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POEM

PEDIATRIC ONCOLOGY EXERCISE MANUAL

FAMILY VERSION

1st Edition

Alberta Health Services
Alberta Children's Hospital Research Institute for Child and Maternal Health
University of Calgary Faculty of Kinesiology
Health & Wellness Lab

Health & Wellness Lab

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Family Version, *1st Edition*

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Always do the warm-up exercises before attempting any individual exercises. It is recommended that you check with your doctor or healthcare professional before commencing any exercise regime. While every effort has been taken in the preparation of this material, the publishers and their respective employees or agents will not accept responsibility for injury or damage occasioned to any person as a result of participation in the activities described in the book.

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Thrive: Physical Activity for Cancer Survivors

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Dr. Carolina Chamorro-Viña completed her Bachelor's degree in Physical Education and Sports in Uruguay. Upon completion, she moved to Spain to complete her Masters equivalent in Exercise Prescription and Health and her Ph.D. in Biomedicine and Health, at the University Europea de Madrid. She is currently working on her Post-Doctoral research supported by Alberta Children's Hospital Department of Pediatrics, Hematology, Oncology and Blood and Marrow Transplant Program and Psychosocial Oncology Research Training (PORT). Her project focuses on the translation of the evidence into community programming. She has created the Pediatric cancer patients Engaging in Exercise for Recovery (PEER) program, a community based-exercise program for children with cancer and now is developing education session for families and professional using POEM as a resource.

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Dr. Melanie Keats is an Associate Professor in Health and Human Performance, Faculty of Health Professions, Dalhousie University. She has a cross-appointment with the School of Physiotherapy and holds a scientific staff appointment with the IWK Children's Hospital in Halifax. She completed her doctoral and post-doctoral training at the University of Calgary. Her research interests include the examination of the impact of physical activity on cancer related health outcomes; investigating the prevalence, determinants, and activity preferences of young cancer survivors; and exploring the effectiveness of novel interventions designed to promote physical activity across the cancer continuum. She serves on several patient advocate and scientific research committees dedicated to enhancing the quality of life of young cancer survivors.

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Dr. S. Nicole Culos-Reed is an Associate Professor in Health and Exercise Psychology in the Faculty of Kinesiology, and Adjunct Associate Professor in the Department of Oncology in the Faculty of Medicine, University of Calgary. Dr. Culos-Reed also holds a Research Associate appointment with the Department of Psychosocial Resources, Tom Baker Cancer Centre. She created and runs the Health & Wellness Lab, which offers wellness resources (educational and programming) and researches the effects of physical activity for cancer survivors. The lab focuses on utilizing an interdisciplinary perspective to understand and improve the quality of life of cancer patients and survivors. Specifically, the goal of her research is to develop physical activity programs that positively impact the myriad of physical and psychosocial factors that cancer survivors experience, ultimately enhancing their quality of life. Dr. Culos-Reed is the Director of the Thrive Centre, a fitness facility for cancer survivors.

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
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“

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
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“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

Alberta Health Services

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.

Alberta Children's HOSPITAL
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PREFACE

Dear Families,

Welcome to the POEM manual. The POEM is the first evidence-based physical activity manual for children with cancer, created by an international and multidisciplinary team. This family version of the manual ensures that patients and families can learn about the benefits of physical activity. We aim to bring POEM out of the realm of academia and distribute it globally so that all pediatric cancer patients and families can benefit.

We know that pediatric cancer patients are at risk for a sedentary lifestyle and the associated health risks. A physically active lifestyle is crucial for children with pediatric cancer, as the risks of a sedentary lifestyle have even more extreme consequences than for healthy children. Our goal is to encourage these patients to engage in appropriate, safe, and enjoyable physical activities in order to improve their quality of life, diminish the cancer treatment side effects, and reduce their risk of comorbid conditions, such as obesity.

This project will advance the health of childhood cancer survivors by closing the gap between research on physical activity benefits through the cancer journey and what survivors, families, clinicians, and educators know and use for the promotion of physical activity. 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 patient's and survivor's needs. As a mom told us, "during treatment you are concerned about your child's life, therefore you do not think about the importance of physical activity in your child's life…you don't even realize that physical activity is an option".

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. The POEM will better inform health care professionals, fitness professionals, and families affected by pediatric cancer about the benefits of physical activity during the pediatric cancer journey. This manual represents the collective work of 27 international authors. Each author was invited to contribute based on his/her leading expertise in the area.

Important information: this manual ***was not created to read from beginning to end***. Read the chapters that might have helpful information for you and your child. ***Chapter 1 through Chapter 4*** have important information that might be useful for most types of cancer. We highly recommend you go over those chapters that might help you better understand the

importance of physical activity, basic terminology and general recommendation. ***Chapter 5*** cites the most common side effects that a child with cancer may develop, and provides recommendations about what types of physical activity are recommended and what precautions to consider. ***Chapter 6*** provides information about cardiotoxicity (i.e., damage to the heart caused by some cancer treatments). ***Chapters 7 to 11*** address specific types of cancer (leukemia, brain tumor, solid tumor), as well as specific protocols and palliative care. In those chapters you can read about the evidence base for physical activity unique to these situations. ***Chapters 12 to 14*** provides tips to engage your child in physical activity, as well as a look at emerging research on alternative types of physical activity, including yoga and active video games.

Recommendations for using this manual: For the purposes of the information to follow, the editors have pre-defined several of the terms that will be used throughout the manual. First and foremost, the editors would like to 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** refers to children and adolescents who are receiving active treatment for their malignancy, while **survivors** refers 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** 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.

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. Textboxes 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 guidelines, and every child will be different. Therefore, recommendations must be adapted on an individual basis around personal and medical characteristics. Before your child starts a new physical activity, please consult with their oncologist or primary physician and obtain medical clearance. Also, as parent or guardian, be sure that the person who will be working with your child has the appropriate understanding of physical activity during a cancer journey, and connect them to your child's oncology or primary physician if needed. Overall, it is recommended to "start low and progress slow", monitoring the patient or survivor carefully.

Physical activity is an important component in the healthy development of any child. In a child with cancer, it may be particularly important for countering many of the negative side effects of cancer and its treatment. Is always better to do some physical activity, even if it is just a couple of minutes, than to do nothing.

POEM
PEDIATRIC ONCOLOGY EXERCISE MANUAL

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

Contents

Chapters

Appendices

Chapter 1

Childhood Cancer: An Overview

Gregory Guilcher, MD

Learning Objectives

After completing this chapter you will know:

- ✓ …what cancer is and its treatment.
- ✓ …the most common types of pediatric cancer, incidence and cure rates.
- ✓ …the treatment side effects and their implications on physical activity.
- ✓ …the importance of physical activity in preventing and alleviating the negative effects of cancer therapy.

Introduction

In order to better understand the rest of the manual, this chapter will help you to understand what cancer is and how it is treated. The main negative side effects of cancer and its treatment, and the impact on **physical activity (PA)** will also be discussed.

What is cancer?

Cancer is a term used to name diseases where abnormal/unhealthy cells grow without control. These cells are known as malignant cancer cells and usually live longer than normal cells in the body [1]. Cancer cells may also travel and invade other parts of the body, in a process known as **metastasis**. A group of cancer cells gathered together is called a **tumor**. Various systems have been developed to categorize cancer in different stages. These systems allow physicians to better decide the most beneficial therapy for your child. Typically, the more advanced the staging, the more aggressive the disease, with a more intensive treatment.

What are the most common types of childhood cancer?

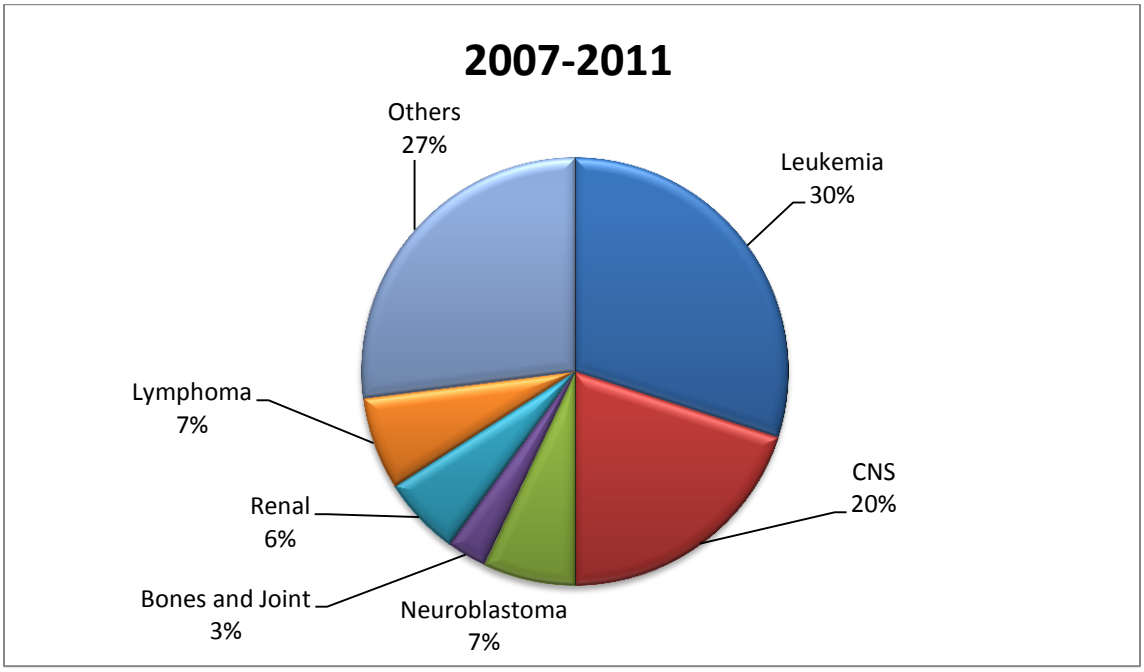
Cancer is one name for a group of more than 100 diseases. Most cancers are named for the organ or type of cells in which they originate. Leukemias and lymphomas are the most common cancers diagnosed in children, followed by **central nervous system tumors.** Within leukemias**, acute lymphoblastic leukemia (ALL)** is most common. Tumors of bone and muscles make up a small proportion of childhood cancer. *Figure 1.1* below shows the common cancer diagnoses in children versus those in teenagers, as seen in *Figure 1.2* [1-4]. As you can see in these figures, some cancers that are prevalent in one age group are rarely diagnosed in the other.

How common is childhood cancer?

- ✓ Pediatric cancer is only 2% of all cancer cases in society [1,2].
- ✓ Approximately 1 in 7,000 children aged 15 and under in North America are diagnosed with cancer each year [1].
- ✓ In Canada, there are approximately 900 new cases of cancer per year in children under 15 years old. There are 1,300 cases in children under 19 years old [1].
- ✓ The occurrence of cancer is highest in children age 3 and under.

