous system (CNS) tumors: tumor of the central nervous system, including brain stem glioma, craniopharyngioma, medulloblastoma, and meningioma.

Certified exercise physiologist (CEP): refer to accredited exercise physiologist. **Chemotherapy:** treatment with drugs that kill cancer cells.

Chemotherapy cycle: some chemotherapy regimens (schedules) consist of a specific number of cycles given over a specific period of time, while others are given for as long as they are effective against the cancer.

Chemotherapy induced peripheral neuropathy (CIPN): characterized by damage to the peripheral nervous system from a chemotherapeutic agent, with each agent manifesting slightly different pathologic changes and symptomatic effects.

Childhood cancer: childhood cancer (also known as pediatric cancer) is cancer in a child. An arbitrarily adopted standard of the ages used are 0–14 years inclusive of age. However, the definition of childhood cancer sometimes includes young adults between 15–19 years old. For the purpose of this manual childhood cancer is define a cancer diagnosed between 0-18 years old.

Clinical trial (CTs): clinical trials are research studies that test new ways to prevent, detect, treat or manage cancer or other diseases. There are may different types such as Case control study (CCS) and Randomized controlled trial (RCTs). For more information visit:

http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/clinical-trials/ **Cognition:** the mental process of knowing, thinking, learning and judging; the psychological result of perception and learning and reasoning.

Cognitive function: pertaining to or characterized by cognition. That operation of the mind which we become aware of objects of thought or perception; it includes all aspects of perceiving, thinking, or remembering.

Cognitive executive deficits: impairments in cognitive function, particularly in executive functioning

Collapsed joint: joints are the part of the skeleton where two bones joint, when a joint collapses it is the flattening of the articular surface of a bone.

Concentric contraction: an overall shortening of the muscle occurs as it

generates tension and contracts against resistance. An example would be the concentric work of the biceps during lifting upward.

Congestive heart failure: is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The cardinal manifestations of congestive heart failure are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema.

Consolidation: treatment that is given after cancer has disappeared following the initial therapy. Consolidation therapy is used to kill any cancer cells that may be left in the body. **Coordination:** is a skill-related component of physical fitness that relates to the ability to use the senses, such as sight and hearing, together with body parts in performing motor tasks smoothly and accurately.

Core Strengthening: a form of exercise that activates core musculature, including transversus abdominus, diaphragm, pelvic floor muscles and multifidi (lower spinal) muscles. Core strengthening is often done with or without conscious focus on breathing. Yoga, Pilates, and Tai Chi are commonly recognized as being forms of core strengthening exercise but a core that is healthy activates with most activities.

Cortical tumor: a tumor found in the cortex of the brain.

Cytopenia: a condition in which there is a lower-than-normal number of blood cells. **Day zero:** in the hematopoietic stem cell transplant process, this is the day in which new stem cells are infused into the host (patient).

Differentiate: describes the processes by which immature cells become mature cells with specific functions. In cancer, this describes how much or how little tumor tissue looks like the normal tissue it came from. Well-differentiated cancer cells look more like normal cells and tend to grow and spread more slowly than poorly differentiated or undifferentiated cancer cells. Differentiation is used in tumor grading systems, which are different for each type of cancer.

Demyelination: the state resulting from the loss or destruction of myelin. Myelin is a mixture of proteins and phospholipids forming an insulation around many nerve fibers, increasing the speed at which impulses are conducted.

Dyspnea: difficult, painful breathing or shortness of breath. See exertional dyspnea. **Eccentric contraction:** a type of muscle contraction that occurs as the muscle fibres lengthen, such as when a weight is lowered through a range of motion. The contractile force generated by the muscle is weaker than an opposing force, which causes the muscle to stretch.

Concentric Contraction: is a type of muscle contraction in which the muscles shorten while generating force. This occurs when the force generated by the muscle exceeds the load opposing its contraction.

Ejection fraction (EF): the proportion of the volume of blood in the ventricles at the end of diastole that is ejected during systole; it is the stroke volume divided by the end-diastolic volume, often expressed as a percentage.

End-of-life (EOL): the last and final stage of the cancer continuum.

Endoprosthesis: an artificial device to replace a missing bodily part that is placed inside the body.

Endurance training (aka aerobic training): activity focused on enhancing cardiorespiratory function.