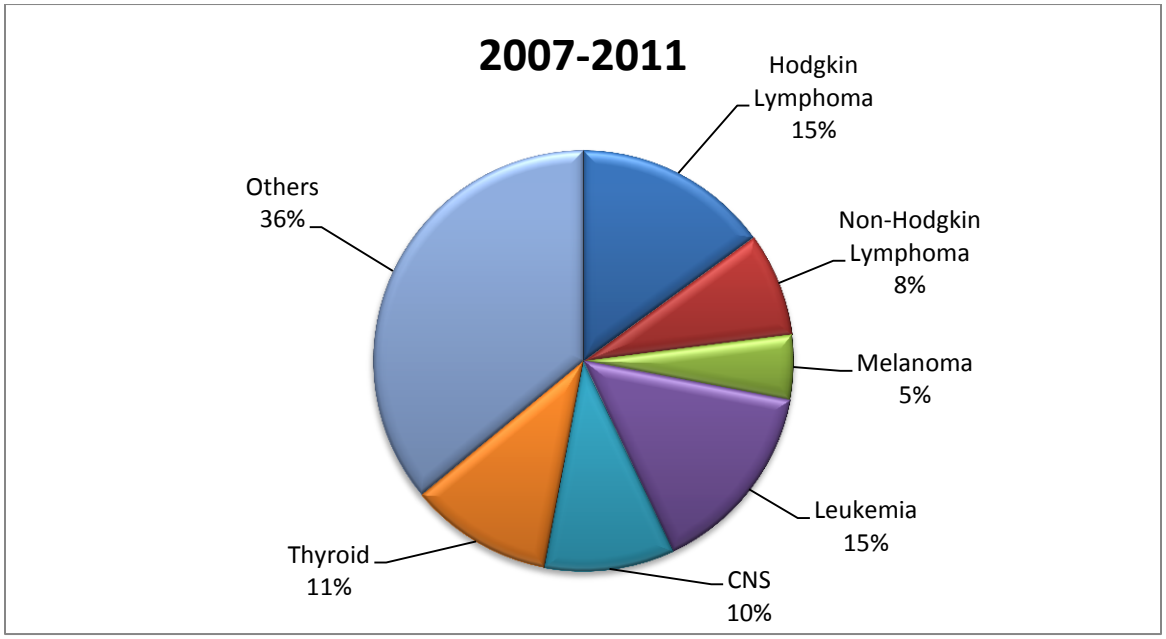
A cancer patient and her sister playing with their mom during a PEER session

Figure 1.1. Cancer diagnoses in children 0-14 years of age.



Note. Data taken from Surveillance Research Program, National Cancer Institute [3] and Gourney et al., [4]. CNS: central nervous system tumor.

Figure 1.2. Cancer diagnoses in adolescents 15-19 years of age.



Note. Data taken from Surveillance Research Program, National Cancer Institute [3] and Gourney et al., [4]. CNS: central nervous system tumor.

What are the cure rates of childhood cancer?

- ✓ In high-income countries, cure rates for childhood cancer are now greater than 80% [1,4,5].
- ✓ One in 300-350 young adults in North America are survivors of childhood cancer [2].
- ✓ Children who live in low-income or developing countries have a lower chance of surviving childhood cancer, due to difficulty accessing a timely diagnosis, care, and essential treatments [6].

What are the causes of childhood cancer?

- ✓ The cause of most childhood cancers is unknown [1,4].
- ✓ Approximately 10% of childhood cancer diagnoses are linked with a genetic cancer predisposition [7].
- ✓ As most pediatric cancers are diagnosed at a very young age, this leaves very little time for the environment to play a role in the development of the disease.
- ✓ There are certain risk factors that are associated with different types of cancers, such as[7]:
  - ✓ Genetic Syndromes
  - ✓ Previous Exposure To Chemotherapy Or Radiotherapy
  - ✓ Family History Of Cancer
  - ✓ Infections

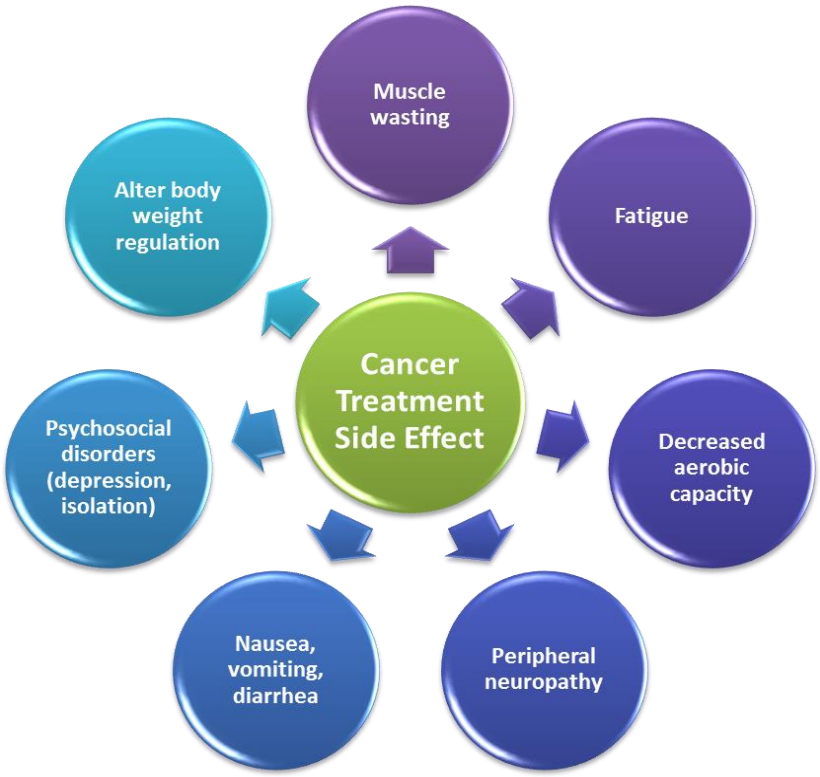
How is cancer treated?

Treatment options typically include one or more of the following: **chemotherapy, immunotherapy, radiotherapy**, surgery and **hematopoietic stem cell transplantation (HSCT).** The goal of cancer treatment is to maximize the chance of cure, while minimizing the **short-term** and **long-term toxicities.** These toxicities, or side effects, can impact your child's ability to engage in PA, and their ability to perform **activities of daily living,** such as climbing stairs. See *Figure 1.3* for a summary of negative side effects [8,9]. For those with cancer that is non-curable, these treatments have the goal of prolonging life and maximizing their quality of life.

Short-term toxicities occur during or shortly after cancer treatment (also known as acute effects, acute toxicities, and early effects).

Long-term toxicities occur months or years after treatment cessation (also known as **late-effects**).

Figure 1.3. Cancer treatment side effects that might impact the ability to perform physical activity.



Note. Compiled from [8-10].

Chemotherapy and how it impacts physical activity

Chemotherapy**,** also known as chemo, is the administration of several drugs to destroy cancer cells. It works by stopping or slowing the growth of malignant cells, which grow and divide quickly [11]. Because most medicines cannot specifically select cancer cells, they may also damage healthy cells, such as skin cells, which also divide quickly. The damage to these healthy cells can cause side effects for your child. See text box and *Table 1.1.*

Short-term side effects of chemotherapy:
- ✓ Inhibit growth of healthy cells
- ✓ Fatigue
- ✓ Nausea
- ✓ Vomiting
- ✓ Diarrhea
- ✓ Immune suppression
- ✓ Loss of appetite

Your child's physician will choose chemotherapy drugs based on several factors, such as the type of cancer and staging, whether or not your

child has previously received chemo, and your child's health condition. Depending on the chemo drugs chosen by the physician, your child may be more prone to develop certain negative side effects that can be carried into the child's survivorship [11]. See *Table 1.1* and *Table 1.2* for more details.

This therapy affects a child's participation in activity, mostly by increasing their fatigue. Energy requirements during PA and at rest can be impacted by cancer and its treatment. There are several drugs used for chemotherapy that are especially relevant to PA and physical ability. They are listed in the *Table 1.1*, along with which cancers they treat and what effects they may have on the child.

Table 1.1. Chemotherapy drugs and their potential side effects.

Drug	What cancers are treated	What it may cause
Corticosteroids	✓ Leukemias ✓ Lymphomas	✓ Central obesity. ✓ Muscle waste. ✓ Osteopenia/osteoporosis. ✓ May result in osteonecrosis (bone death).
Vincristine and Vinblastine	✓ Leukemias ✓ Lymphomas ✓ Brain tumors ✓ Solid tumors	✓ Peripheral neuropathy, sensory, or motor in nature (i.e., peripheral nerve weakness or reduced sensation). This is damage to nerves.
Methotrexate	✓ Leukemias ✓ Lymphomas ✓ Some bone tumors	✓ Adverse effects on the central nervous system. ✓ Osteopenia/osteoporosis.
Bleomycin and Nitrogen mustard compounds	✓ Hodgkin lymphoma ✓ Germ cell tumors	✓ Toxic to lungs. ✓ Breathing problems. ✓ Pulmonary fibrosis (scarring in the lungs).
Anthracyclines	✓ Leukemias ✓ Lymphomas ✓ Solid tumors	✓ Cardiac late-effects. ✓ Weakening of the heart muscle. ✓ Potential for cardiac failure.

Note. Compiled from [11].

Table 1.2. Chemotherapy side effects and their implications for physical activity.

Side Effect of Chemotherapy	What it is	Symptom (s)	Physical Activity Impact
Anemia	✓ Low red blood cell or hemoglobin levels	✓ Tiredness	✓ Decreases ability to do PA for an extended period of time or at high intensities, because of fatigue (extreme tiredness sensation).
Leukopenia	✓ Low measures of white blood cells	✓ Predisposed to infection.	✓ Physician might discourage group activities, due to their increased risk of infection.
Muscular Deconditioning [11]	✓ Loss of muscle mass	✓ Weakness.	✓ Makes activities more difficult. Causes intolerance to PA, and early fatigue.
Osteopenia [11]	✓ Loss of bone mass	✓ Prone to fractures.	✓ Needs to be careful with any PA that involves contact, and to diminish the risk of falls.
Fatigue [12,13]	✓ Is an abnormal sensation of tiredness that impedes your child to perform activities of daily living and PA, such as playing with their peers. Prolongation of this inactive lifestyle might worsen the fatigue, due to physical deconditioning.	✓ Intolerance to PA or lack of energy to do PA. Your child might feel the need to rest for extended periods of time. ✓ Decreased appetite.	✓ Start with small amounts of PA and a really low intensity. Alternate small bouts of PA with enough resting time.

Note. See *Chapter 5* to know more details about these side effects and their implication for PA.