Engraftment: in an hematopoietic stem cell transplant is the day in which new blood-forming cells (i.e., HSCs) begin to grow and make sufficient number of healthy blood stem cells to normalize the patient's blood cell counts (neutrophils, platelets, and erythrocytes). We see neutrophil and platelet engraftment. Neutrophil engraftment is defined as the first day of three consecutive days where the neutrophil count (absolute neutrophil count) is 500 cells/mm3 ($0.5 \times 109/L$) or greater. A platelet count of 20,000 to 50,000/microliter for three day without blood transfusion is sign of platelet engraftment.

Engraftment syndrome: is an early complication of hematopoietic stem cell transplantation that occurs around neutrophil engraftment time and is attributed to the sudden cytokine discharge associated with robust engraftment of transplanted cells. This include the presence of two or more of the following symptoms usually 96 hours before neutrophil engraftment time: fever with no detectable infectious, erythematous skin rash not related to drug reactions or viral infection , weight gain of 2.5-5% (above baseline of admission) and albumin drop to 90% of pretransplant levels, and dyspnea, hypoxia and pulmonary infiltrates .

Ewing sarcoma: a type of cancer that forms in bone or soft tissue.

Executive function: executive function is a set of mental processes that helps connect past experience with present action. People use it to perform activities such as planning, organizing, strategizing, paying attention to and remembering details, and managing time and space.

Exercise: physical activity performed in one's discretionary time on a repeated basis over an extended period of time with the goal of improving fitness or health.

Exertional dyspnea: difficult, painful breathing or shortness of breath as a result of exertion. See dyspnea.

Fatigue: refer to cancer related fatigue.

Graft versus host disease (GVHD): a disease caused when cells from a donated stem cell graft attack the normal tissue of the transplant patient.

Graft versus leukemia (GvL): the donor's immune cells may recognize residual leukemia, lymphoma or cancer cells as being different and destroy them.

Graft versus tumor (GvT): the donor's immune cells may recognize residual leukemia, lymphoma or cancer cells as being different and destroy them.

Growth hormone: a protein made by the pituitary gland that helps control body growth and the use of glucose and fat in the body. Also called somatotropin.

Health-related fitness (HRF): is the ability to become and stay physically active. It has five components: cardiovascular fitness, muscular endurance, muscular strength, flexibility, and body composition. Together, these components promote optimum health and prevent the onset of disease and problems associated with inactivity.

Hematology: the study of blood and blood forming organs.

Hematopoietic Stem Cell Transplant (HSCT): also known as bone marrow transplant. The transplant of an immature cell that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets. Hematopoietic stem cells are found in the peripheral blood and the bone marrow.

Hematopoiesis: the formation of new blood cells.

High-dose chemotherapy: an intensive drug treatment to kill cancer cells, but that also destroys the bone marrow and can cause other severe side effects. High-dose chemotherapy is usually followed by bone marrow or stem cell transplantation to rebuild the bone marrow.

High-dose radiation: an amount of radiation that is greater than that given in typical radiation therapy. High-dose radiation is precisely directed at the tumor to avoid damaging healthy tissue, and may kill more cancer cells in fewer treatments.

Hippocampus: a layer of gray matter lying along the floor of the lateral ventricle of the brain, comprised of cholinergic and possibly glutamatergic fibers, believed to be the critical brain structure underlying learning and memory.

Human leukocyte antigen (HLA): is what the immune system uses to distinguish between self and non-self. The HLA molecules are cell surface receptors that present antigens to T lymphocyte cells, initiating an immune response. The T cells only respond to foreign peptides, so differences in the HLA between donor and recipient will make T cells respond

Immunotherapy: a type of biological therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some types of immunotherapy only target certain cells of the immune system. Others affect the immune system in a general way.

Induction therapy: the first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, induction therapy is the one accepted as the best treatment. If it doesn't cure the disease or it causes severe side effects, other treatment may be added or used instead. **In-patient:** admitted to hospital and assigned a hospital bed/room.

Intellectual quotient (IQ): a score derived from a standardized test designed to assess an individual's intelligence as compared to the general population.

Intrathecal therapy (IT) or intrathecal chemotherapy: treatment in which anticancer drugs are injected into the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord.

Isolation Phase: state of being separated from others due to lowered immunity.