See *Chapter 5* to learn more about these side effects and their implications for PA. Also see *Chapter 6* to learn more about cardiotoxicity. See *Appendix A* for medication list.

Radiation and how it impacts physical activity

Radiation therapy is the use of high energy x-rays, which kills fast growing cells, such as cancer cells. Similar to chemotherapy, radiation can hurt healthy cells in the body [14]. It differs from chemotherapy because it usually only targets a specific area in the body, however, it still has toxic effects on the healthy tissues located in that area. Normal tissue growth and health can be affected, and for this reason, efforts are made to spare children radiation therapy whenever possible. It is typically used in combination with another treatment [14]. Doctors will consider the child's age and the area to be radiated. They will also try to avoid areas that are vulnerable to radiation. See *Table 1.3* for more details.

Side effects of radiation:
- ✓ Local tissue and/or skin inflammation
- ✓ Fatigue
- ✓ Wasting of tissue within the treatment area
- ✓ Radiation-induced second cancers
- ✓ Neurocognitive delay (learning issues)

Table 1.3. Side effects of radiation.

Affected area	Negative effects	How this may impact physical activity
Brain [14,15]	✓ **Cognition** is vulnerable when the brain is developing. Children under three are spared radiation if possible. ✓ Growth and neurologic complications ✓ Risk for obesity [14, 15]	✓ When cognition is affected learning problems might appear. This can affect the child's ability to socialize, understand, and participate in organized activities. ✓ Asymmetric development between right and left sides might happen. This can lead to balance issues and scoliosis. ✓ Obesity is a drawback for PA participation.
Heart and Lungs [16]	✓ Scarring on the organs	✓ Cardio-respiratory long-term effects, such as scarring, may impact their PA tolerance.

Note. This table was compiled from [14-16].

Surgery and how it impacts physical activity

Doctors use surgery as an attempt to maximize the chances of a cure on solid tumors, and it is usually used along with other treatment options, such as chemotherapy or radiotherapy. Surgeries are commonly used to remove central nervous system tumors, abdominal masses, and musculoskeletal tumors. The negative side effects of surgeries will vary with each child,

depending on several factors, such as the area affected by cancer, and the type of surgical procedure. Refer to *Chapter 5* for more details. Surgeries may also put your child's motor skills and PA tolerance at risk. This reduced tolerance can be caused by:

Many complications and side effects depend on the site of the tumor and specific surgical procedure.

- ✓ Loss of lung volumes, because of lung resection or thoracic deformity
- ✓ Learning problems or delay, because of neurosurgery (brain surgery)
- ✓ Functional and/or structural problems, because of surgeries that involved the musculoskeletal system

Surgeons, physiotherapists, and fitness instructors must be in communication in order to maximize rehabilitation, shorten the recovery period, and ensure that your child can return to being physically active in a safe and feasible manner.

Immunotherapy and how it impacts physical activity

Immunotherapy takes advantage of the immune system mechanism and its response to destroy cancer cells. It is becoming the preferred method in treating aggressive neuroblastomas, and some lymphomas [17,18]. Children undergoing immunotherapy may be at a higher risk for infection. Because of this, special isolation may be necessary that will decrease the child's participation in PA.

Potential side effects:
- ✓ Allergic reactions
- ✓ Leaky blood vessels
- ✓ Immune suppression
- ✓ Risk of secondary lymphoma

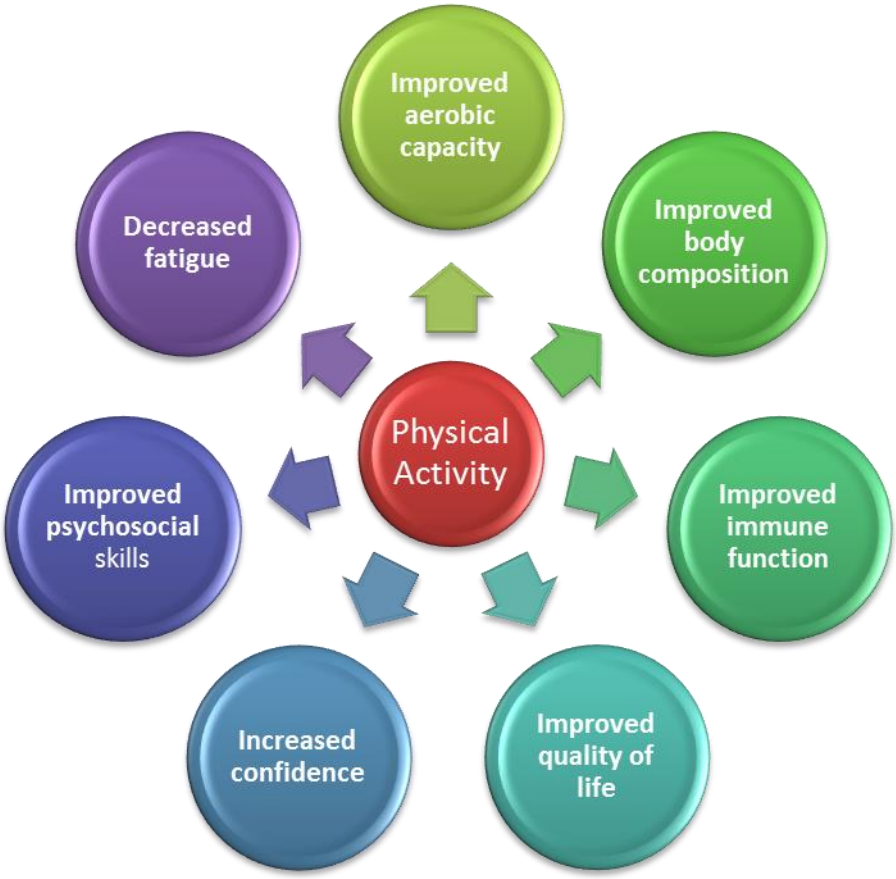
Hematopoietic stem cell transplantation and implications for physical activity

Hematopoietic stem cell transplantation (HSCT) is a therapy that helps with the recovery from high doses of chemotherapy and/or radiation. It can also be used as a form of immunotherapy to fix underlying blood and immune disorders. There are two common strategy types of HSCT, autologous HSCT and allogenic HSCT. Autologous HSCT is where stem cells can be re-introduced into the same person they came from. This strategy is typically used after high doses of chemotherapy to allow for those doses to be safely received. On the other hand, allogenic HSCT, is where stem cells can be donated from another person, and this method is used to treat leukemias, bone marrow failure, and immunologic disorders. For more information and implications for PA, refer to *Chapter 8.*

Benefits of physical activity in pediatric cancer

Currently, PA is being investigated in research, and promising preliminary results have been identified [9,19]. *Figure 1.4* shows the benefits of PA. Children with cancer often adopt a sedentary lifestyle that may worsen their already decreased fitness conditioning. Sedentary lifestyle is a modifiable risk factor that prevents and reduces some side effects, such as decreased bone mineral density [20-22] and aerobic capacity [23]. See *Chapter 2* for more details.

Figure1.4. Benefits of physical activity in pediatric oncology.



Note. Compiled from [9,19,24,25].

The time for activity is now

Children who undergo cancer therapy have already undertaken immense risk, but have also shown perseverance against incredible challenges in an effort to live longer. The focus on healthy living can start with a cancer diagnosis, to not only increase the opportunity for a cure, but also to promote lifelong healthy decisions beyond the cessation of cancer treatment.

Short and long-term toxicities of cancer therapies can result in barriers to active lifestyles. Participation in PA from the beginning of treatment through survivorship is an important step in the fight against cancer, and its therapeutic negative side effects.

Additional Resources:

- ✓ National Cancer Institute**: www.cancer.gov.**
- ✓ Canadian cancer society: **www.cancer.ca.**

Take Home Message

Cancer in children and teenagers is relatively rare and cure rates are high. Current treatments still carry both short and long-term toxicities. Due to the intensity of these therapies and the time away from educational, social, and athletic activities, children that are diagnosed and treated for cancer are at a high risk of missing opportunities with their peers. Physical activity is a safe and essential part of any child's lifestyle, and this should not be thought of differently for any child whose life is affected by cancer and its treatments. There are methods of modifying physical activity to be safe and beneficial for children that will improve the negative side effects associated with the cancer and its treatment.

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Chapter 2

The Benefits of Physical Activity in Childhood Cancer

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

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

iv) Neurocognitive: Taryn Fay-McClymont, PhD, R Psych

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 on 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 cognition.

Introduction

Advancements in the treatment of most types of **childhood cancers** has increased the five-year survival rate from less than 30% in 1960 to more than 80% today [1]. Unfortunately, the cancer treatments needed to achieve a cure may cause countless negative side effects, such as heart and lung damage, muscle and bone abnormalities, fatigue, problems thinking and problem solving, and social isolation [1,2]. These physical and psychosocial side effects have been linked to a decreased ability to perform **activities of daily living** and overall well-being [3-5].

Recently, **physical activity (PA)** has emerged as a promising complementary therapy to ease some of these side effects [6,7]. For example, there is growing evidence for the ability of PA to improve strength, **cardiorespiratory fitness**, fatigue, and well-being [3,4,6-8]. Importantly, no serious negative outcomes have been reported [3,5,9,10]. PA has also been identified as an activity that might enhance the feeling of normalcy for children with cancer, as their lives are often dramatically changed by their disease and its treatments [11]. In other words, PA gives children the opportunity to play games and engage in other common activities that they used to play before being diagnosed [12]. In addition, PA is a key factor in the development of any healthy child, as it is associated with improved general health, disease prevention, positive social development and mental health [3,11]. Given the potential negative side effects associated with a cancer diagnosis and its treatments, PA plays a very important role. This chapter will discuss the benefits of PA with regards to the outcomes related to health-related fitness (physiological), fatigue, psychosocial, and thought and memory function (neurocognitive).

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 health-related fitness is affected by both cancer and its treatments [5,6]. To our knowledge, only 14 studies to date have assessed health-related fitness outcomes in pediatric populations. See *Table 2.1* for a summary of the interventions, populations in which the interventions were performed, and a summary of outcomes obtained.

The majority of the studies conducted their interventions 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 [13].

Cardiovascular fitness, also known as **aerobic fitness, cardio-respiratory endurance, maximal aerobic capacity, maximal oxygen consumption (VO_2 max), or peak oxygen consumption (VO_2peak)**, is the ability of the body's circulatory and respiratory systems to supply fuel during sustained PA [14]. 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 heart diseases and complications [14].

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 **VO_2 peak** of 24 mL/kg^{-1}/min^{-1}, which is below the expected VO_2 peak for healthy children (45 mL/kg^{-1}/min^{-1}) [15-17]. Fortunately, this decrease in VO_2 peak seems to be reversible. An increase of 6 mL/kg^{-1}/min^{-1} has been reported in research after 16 weeks of aerobic and strength training in children with ALL during the maintenance phase of treatment (age range 4-7 years) [17].

Muscular strength is the ability of the muscle to exert force during an activity [14]. Muscular endurance is the ability of the muscle to continue to perform without fatiguing [14]. Because muscular strength and endurance are so closely related, they will be discussed together in this chapter.

Decreased muscular strength and endurance are common side effects of cancer and its treatments, specifically if your child was treated with corticosteroids, or was immobilized for prolonged periods [19]. Research has found resistance training is safe in pediatric cancer populations, and promotes improved or maintained muscular strength and endurance [3,6]. For example, in a study performed during HSCT in which children with cancer were hospitalized for about 30 days and most of the time they were lying on their beds, maintenance of strength after a PA intervention was detected [20]. This is very important, because a decrease in strength is usually expected. Important to note, supervised PA interventions seem result in more strength gains compared to home-based interventions [4].

Cancer patients are forced to reach their maximum oxygen consumption in order to perform activities of daily living.
Activities of daily living 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}/min^{1}, therefore, 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 these activities would require the patients to be working at 100% of their VO_2peak, and they are able to tolerate this intensity just for a few minutes [18].

Body composition refers to the relative amount of muscle, fat, bone, and other vital components of the body [14]. It is important to maintain a healthy body weight, as both increases and decreases in weight are related to other risk factors. For example, substantial weight gains are associated with greater risk of the development of other comorbid conditions [21]. This is concerning, as there is an increasing prevalence of overweight and obesity in survivors of pediatric cancer, mainly in ALL patients [22-25]. In contrast, decreases in body weight during treatment may occur due to malnutrition, and/or chemotherapy-induced toxicities (such as mucositis and diarrhea) [26]. PA seems to be a method to maintain a healthy weight, whether the side effects of treatment cause weight loss or weight gain [9].

Flexibility is the range of motion around a joint [14]. Sufficient flexibility around the joints can help prevent injuries through all stages of life [14]. A common side effect of cancer therapy is limited **range of motion**. For example, some **chemotherapy** drugs **induce peripheral neuropathy (CIPN)** and that might reduce ankle dorsiflexion ROM. The diminished ankle dorsiflexion range of motion will affect a child's gait, causing them to trip when walking or have difficulty climbing stairs. Refer to *Chapter 5* for more details on CIPN. An improvement in ankle range of motion was seen after a 12 week PA intervention where the children performed daily ankle stretching (held for 30 seconds), and lower extremity strengthening, 3 days a week [27]. An improvement of hamstring flexibility was also reported after a PA intervention [8,13]. See *Table 2.1* for more information about the PA interventions.

Other physiological variables impacted by PA

Physical function, which is commonly negatively affected in children with cancer, is defined as, the ability to perform tasks of daily living [15,16,28]. This variable has been measured with different tools in pediatric cancer and has only been addressed in a few studies [15-17,27-29]. Overall, PA seems to improve physical functioning, however, more research is needed [5]. To

summarize, PA is safe, feasible, and beneficial throughout the childhood cancer journey. Preliminary results suggest PA improves cardiovascular fitness, muscular strength, muscular endurance, flexibility, range of motion and physical functioning. Early research suggests that PA does not negatively impact immune function. Future research on PA prescription will help our understanding of potential improvements and the development of optimal PA programs for this population.

Finn, age 7. Soccer game

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

Author	Population	Intervention	Result
Perondi et al. [25]	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 sets x 15 rep of bench press, leg press, lateral pull down, leg extension, and seated row. • 2nd wk ongoing: 4 sets x 6-10 rep of same exercises described above. **- Aerobic training:** 10 min warm up + 20 min at moderate intensity.	- Strength ↑ 50 to 73% in all the muscles tested
Tanir et al. [70]	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 extension, foot dorsiflexion, and internal and external rotation of the foot. **- PRT:** • 3 times/day, 3/wk. Exercises: squatting (30 rep) and walking on the heels (10 rep, 3x, back and forth). **- Aerobic exercises:** 30 min, 3/wk. Exercises: ride a bike, walk, run, jump and dance. Intensity not reported.	- IG: ↑ aerobic capacity, functional capacity and strength. - CG: ↔ aerobic capacity, functional capacity, and strength.
Marchese et al. [27]	ALL (maintenance phase) (5-15 yr) N= 28 IG= 13	**- Duration:** 12 wk. 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 sec, 5 days/wk), lower extremity strengthening (10 rep, 3 days/wk), and aerobic fitness on a daily basis. Intensity was not reported	IG: ↑ ankle ROM and knee extension strength. Aerobic capacity ↔. CG: ↔ aerobic capacity, strength, and ankle ROM.

Note. PRT: progressive resistance training; N: number of participant; IG: intervention group; CG: control group; ROM: range of motion; BMI: body mass index; HSCT: hematopoietic stem cell transplantation; rep: repetitions; yr: year(s); wk: week(s); min: minute(s); ↔: maintain/ no change; ↓: decrease; ↑: increase/improve

San Juan et al.[16]	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, 8-15 rep, 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 low intensity, to 30 min at moderate intensity.	IG: ↑ functional capacity and strength.
San Juan et al.[17]	Same as above	**Same study as above with the same participants over 16 wk.**	IG: ↑ functional capacity, aerobic capacity and strength.
San Juan et al.[29]	HSCT patients (IG: 8 ± 4 yr, CG: 7 ± 3 yr) N= 15 IG= 8 HSCT CG= 7 healthy children	**- Duration:** 8 wk. Supervised in-hospital intervention **- Frequency:** 90 min/ 3/wk. **- PRT:** • 1 set, 8-15 rep, 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 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 low intensity, to 30 min at moderate intensity.	Aerobic capacity was lower in HSCT patients than in CG. IG: ↑ aerobic capacity and strength.
Moyer-Mileur et al.[72]	ALL (standard risk) (4-10 yr) N= 14 IG= 6	**- Duration**: 12 months. 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:** 15-20 min of moderate-to-vigorous activity at least 3/wk.	IG vs. CG: ↑PA min and aerobic capacity. IG and CG: ↔ flexibility and upper body strength.

Rosenhagen et al. [20]	HSCT patients (15.3 ± 3.7 yr) N=23 IG= 13	**- 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 were used to prescribe exercises. **- Aerobic training:** Stationary bicycle ergometer with minimal resistance of 6 watts for a minimum of 10 min. The resistance of the bicycle was increased in the next class only if participant reached 10 min. Intensity of training: moderate. Participant trained for a median of 18 minutes.	IG: ↑ aerobic capacity. ↔ Strength. CG: not reported. Regular PA during isolation phase of HSCT is feasible, safe, and counteracts the side effects of immobilization, like muscular atrophy.
Keats & Culos-Reed. [8]	Mixed cancer types (14-18 yr) N=10 IG= 10	**- Duration:** 16 wk, with follow up assessment at 3 and 12 months. **- Frequency:** 90 min, 1/wk. **- Week 1- 8:** 30 min educational sessions, 45 min aerobic training, 15 min of core (back and abdominals), strength training. - **Week 9-16**: Variety of non-competitive PA. Informal lifestyle education was provided.	↑ upper body strength, flexibility, and aerobic capacity. This increment was maintained in the 3 and 12 month follow up assessments.
Shore & Shephard. [45]	Most of them ALL (IG: 14 ± 0.6 yr, CG: 13 ± 3.1 yr) N=6 IG=3	**- Duration:** 12 wk. Supervised 1/wk + Home –based intervention 2/wk. **- Frequency**: 35 min, 3/wk. **- Aerobic exercises:** 30 min, 3 /wk at moderate to high intensity. **- Stretching:** 2-3 min, 3/wk.	↔ aerobic capacity.
Takken et al. [41]	ALL survivors (6-14 yr) N=9 IG=9	**- Duration:** 12 wk. Home–based intervention (2/wk) + supervised exercise session with physiotherapist (2/wk). **- Frequency**: 45 min, 4/wk. **- Aerobic exercises:** Exercise intensity increased every 4 wks, started at moderate intensity, and finished with moderate to high intensity. **- PRT and flexibility:** Exercises were included but not described.	↔ 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 boring.

Chamorro- Viña et al. [9]	HSCT in isolation phase (4-16 yr) N= 20 IG= 7 CG= 13	**- 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, 8-15 rep 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**: Ranged from 10 to 40 min dependent on child's status. Intensity controlled by heart rate monitor, between low and moderate.	IG: ↑ BMI and weight, ↑ fat free mass and body fat. ↑ Aerobic fitness and strength. CG: ↔ BMI, body fat and weight, with a trend to decrease.
Hartman et al. [71]	ALL (1-18 yr) N= 41 IG= 20	**- Duration**: 2 yr intervention. Home based–exercise program with an individual physiotherapist follow up every 6 wk. **- Frequency:** 7/wk . - Parents were supplied with an exercise list enabling them to select exercises most appropriate for their child. Children had to perform 1/day, exercises to maintain hand and leg function and 2/day, jumping and stretching exercises.	↓ BMI and percentage of body fat to normal values in the IG, and in the CG 1 year post-treatment. These changes were more pronounced in the IG.
Wurz et al. [13]	Mixed cancer sample Out-patient (5-17 yr) N=8 IG=4	**Duration:** 12 wk. Supervised group yoga program. **Frequency:** 60 min, 2/wk. **Intervention:** Each session consisted of warm-up, standing poses, group activities, supine/seated/kneeling poses, prone poses, and a final resting pose**.**	IG: ↑ functional mobility, ↑ hamstring flexibility, ↔ Ankle dorsiflexion ROM.

Note. PRT: progressive resistance training; N: number of participant; IG: intervention group; CG: control group; ROM: range of motion; BMI: body mass index; HSCT: hematopoietic stem cell transplantation; rep: repetitions; yr: year(s); wk: week(s); min: minute(s); ↔: maintain/ no change; ↓: decrease; ↑: increase/improve.

ii) Fatigue

Fatigue has been argued to be an under-recognized and undertreated symptom in pediatric oncology [30,31].

Patients and survivors may experience lifestyle changes, such as being socially isolated or unable to concentrate, because of the fatigue [30,32,33]. Children primarily report early fatigue during games and outdoor activities [4].

While the underlying mechanisms of **cancer related fatigue** are not understood well [30,32], it is most likely a multidimensional, multi-factorial, and highly subjective phenomenon [30,32,34]. Regardless of the cause, cancer related fatigue is a distressing symptom [33,35] negatively affecting the survivors´ well-being and ability to perform activities of daily living [3,4,8,32-34,36-38].

Fatigue can be defined as, an unusual sense of whole body tiredness, weakness, lack of energy, and an unusual need for rest.