Isometric Contraction: A form of exercise in which tension develops in the

muscle but no mechanical work is performed. There is no appreciable joint movement, and the overall length of the muscle remains the same.

Late-effects: (aka side effect) are those that were not apparent during primary treatment but become apparent at some later time.

Left ventricle: the left side of the heart that receives the arterial blood from the left atrium and contracts to force it into the aorta.

Leukopenia: a condition in which there is a lower-than-normal number of leukocytes (white blood cells) in the blood.

Loads: (aka resistance) weight lift in a progressive resistive training.

Long-term effects (toxicities): refer to late effects.

Long-term survivor: as those survivors who have been cancer free for at least 5 years.

Limb sparing surgery: also called limb-salvage surgery is a surgery to remove a tumor in a limb (arm or leg) without removing the whole limb. The bone and tissue around the tumor may also be removed, and an implant may be used to replace the part of the limb removed. Limb-sparing surgery is done to help save the use and appearance of the limb. It is used to treat cancers of the bone and soft tissue.

Limb biological reconstruction: could be defined as a procedure wherein limb-sparing surgery is performed using biological (usually one's own) tissue to reconstruct a limb. An example of this would be a fibular auto-graft, where one's own fibula is used to replace a portion of a removed (cancerous) femur.

Limb salvage surgery: The removal of a neoplasm that otherwise would be treated by amputation. Limb salvage usually requires two separate but equally important procedures: (a) "adequate" removal of the tumor and (b) bone and soft-tissue reconstruction.

Lymphoid: referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop.

Maintenance chemotherapy: treatment that is given to help keep cancer from coming back after it has disappeared following the initial therapy. It may include treatment with drugs, vaccines, or antibodies that kill cancer cells, and it may be given for a long time. See also ALL Treatment Phases.

Maintenance phase: This is the third phase of acute lymphoblastic leukemia (ALL) treatment. The goal is to kill any remaining leukemia cells that may regrow and cause a relapse. Often this phase of treatment are given in lower doses than those used during the remission induction and consolidation/intensification phases. Not taking medication as ordered by the doctor during maintenance therapy increases the chance the cancer will come back. This is also called the continuation therapy phase.

Major histocompatibility complex (MCH): a genetic system that allows large proteins in immune system cells to identify compatible or foreign proteins. It allows the matching of potential organ or bone marrow donors with recipients

Malignant: Cancerous. Malignant cells can invade and destroy nearby tissue and spread to other parts of the body.

Maximal aerobic capacity: refer to a maximal oxygen consumption.

Maximal oxygen consumption (VO2max): it is the maximum amount of O2 that can be utilized, typically during an incremental test to exhaustion (although if the exercise intensity is high enough, VO2max may be eventually attained). VO2max is normally expressed as an absolute (L·min-1) or relative (mL·kg-1·min-1) rate and it reflects the cardiorespiratory physical fitness of a person. VO2 max is influenced by central and peripheral components. The central component involves the ability of your lungs, heart and vascular system to deliver oxygen to your muscles via your blood stream. The peripheral component involves the ability of your muscle cells to extract oxygen from your blood and use it to make ATP, the fundamental unit of energy. VO2 max values are lower in women, and decrease incrementally with age.

Metabolic syndrome: a condition marked by extra fat around the abdomen, high levels of blood glucose (sugar) when not eating, high levels of triglycerides (a type of fat) in the blood, low levels of high-density lipoproteins (a type of protein that carries fats) in the blood, and high blood pressure. People with metabolic syndrome are at increased risk of diabetes mellitus and diseases of the heart and blood vessels.

Methaphyses: the metaphysis is the wide portion of a long bone between the epiphysis and the narrow diaphysis. It is considered a part of the growth plate, the part of the bone that grows during childhood and as it grows, it ossifies near the diaphysis and the epiphyses.

Metastasis: the spread of cancer from one part of the body to another. A tumor formed by cells that have spread is called a "metastatic tumor" or a "metastasis." The metastatic tumor contains cells that are like those in the original (primary) tumor.

Muscle atrophy: is the wasting or loss of muscle tissue.

Muscular strength: is the ability of the muscle to exert force during an activity.

Muscular endurance: is the ability of the muscle to continue to perform without fatiguing. **Myeloid:** having to do with or resembling the bone marrow. May also refer to certain types of hematopoietic (blood-forming) cells found in the bone marrow.