A PEER participant working on strength training

PA programs may have the potential to reduce cancer related fatigue [5,6,39]. Several studies have examined the effects of PA interventions on survivors´ fatigue scores and preliminary results are promising. See *Table 2.2* for more details. However, while PA programs may be beneficial for childhood cancer survivors suffering from fatigue, we still do not know how PA affects fatigue and what kind of PA is the most advantageous.

Table 2.2. Clinical physical activity interventions in pediatric oncology with fatigue as a main outcome.

Authors	Demographics	Sample	Intervention	Fatigue Results
Rosenhagen et al.[20]	See *Table 2.1* for a description of demographics, sample and intervention.			Fatigue ↓ (trends) in IG during intervention.
Yeh et al.[40]	**IG**=12 (11.01 ± 3.56 yr) **CG**=10 (12.48 ± 3.86 yr)	ALL	Home-based (maintenance chemotherapy*).* **IG:** 6wk; 3/wk, 30min; moderate endurance PA at with PA video. **CG:** Standard care.	General fatigue score ↓ in IG vs. CG, at 1-month follow up.
Blaauwbroek et al.[32]	**IG=** 46 (29.8 ± 8.6 yr) **CG**=30	**IG:** Mixed cancer survivors **CG:** Healthy controls	**Home-based** *(survivorship).* **IG:**10 wk; telephone counselling and feedback from pedometer.	Fatigue ↓ in IG during intervention and at follow up/wk 36.
Takken et al.[41]	See *Table 2.1* for a description of demographics, sample and intervention.			No significant changes in fatigue (improvement of 11%).
Keats et al.[8]	See *Table 2.1* for a description of demographics, sample and intervention.			Fatigue: general fatigue ↓ during intervention and at 3-month follow-up; total fatigue and sleep/rest fatigue ↓ at 12-month follow-up.
Hinds et al.[42]	**IG=**14 (13.08 ± 2.55 yr) **CG** =15 (11.92 ± 3.24 yr)	Solid tumor, AML	**Supervised, in-hospital** (*during medical treatment*). **IG:** 2-4day; 2/day, 30min; endurance training on stationary bike.	No effect on fatigue.

Note. ↓: Improvement/decrease in symptom; IG: intervention group; CG: control group; yr: year(s); wk: week(s); min: minute(s). Adapted from Baumann et al. [5].

iii) Psychosocial

Treatments in pediatric oncology patients result in numerous negative physical and psychosocial outcomes that, ultimately, negatively impact their **quality of life (QOL)** [43,44]. Although 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 [8,16,20,27-29,45,46]. To date, no studies have found any detrimental psychosocial effects from PA. More importantly, most studies have found improvements, such as [8,20,27-29,46]:

- ✓ Increased And Improved Social Interaction
- ✓ Improved Self-Esteem
- ✓ Decreased Anxiety
- ✓ Improved Mental Health
- ✓ Increased Comfort
- ✓ Increased Resilience

Quality of life: defined as an 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.

Yoga is an alternative form of PA. The four studies conducted in pediatric oncology [13,47-49] have shown positive psychosocial benefits. Please, refer to *Chapter 12* for more details. With regards to the benefits of traditional PA, a summary of the psychosocial benefits can be seen below in *Table 2.3*. Refer to *Appendix C (infographics).*

Table 2.3. Physical activity and psychosocial outcomes.

Authors	Demographics	Sample	Intervention	Results
Rosenhagen et al. [20]	See *Table 2.1* for a description of demographics, sample and intervention.			↑ QOL (trend)
Gohar et al. [28]	IG= 9 (2-14 yr)	ALL; 2wk from diagnosis	**Supervised, in-hospital and home-based program**; physical therapy 6-7month.	↑ QOL
Speyer et al. [46]	IG= 30 (9-18 yr)	Mixed cancer patients; during hospital stay	**Supervised, in-hospital; adapted PA.** >3/wk; 30min.	↑ Child self-report QOL. ↑ Parent-proxy report QOL.

San Juan et al. [29]	See *Table 2.1* for a description of demographics, sample and intervention.	↑ Comfort and resilience (self-report). ↑ Satisfaction and achievement (parent-proxy report).
Keats & Culos-Reed. [8]	See *Table 2.1* for a description of demographics, sample and intervention.	↑ QOL, and at 3-month and 12-month follow up, ↑QOL.
San Juan et al. [17]	See *Table 2.1* for a description of demographics, sample and intervention.	No improvement.
Marchese et al. [27]	See *Table 2.1* for a description of demographics, sample and intervention.	No improvement.
Shore & Shepard. [45]	See *Table 2.1* for a description of demographics, sample and intervention.	↓ Symptoms of anxiety.

Note. ↑: Improvement; ↓: Decrease; ALL: acute lymphoblastic HSCT: hematopoietic stem cell transplant; leukemia; IG: intervention group (are those who received PA interventions); CG: control group (group did not receive the PA intervention); QOL: quality of life; wk: week(s); yr: years.

iv) Neurocognitive

Children with **brain tumors** or ALL are at the most risk for neurocognitive late-effects because of the administration of therapies into the brain or spinal cord, such as cranial **radiation therapy**, and/or **intrathecal chemotherapy** [50,51]. These therapies are often associated with the disruption of normal brain development. Cognitive problems can include **attention** difficulties, **decreased working memory and processing speed, and impaired executive functioning**. As a consequence of the cognitive side effects of treatment, socialization problems, and decreases in academic achievement and well-being might be expected years after completion [52-55]. See *Chapter 10* for more details.

Neurocognitive is related to cognitive function.

Cognitive function is the ability (or lack of) to think, learn, and memorize.

While there are many studies that demonstrate neurocognitive deficits in childhood cancer survivors, very few studies have addressed recovery or prevention.

The evidence of positive and long-term effects of PA on cognition in children is growing. The literature on neurocognitive benefits of PA in pediatric cancer patients and survivors is just beginning. In this chapter, we summarized the neurocognitive benefits of PA seen in healthy children and animals, animal models in which researchers reproduce the side effects promoted by cancer, and in pediatric cancer. See *Table 2.4* and *Figure 2.1* for a summary of research outcomes.

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.

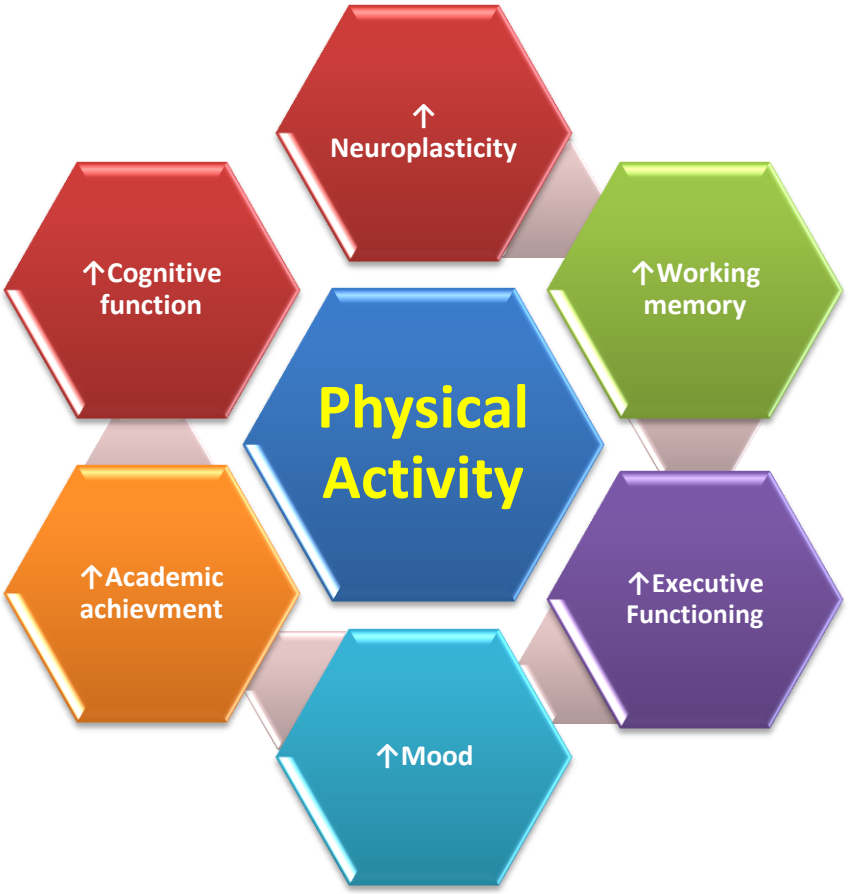
Table 2.4. Summary of research evidence regarding physical activity effects on neurocognition.

Evidence from	Showed	Definitions
Animal and/or human research [54,56-61]	✓ Increase neuroplasticity ✓ Increase white matter tracts ✓ Improve cognitive functions ✓ Positive effects on hippocampus	✓ **Neuroplasticity:** The brain's ability to reorganize itself by forming new neural connections throughout life. ✓ **White matter:** is a substance in the brain that coordinates communication between different grey matters areas in the brain. Using a computer network as an analogy, the computers will be the grey matter; meanwhile, the cables to connect them all will be the white matter. ✓ **Working memory**: is the part of short-term memory that is concerned with immediate, conscious perceptual and linguistic processing.
Healthy children [58,59,62-67]	✓ Improve mood ✓ Improve **cognitive functions** ✓ Improve executive functioning ✓ Children with higher fitness level obtain better academic achievement	
Mice model imitating side effects of cancer and it's treatment [54]	✓ PA after radiation demonstrated an increase of almost 300% in new neurons compared with those mice that did not have access to a running wheel.	
Cancer patients [68]	✓ Higher levels of aerobic capacity in pediatric cancer patients were associated with better working memory.	

Note. Compiled from [54-69].

By understanding the benefits of PA on brain development and cognition in healthy children and animals, we can begin to understand the positive effects PA may have on preventing or improving some of the negative neurocognitive side effects we observe in pediatric cancer patients and survivors.

Figure 2.1. Neurocognitive benefit of PA.



Take Home Message

- ✓ Physical activity is safe and feasible. Preliminary results suggest it improves cardiovascular fitness, muscular strength, muscular endurance, flexibility, range of motion and physical functioning, without affecting the immune system.
- ✓ Cancer-related fatigue is a common symptom 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.
- ✓ Physical activity potentially enhances quality of life and specific psychosocial domains. Future research is necessary to more clearly clarify potential benefits, and outline effective methodologies and measurement tools.
- ✓ 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 Childhood Cancer Journey

Julia Beulertz, PhD candidate & 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 physical activity strategies and their benefits on physiological and psychosocial outcomes.

Introduction

Physical activity (**PA**) plays an important role in a child's development (physical, mental and social). Having good physical fitness (i.e., strength, aerobic capacity, and flexibility) allows children to participate in **activities of daily living**, such as climbing stairs and playing sports without getting tired [1]. Impaired physical functioning due to cancer and its treatment may lead to low levels of PA [2]. Having low levels of PA may decrease the already low levels of physical functioning, and increase the risk of developing health problems (e.g., cardiovascular disease, osteoporosis, diabetes) [3]. For that reason, children and youth with cancer must be encouraged and motivated to have an active lifestyle.