Myocardial fibrosis: is define by a significant increase in the collagen volume factor of the myocardial and leads to impaired cardiac diastolic and systolic function and is related to adverse cardiovascular events.

Neo-adjuvant chemotherapy: chemotherapy that enhances the effect of a particular medical treatment.

Nephroblastoma: synonymous with Embryoma, or Wilms' tumour. Malignant renal (kidney) tumour of early childhood.

Neuroblastomas: cancer that arises in immature nerve cells and affects mostly infants and children.

Neurocognitive outcomes: this term encompasses a large number of problems and issues associated with intellectual functioning and information processing.

Neurogenesis: involves proliferation, differentiation, and/or maturation of neural cells. **Neuron:** type of cell that receives and sends messages from the body to the brain and back to the body. The messages are sent by a weak electrical current.

Neutropenia: is an abnormally low count of neutrophils, a type of white blood cell that helps fight off infections.

Non-Curative Cancer: A form of cancer where a procedural cure has yet to be identified. **Open chain strengthening:** open chain strengthening: Exercise in which a distal (i.e. foot is distal to or further from the knee) segment of the body moves freely in space.

Osteonecrosis: a condition in which there is a loss of blood flow to bone tissue, which causes the bone to die.

Osteopenia or low bone mineral density: a condition in which there is a lower-than-normal bone mass or bone mineral density (the amount of bone mineral contained in a certain amount of bone). Osteopenia is a less severe form of bone loss than osteoporosis.

Osteoporosis: a condition that is marked by a decrease in bone mass and density, causing bones to become fragile.

Osteosarcoma: a cancer of the bone that usually affects the large bones of the arm or leg. **Out-patient:** Accessing ambulatory hospital services but not assigned bed/room for the purpose of staying day/night.

Oxygen uptake reserve: from the maximal oxygen consumption (VO2 _{max}), subtract your resting oxygen consumption (found by multiplying 3.5 by your total weight in kilograms) to get your VO2 reserve. The higher your VO2 reserve, the more intense the exercise you're capable of doing

Palliative care (aka supportive care, comfort care and symptom management) : an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Pallor: pale

Peak oxygen consumption (VO2peak): it is the highest value of oxygen consumption attained on the particular test, most commonly an incremental or other high-intensity test, designed to bring the subject to the limit of tolerance. Although, it is the highest value achieved during a particular test, it is not necessarily the maximum value attainable by the subject.

Physical activity (PA): any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level.

Physical fitness: the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure-time pursuits and respond to emergencies. Physical fitness includes a number of components consisting of cardiorespiratory endurance (aerobic power), skeletal muscle endurance, skeletal muscle strength, skeletal muscle power, flexibility, balance, speed of movement, reaction time, and body composition.

Physical performance: (aka physical function) is a reflection of their overall health, and the impact of several chronic diseases common among the elderly or cancer patients, such as osteoporosis and coronary heart disease, on the ability to function without limitations in the course of daily life.

Physical functioning: refer to physical performance

Physical therapy: The use of exercises and physical activities to help condition muscles and restore strength and movement.

Plyometric exercises: High intensity, high-velocity resistance exercise characterized by a resisted eccentric muscle contraction followed by a rapid concentric contraction and designed to increase muscular power and coordination, also known as stretch-shortening drills. An example would be box jumping.

Processing speed: the rate at which cognitive functioning occurs.

Progressive resistance training: an exercise regimen in which the participant progressively increase the amount of weight lifted and or/the amount of repetitions. The more repetitions, the greater the endurance development. The more weight lifted, the greater the strength development.

Props: is any object that helps you stretch, strengthen, balance, relax, or improve your body alignment.

Proprioceptive neuromuscular facilitation (PNF): a method of stretching muscles to maximize their flexibility that is often performed with a partner or trainer and that involves a series of contractions and relaxations with enforced stretching during the relaxation phase. **Prosthesis:** an artificial body part, such as a leg, a heart, or a breast implant.

Pulmonary fibrosis: scarring throughout the lungs that can be caused by many conditions. **Prophylaxis:** an attempt to prevent disease.

Quality of life (QOL): the World Health Organization defines quality of life as individuals perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment.

Radiation therapy: the use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that travels in the blood to tissues throughout the body.

Randomized controlled trials (RCTs): a study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial.