Physical function (**physical performance**) is a reflection of their overall health, and the impact of several common chronic diseases, such as osteoporosis and coronary heart disease, on the ability to perform activities of daily living.

Aerobic capacity is the ability to transport and use oxygen. The higher the aerobic capacity, the less fatigue results from performing a given activity. When we train to improve our aerobic capacity we can say that we are doing endurance training, such as running, walking, or playing sports, basically anything that makes our heart pump faster.

Physical Fitness is 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 and the most important are, aerobic capacity, muscle endurance, muscle strength, flexibility, and body composition.

Inactivity in Childhood Cancer Survivors

Nearly half of the survivors of childhood cancer do not meet the general PA guidelines for children [4-8] (see *Appendix B for PA guidelines*). Children with cancer also tend to be more inactive and the intensity of their activities tend to be lower than their healthy peers [5,6,8].

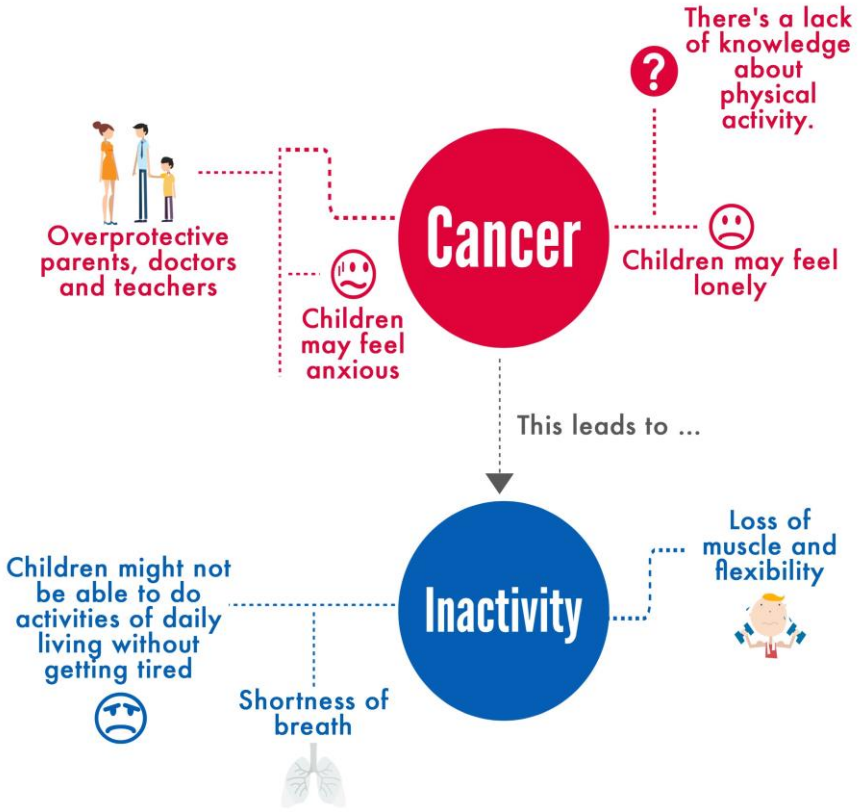
There are many possible reasons for inactivity in children with cancer and survivors (see *Figure 3.1*). The main explanations are:

- ✓ Children are inactive because of the side effects of their cancer treatment, such as anemia, muscle weakness, and shortness of breath. These side effects cause high levels of fatigue and can make it difficult to engage in PA [8].
- ✓ Low self-confidence. Their treatment causes them to miss an important phase, in which the majority of kids engage in a sport. Once they finish their treatment and want to join their peers in different activities, they do not have the knowledge to participate [8].
- ✓ Overprotective parents, physicians, and educators try to keep the child from being active, because they think the child should be resting. This can also be related to the fact that there is a lack of knowledge about the role of PA during the pediatric cancer journey [6,8].
- ✓ Patients may also become more worrisome, anxious, or lonely. This could discourage them from being active. Lower levels of PA can decrease physical functioning, which can lead to an even more inactive lifestyle [2].

Did you know that these factors can increase your child's risk of being more inactive?

- ✓ Having blood, bone, or central nervous system cancer [8,9]
- ✓ Having an amputation [5]
- ✓ If he or she received more than 20 **gray (Gy)** of cranial radiation
- ✓ If he or she received a specific chemotherapy, such as vinca-alkaloide, platinum, anthracycline [5]
- ✓ If your child is female [10]
- ✓ If your child has problems that affect their intellectual function [7]
- ✓ If your child experiences cancer-related fatigue [11]

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



Note. Compiled from [5,6].

Physical Activity Interventions in Childhood Cancer

Over the last 15 years, several studies on therapeutic PA programs in pediatric cancer populations have been published. Most of these studies have been conducted in **acute lymphoblastic leukemia (ALL)** patients. Overall, modified PA programs could help reduce inactivity and the side effects of childhood cancer [1]. PA programs should be designed to help children perform activities of daily living without getting tired. Therefore, programs that focus on maintaining or improving muscular strength, muscular endurance, aerobic capacity, and flexibility might help improve physical functioning in children affected by cancer. We recommend that health care professionals or exercise specialists with training in pediatrics and chronic conditions (or cancer-specific training) should conduct these programs [12].

A PEER participant working on balance with her mom's help

Muscular strength is defined as, the maximum amount of force that a muscle can exert against some form of resistance in a single effort.

Muscular Endurance is the ability of a muscle or group of muscles, to work continuously for a long time without tiring.

Physical activity during medical treatment

From the **isolation phase** of **hematopoietic stem cell transplantation (HSCT)** to later phases of treatment like the maintenance phase for ALL patients, adapted PA programs have not shown any negative effects on cancer patients [13,14]. Maintenance, or improvements in aerobic capacity, muscle strength, stabilization of weight, joint range of motion, level of activity, well-being, and fatigue levels have also been reported along these phases of treatment [13-21]. We also want to highlight that moderate-intensity PA during hospital stays for HSCT did not alter

the recovery of the immune system in these children [13]. See *Appendix C for our infographic of PA benefits.*

PA programs during medical treatment involved supervised activity [15-18,22-24], home-based programs [19,20], or a combination of supervised and home-based programs [25-27]. Most programs included mixed PA focusing on the development of aerobic capacity, strength, and flexibility (see *Appendix C for our infographic of types of PA*). A supervised yoga program has also shown to be beneficial (refer to *Chapter 12 for more information on yoga in childhood cancer)* [22].

Physical activity during survivorship

During survivorship, research has generally focused on supervised programs [3] or a combination of both supervised and home-based programs [28,29]. Positive effects have been seen in well-being, fatigue, and activity levels. Physical changes have also been seen, such as increased strength, flexibility, and improved aerobic capacity. These changes can help survivors perform activities of daily living without getting tired.

Jacey, age 5

Additional Resources:

- ✓ Kelly AKW. Physical activity prescription for childhood cancer survivors. Current Sports Medicine Reports. 2011; 10(6): 352-359 [30].
- ✓ Gotte M, Taraks S, Boos J. Sports in pediatric oncology:The role(s) of physical activity for children with cancer. J Pediatr Hematol Oncol. 2014; 36(2): 85-90 [31].

Take Home Message

Specific physical activity programs are needed, because the physical activity levels in children affected by cancer are low. Research shows that physical activity interventions are possible, safe, and beneficial for childhood cancer patients and survivors. However, more research is needed in this area in order to find the best possible physical activity for each cancer patient.

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Chapter 4

General Physical Activity Recommendations for Childhood Cancer

Tim Takken, PhD & Marco van Brussel, PhD

Learning Objectives

After completing this chapter you will know:

- ✓ …side effects of treatment on fitness levels.
- ✓ …the role of physical activity and exercise for improving the ability to perform activities of daily living, strength and the ability of the heart and lungs to provide oxygen to the body.
- ✓ …the physical activity guidelines provided should be personalized for your child, supervised, and should take into account any possible side effects of treatment.

Introduction

Childhood cancer usually occurs at the age when children are first introduced to **physical activity (PA).** When a child develops cancer at this important time in his or her life, it limits his or her PA involvement. This can set the foundation for future inactivity and related health problems. This can also affect a child's sense of self-confidence, wellbeing, and relationships with others [1].

Cancer treatments are often accompanied by a wide range of **short and long-term side effects,** such as:

- ✓ Decreased brain and nerve function
- ✓ Trouble remembering, learning new things, concentrating, or making decisions
- ✓ Decreased ability to pump oxygenated blood to the body, because of anemia and/or cardiopulmonary **toxicity**

Toxicity is defined as, the extent to which something is poisonous or harmful.

- ✓ Increased risk of fractures
- ✓ Loss of muscle mass, weakness and decreased flexibility
- ✓ A secondary cancer

The side effects mentioned above might become worse if your child adopts an inactive lifestyle [2]. On the other hand, if PA begins during, or soon after treatment, it can lessen the impact of the side effect [3-5]. Please see *Chapter 2* for an explanation of PA benefits. In-hospital PA programs that are structured, personalized, and supervised seem to be the most effective and safe for childhood cancer patients [6,7]. There is little information to develop specific guidelines for each cancer type, but it is important that PA is individually designed for your child.

A sibling of a PEER participant

General Physical Activity Guidelines

The recommendations that we provide here are based on existing literature in healthy children [8,9,10,11]. They have been adapted based on specific childhood cancer information, and our own clinical experience with PA [4, 8,12].

Currently, there are no universally accepted training guidelines for children with cancer. We recommend using what we have provided in this chapter as a framework for an individualized, disease-specific, training program for each child.

Aerobic training

Table 4.1. General aerobic recommendations modified for pediatric cancer survivors.

	Aerobic training	Interval training
Frequency	2-5 times/week	2-3 times/week.
Intensity	Moderate (RPE 2-5) to vigorous (RPE 6-7)	3-5 minutes of light to moderate; interrupted 6-8 times by 1-3 minute bouts of intense PA.
Time	20-70 minutes	In total 20-70 minutes.
Type	Running, jumping, cycling, swimming, football	Running, jumping, cycling, swimming.

Note. Adapted from 8 and 9. RPE: Rating of Perceived Scale (OMNI 1-10); Interval training can be used alternatively with aerobic training.

Interval training is simply alternating bursts of intense activity with intervals of lighter activity.

Children playing soccer at a PEER session

Moderate aerobic training requires some effort, but children can still speak easily while doing it. E.g., fast walking, riding a bike, and active play.

Vigorous aerobic training requires more effort, and makes children breathe harder and faster (‘huff and puff’).
E.g., running, chasing and playing tag, and sports like soccer.