Range of motion (ROM): is a measurement of movement around a joint.

Reinduction therapy: treatment for relapse. Using either a four-drug reinduction regimen (similar to that administered to newly diagnosed high-risk patients) or an alternative regimen including high-dose methotrexate and high-dose cytarabine.

Remission: disappearance (not a cure) of detectable disease.

Repetitions: the number of times a person lifts a weight in muscle-strengthening activities. Repetitions are analogous to duration in aerobic activity.

Repetition maximum (RM): in strength tainting is the maximum amount of force that can be generated in one maximal contraction

Restrictive lung disease: decrease in the total volume of air that the lungs are able to hold, is often due to a decrease in the elasticity of the lungs.

Resistance training: is any exercise that causes the muscles to contract against a resistance with the expectation of increases in strength, mass and/or endurance.

Rotationplasty: surgery used to remove a tumor in or near the knee joint, often in young people who are still growing. The knee and part of the thigh are removed. The part of the leg that remains below the knee is then attached to the part of the leg above the knee, with the foot facing backward and the ankle joint acting as a new knee. The patient is then fitted with an artificial lower leg and foot.

Sarcopenic obesity: a form of obesity which is operationally defined as excess weight and reduced muscle mass and/or strength, a combination that occurs in 4 to 9% of obese patients. **Scoliosis:** abnormal lateral curvature of the spine

Short-term effects (toxicities): synonymous with acute effects (toxicities) and early effects. Occur during or shortly after cancer treatment.

Soft tissue sarcoma: a cancer that begins in the muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body.

Strength: a health and performance component of physical fitness that is the ability of a muscle or muscle group to exert force.

Supportive care: refer to palliative care

Survival length: time of diagnosis until death.

Systolic dysfunction: systolic dysfunction is characterized by a decrease in myocardial contractility.

Terminal Cancer: Cannot be cured and will cause death.

Thrombocytopenia: lower-than-normal number of platelets in the blood. It may result in easy bruising and excessive bleeding from wounds or bleeding in mucous membranes and other tissues.

Thrombotic microangiopathy: is a rare but serious medical disease. It is a pattern of damage that can occur in the smallest blood vessels (cappillars) inside many of your body's vital organs – most commonly the kidney and brain.

Valsalva maneuver: the Valsalva maneuver is performed by attempting to forcibly exhale while keeping the mouth and nose closed.

Veno-occlusive disease: disease is an uncommon, but serious liver problem. The blood vessels that transport blood through the liver become inflamed and blocked. This causes the liver to swell. Because of the lack of blood supply, the liver cannot remove toxins, drugs and other waste products from the blood, which is one of the liver's essential functions. Eventually, fluids build up inside the liver, making it more tender. The kidneys may keep excess water and salt, causing the arms, legs and abdomen to swell. In most cases, is not severe, and the damage to the liver can be reversed.

Visuo-spatial abilities: relating to, or being thought processes that involve visual and spatial awareness.

Weight-bearing: describes the amount of weight a body part is applying against any given surface. Standing on one leg, a person applies 100% weight bearing through that foot. A weight

bearing status or restriction refers to a limitation imposed by a surgeon to protect an operated or broken limb from injury, deformity or instability. These are further categorized as:

• Full weight bearing (FWB): no limitation in weight.

• Weight-bearing as tolerated (WBAT): limited only by the person's own perception of discomfort or pain. From a safety and practical perspective, functionally equivalent to FWB (above).

• **Partial weight bearing (PWB):** classically understood as about 50% on one's own body weight, but sometime surgeon will specify a specific weight (i.e. "up to 30lbs of pressure). Teaching of this easiest by using a weight scale.

• **Feather weight bearing (FeWB):** toe-touch or light weight, often described as "imagine there is an egg under your foot that you cannot crush". Practically the person is allowed to touch the floor only enough to help with balancing themselves. Will require crutches or other ambulatory device to walk.

• **Non-weight bearing (NWB):** not allowed to put weight through a body part. Will require crutches or other ambulatory device to walk.

Weight-bearing exercise: exercise during which the body works against the force of gravity and the feet and legs carry a person's weight. Weight-bearing exercise can be high impact as jump and run or low impact as climb stairs or walk.

Working memory: short term memory related to the storage, processing and recall of information required for the accomplishment of immediate cognitive tasks.



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POEM Editors