Progressive resistance training

Table 4.2. General resistance training recommendations modified for pediatric cancer survivors.

	Strength (Resistance) Training
Frequency	2-3 times per week.
Intensity	Moderate to high. 50 to 70 % of 1**RM**. See text box below.
Time	2-3 minutes per each major muscle group (about 8-20 repetitions). In total, 20-30 minutes (can be interchanged with aerobic training and games).
Type	Push-ups, sit-ups / crunches, pull-ups, handgrips, squats, climbing, martial arts, rowing etc.

Note. RM: maximal repetition. Adapted from [12].

Resistance training intensity	Number of repetitions
50%	25
60-70 %	18-20
75%	12
80%	8-10

Use this table to calculate the intensity of your child's strength training.

Flexibility training

The effect of PA on the improvement of flexibility in children with cancer has not been well studied. However, in children with cancer, flexibility can be affected and thus impacts the ability to perform activities of daily living. For that reason, we ask you to incorporate flexibility training as part of your child's daily PA.

It is very important to consider your child's limitations when making a program. Healthcare professionals, **certified exercise physiologists**, and other exercise professionals can assist in designing appropriate PA programs for your child.

Practical tips to get your child enrolled in a PA programs
Information from your doctor/oncologist:
✓ Inform your doctor that you might start a PA program. ✓ Ask your doctor if your child has any contraindications for engaging in PA, like cardiotoxicity. ✓ Ask your doctor if your child has anemia, thrombocytopenia, or immune system suppression. These conditions can limit the ability of your child to do PA. ✓ Ask your physician or primary nurse to give you a short report about the treatment that your child has received, and write down any side effects that your child has developed because of the cancer treatment. ✓ Ask your physician to reply to any questions from the fitness professional working with your child.
Ensure the fitness professionals who are working with your child:
✓ Have medical clearance from appropriate health care professionals (e.g. oncologist/ cardiologist). ✓ Know your child's relevant medical information (current health status, medical treatment, and side effects that might impact your child's PA conditions). See *Appendix F and G (client intake form and physician clearance)* for more information. ✓ Know how to adapt a PA program for your child's specific needs. ✓ Know that your child may have higher fatigue levels and slower recovery times. ✓ Know that fitness testing by an experienced certified exercise physiologist is recommended before starting PA. ✓ Ask your child's physician if they have any questions regarding your child's health status and any reasons for not being active. ✓ Keep PA fun!

Additional Resources:

- ✓ San Juan AF, Wolin K, Lucia A. Physical activity and pediatric cancer survivorship. Recent Results Cancer Res. 2011; 186: 319-347.
- ✓ Braam KI, van der Torre P, Takken T, Veening MA, van Dulmen-den Broeder E, Kaspers GJ. Physical exercise training interventions for children and young adults during and after treatment for childhood cancer. Cochrane Database of Syst Rev. 2013; 4: Cd008796.

Take Home Message

Physical activity appears feasible and effective in pediatric cancer patients and survivors. Programs should be individualized and consider your child's cancer type and treatment and their side effects. Exercises should be progressive, developmentally and age-appropriate, enjoyable and involve a variety of activities. These general recommendations may provide a framework for creating personalized physical activity programs.

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Chapter 5

Practical Aspects of Physical Activity in Childhood Cancer

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Learning Objectives

After completing this chapter you will know:

- ✓ …the side effects related to pediatric cancer treatments that affect children, adolescents, and young adults' physical activity.
- ✓ …the areas of emphasis and caution when participating in physical activity for major side effects of treatment.
- ✓ …when symptoms during physical activity warrant referral to a medical professional.

Introduction

Every cancer treatment is different (protocol, severity, etc.), and every child responds in their own unique way. Many children will not experience serious symptoms when they perform **physical activity (PA);** however, it is important to understand the possible side effects of specific treatments in order to be safe and successful. This chapter will cover common side effects related to childhood cancer and its treatment. The sections covered include: i) **chemotherapy-induced peripheral neuropathy (CIPN),** ii) **osteopenia/osteoporosis**, iii) **osteonecrosis**; iv) cardiac toxicity, v) pulmonary toxicity, vi) hypertension, vii) pancytopenias, viii) bone tumor effects, ix) sensory impairments, and x) chronic graft-versus-host disease. Each of these medical terms will be explained and each section will provide practical advice on which activities to emphasize, and which activities to be careful about. A child may have one, many, or none of the side effects described. If you or your child notices symptoms caused by the side effects described, we recommend you discuss them with your oncologist, rehabilitation therapist, or exercise professional. These professionals will help you apply the recommendations provided based on your child's age, abilities and risk factors. Most forms of PA are safe for cancer survivors. Research tells us that, in most cases, the benefits for PA

outweigh the possible risks. The definitions provided in the box below will help you to understand the recommendations provided in this chapter.

Progressive Resistance Training: an exercise program in which someone gradually increases the amount of weight lifted, and or/the amount of repetitions. The more repetitions done, the more a person develops endurance. The more weight lifted, the greater the strength development.
Weight-bearing exercises: are exercises which force you to work against gravity. Some examples of weight-bearing exercises include, weight training, walking, tennis, and dancing. Examples of exercises that are not weight-bearing include, swimming and bicycling.
Aerobic activities or aerobic exercise: activities that involve repetitive use of large muscles groups, such as walking, running, and dancing, where your breathing is faster and deeper. Your heart beats faster during aerobic activity. This type of exercise might help your child bring up their endurance and allow them to do more PA or even daily activities without getting tired as easily.
Core strength training: there are several definitions of this. However, for the purpose of this manual, we will define it as a strength program that includes work of the muscles around the spine, hips and pelvis, such as abdominals and muscles of the back.
Isometric exercise: an exercise where a muscle contracts without moving a joint.

i) Chemotherapy-induced peripheral neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is characterized by damage to the **peripheral nervous system** from the use of chemotherapy [1,2]. The most common chemotherapy drugs known to cause CIPN are, vincristine, cisplatin, bortezomib, and thalidomide [3].

The **peripheral nervous system** consists of nerves that connect the central nervous system (brain and spinal cord) to different organs in our body, such as the eye, ear, muscles, blood vessels, and glands.

This damage can cause numbness, tingling, pain, weakness, or lack of coordination. These symptoms could affect PA participation, and the ability of your child to perform activities of daily living, such as climbing stairs or walking, during, and even after cancer treatment. If you know or suspect that your child has CIPN, ask your physician about the limitations your child might have when exercising. Fortunately, physical therapy and certain types of PA can help overcome some of the limitations to perform activities of daily living, that patients and survivors affected by neuropathy could have[4,5]. The table below shows the PA areas to emphasize, and lists the cautions that must be recognized. If your child has functional

limitations due to their CIPN, consider consulting a physical therapist in order to set up a safe and effective exercise program.

Supervision during PA is highly recommended, because a child affected by CIPN has a high risk of falling. Orthotics or ankle braces may be recommended during activities that may challenge their ankle stability.

Table 5.1. Areas of emphasis and caution in patients and survivors with CIPN.

Emphasize:
✓ Stretching to improve ankle movement (e.g., ankle flexibility to improve walking, refer to *Appendix 5.A*).
✓ Strengthening of ankles, toes, wrists, and hands.
✓ Balance training (refer to *Appendix 5.B*).
✓ Aerobic exercises. Be careful about your choice of PA. For example, walking may not be the best choice because the ankles may become tired before their body works hard enough to challenge the heart. Biking or swimming may be better to increase heart rate.
Caution:
✓ Strength training requiring handgrip, because your child might not have enough strength to hold it. Use of elastics bands is a possibility when hands are weak.
✓ PA over uneven surfaces like grass or sand, because of balance problems.
✓ Difficult balance activities like those performed on unstable surfaces (bosu, fit-ball).
✓ Activities that require the ankles to work hard.

Note. Compiled from [2,4-9].

ii) Osteoporosis, Osteopenia (or low bone density)

Osteoporosis, or osteopenia, is a disease that affects the strength of your child's bones and increases their risk of fractures. See risk factors for cancer patients in text box. The diagnosis of low bone density osteopenia, or osteoporosis depends on age, the strength of the bone, and the child's history of fractures [10]. An oncologist or endocrinologist can assist a family in understanding a child's risk for this side effect.

Risk factors for low bone mineral density:
- ✓ ≥ 9 g/m^2 of corticosteroids
- ✓ ≥ 40 g/m^2 of methotrexate
- ✓ >18 Gy cranial radiation
- ✓ Reduced PA during, and after treatment

PA can improve this known late effect of cancer treatment. Since 60% of osteoporosis risk is determined by the bone strength in adolescence [11], and much of that bone strength is formed around ages 12.5 in girls and 14 in boys [12], a child must not wait until treatment is finished to begin to exercise. Strength training, sports (e.g., basketball, soccer) and high impact exercises (e.g., running, jumping) are beneficial to form bones, but they also might increase fracture risk or other injury. Therefore, there should be a balance between an emphasis on weight-bearing exercises, and reducing risk of falls and fractures as a result of low bone density. Seeing a physical therapist is beneficial to individualize your child's exercise program based on his/her pain and mobility status. Since children have the ability to strengthen bones, some activities may be beneficial in children that may not be allowed in adults.

Often, bone density is not tested unless there is a history of fracture or pain issues. See risk factors in the text box [10,13,14]. You should understand the areas of emphasis and caution when thinking about PA. Refer to *Table 5.*2 and *Table 5.3* for specific recommendations.

Table 5.2. Areas of emphasis and caution in patients and survivors with low bone mineral density.

Emphasize:
✓ Weight-bearing exercises (during and after treatment). ✓ Progressive resistance exercise focused on strength development (8-12 repetitions. More loads and fewer repetitions are better). ✓ Balance training (to decrease risk of falls). ✓ Core strength. ✓ High impact sports/exercises at least 3 times week, if it is safe (e.g., running, jumping, basketball, handball, or gymnastics). Consult with your medical team to determine if this is appropriate. ✓ Safety and confidence to challenge themselves.
Caution:
✓ Contact sports (depending on severity of low bone density). ✓ Activities or sports that could increase the risk of an injurious fall.

Note. Compiled from [11-13,15-19]

Table 5.3. Areas of emphasis and caution in patients and survivors with osteoporosis.

Emphasize:
✓ **Core strength** (especially trunk extension). ✓ Progressive resistance exercises with an emphasis on strength. Do it as much as tolerable. Do not stress until the point of fatigue. ✓ Gait steadiness. ✓ Balance. ✓ Aerobic exercise. ✓ Flexibility.
Caution:
✓ Exercises causing spinal flexion, rotation (twisting), or side-bending. ✓ Exercises that cause spinal movement and cause pain. ✓ High impact activities (bouncy or jerky movements, especially in adult survivors of childhood cancer). ✓ Balance activities without support. ✓ Heavy lifting (when a spotter is needed or unable to lift 10 reps), or lifting overhead. ✓ Activities that increase the risk of falling.

Note. Compiled from [14,20-22].

Children with osteoporosis may be able to do high impact activities because they may be able to increase their bone density. Since these activities also increase the risk of fractures, they should be performed with caution and supervised by a physical therapist or specialized fitness professional. Please consult with an oncologist, orthopedic surgeon, or physical therapist to determine what is safe for your child.

iii) Osteonecrosis

Osteonecrosis (**ON**) is the death of a segment of bone, which occasionally occurs in children with cancer. If it occurs, osteonecrosis usually affects the hips or knees. See text box for risk factors [23]. The condition may not show any symptoms; however, if severe, it can lead to pain, decreased mobility, and break down of the joint, which may require joint replacement [23-26]. Osteonecrosis results in changes to a joint that require an individualized PA program to protect the bone, strengthen the muscles around the joint or joints, and reduce pain. Because each

child will require specific adaptations, communication with the medical team is necessary for proper exercise recommendations.

Risk factors for ON:
- ✓ Corticosteroids during cancer treatment
- ✓ Children older than 10 years affected by ALL or non-Hodgkin lymphoma
- ✓ Children who received hematopoietic stem cell transplant

In general, people with osteonecrosis should think of pain as their guide during PA and keep frequent follow-ups with medical providers to manage symptoms. Pain may be intermittent or inconsistent; however, it should not be ignored. The use of a pain scale is recommended. See *Appendix D.*

Table 5.4. Areas of emphasis and caution in patients and survivors with osteonecrosis.

Emphasize:
✓ PA without pain. ✓ Work the affected joint range of motion. If possible for your child, let him/her do the exercise. If your child is not able to do the exercise, you may move it for them. ✓ Progressive resistance training (to increase support around joint). ✓ Aerobic activity (biking or swimming). ✓ Flexibility.
Caution:
✓ PA with pain or increase in pain. ✓ Follow individual orthopedic weight-bearing precautions. ✓ High impact PA.

Note. Compiled from [27-30].

iv) Cardiotoxicity

Children with cancer, on/off treatment, may be at risk for cardiac disease as a side effect of chemotherapy or radiation [31,32]. For more details regarding cardiotoxicity, please refer to *Chapter 6.* Although PA is generally safe and beneficial for cancer patients and survivors, those at risk of cardiotoxicity should be educated to understand symptoms of cardiac dysfunction. In children exposed to therapies that cause cardiotoxicity (e.g., anthracycline, cisplatin, cyclophosphamide), it is important to emphasize aerobic and strengthening components of PA**.** Heart rate and blood pressure should be monitored during exercise if any symptoms are experienced, or if there is concern. The program may need to be modified if an abnormal heart rate or blood pressure response is noted (e.g., no change in heart rate with effort, falling systolic blood pressure, > 250 mmHg systolic blood pressure, >125 mmHg diastolic blood pressure)[33].

Table 5.5. Areas of emphasis and caution for patients and survivors exposed to cardiotoxic therapies.

Emphasize:
✓ Full evaluation by cardiologist or physician if child is at a high risk (exposed to doses >250 mg/m^2 of anthracycline). ✓ Monitoring aerobic exercise (if history of symptoms). ✓ Progressive resistance training with ability to lift weight at least 10 repetitions (i.e., using a lighter weight and more repetition is recommended), at least three times a week. ✓ Breathing through the movement. Never hold the breath. ✓ Engaging muscles when lifting and lowering the weight.
Caution:
✓ Strength training with heavy loads (especially those at high risk of cardiotoxicity). ✓ Isometric training. ✓ Valsalva maneuver (holding your breath). ✓ Exercising with cardiac dysfunction symptoms (see textbox below).

Note. Compiled from [19 34-40].

Symptoms Related to Cardiac Dysfunction

Persons with any of these symptoms should consult with a cardiologist for further recommendations:

- ✓ Shortness of breath
- ✓ Swollen ankles/feet
- ✓ Heart palpitations
- ✓ Heart racing
- ✓ Dizziness
- ✓ Chest pain

v) Pulmonary toxicity

Pulmonary toxicity is damage to the lungs caused by the cancer therapy. This damage may cause **pulmonary fibrosis** or **restrictive lung disease** [41,42]. Symptoms include:

- ✓ Shortness of breath
- ✓ Chronic cough
- ✓ Wheezing [41-43]

It is important to understand that a person with cancer could have both cardiac and pulmonary toxicity resulting in a decreased capacity to do PA (**exercise intolerance**). If a person has any of the symptoms mentioned above, heart rate, blood pressure, and oxygen saturation should be monitored by a trained professional (e.g., certified exercise physiologist, physical therapist, nurse or physician). Research in people, with or without cancer, affected by pulmonary disease, shows that PA is beneficial in exercise tolerance and well-being [44-47].

Risk factors for pulmonary toxicity:

- ✓ History of radiation
- ✓ Thoracic surgery
- ✓ Alkylating chemotherapy agents

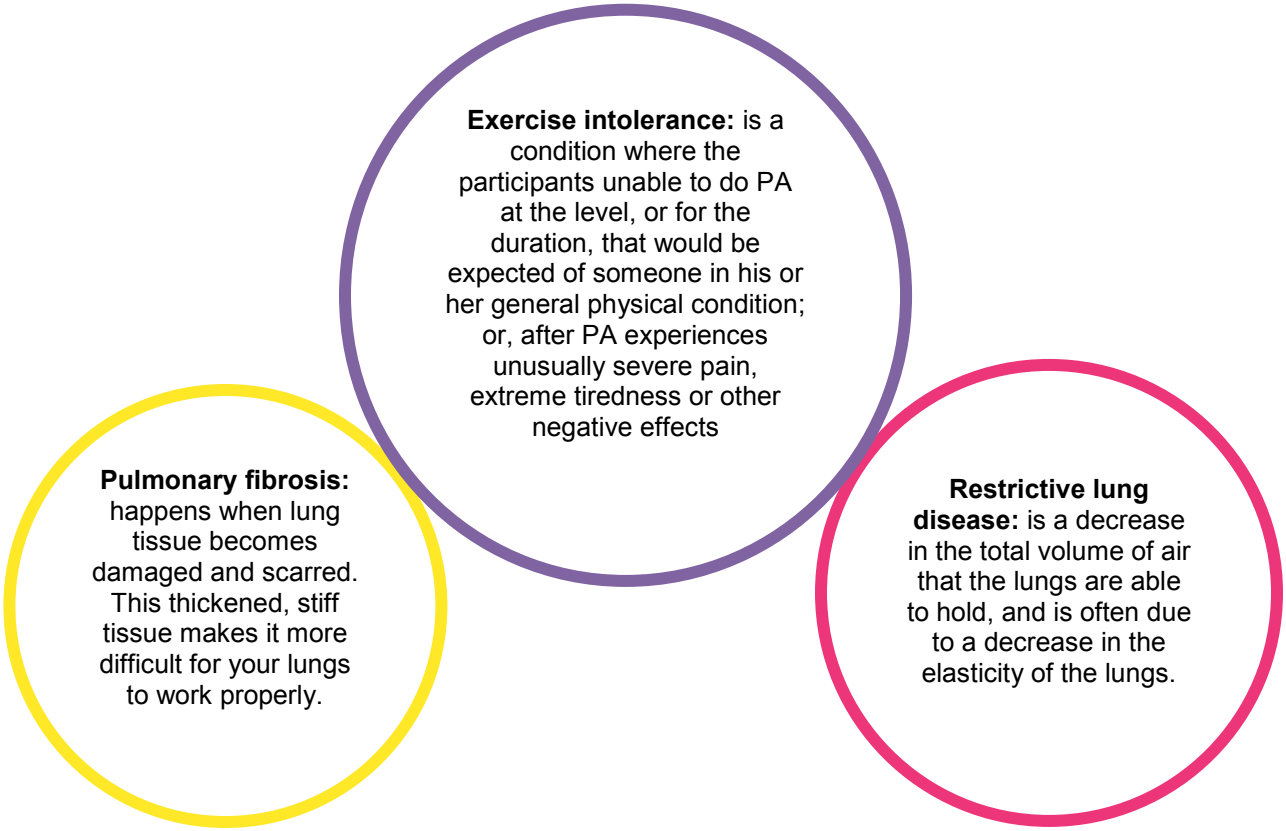

Table 5.6. Areas of emphasis and caution in patients and surivors with pulmonary toxicity.

Emphasize:
✓ Aerobic activity (walking, running, swimming). ✓ Flexibility. ✓ Progressive resistance training.
Caution:
✓ Exercise intolerance (if seen, consult physician). ✓ Difficult or painful breathing, shortness of breath, as a result of exertion.

Note. Compiled from [41-43, 44-47]. Portable oxygen should not be a reason for a person to avoid participating in a PA program. However consult with your child's physician.

vi) Hypertension

Children and adolescents with cancer are at risk for hypertension during and after treatment [48]. Measurement of hypertension in children/adolescents is different than in adults. Hypertension in children has been defined as, systolic blood pressure and/or diastolic blood pressure, that is at or above the 95th percentile.

Risk factors for hypertension:
- ✓ ALL diagnosis
- ✓ Hematopoeitic stem cell transplant
- ✓ Renal toxicity (e.g., ifosfamide, carboplatin, and cisplatin)
- ✓ Treatment with corticosteroids

Pediatric blood pressure norms are available at http://www.nhlbi.nih.gov/health-pro/resources/heart/blood-pressure-measurement-children.htm.

If your child has hypertension, see *Table 5.7* for recommendations and precautions for PA.

Table 5.7. Areas of emphasis and caution in patients and survivors with hypertension.

Emphasize:
✓ Daily aerobic activities at a moderate intensity (rated perceived exertion scale (RPE) between 3-7 or use talk rule described in anemia section in this chapter). ✓ Progressive resistance training. ✓ Weight loss if needed. ✓ Exercise stress test if other cardiovascular risk factors are present, such as treatment with anthracyclines, or trunk radiation.
Caution:
✓ Competitive sports for patients and survivors with uncontrolled hypertension. ✓ High intensity exercise in adult survivors of childhood cancer without exercise stress testing first, such as power lifting, climbing etc. ✓ Valsalva maneuver (holding your breath).

Note. Compiled from [48-52].

vii) Pancytopenias: Anemia, Thrombocytopenia, and Leukopenia

Pancytopenias, or low blood counts, is a disorder consisting of **anemia** (low hemoglobin), **thrombocytopenia** (low platelets), and **leukopenia** (low white blood cell count) [53]. Mild forms of pancytopenia are common among all children with cancer, either as a part of their primary disease (as in leukemia), or as an effect of chemotherapy or radiation [54]. Severely low

counts of hemoglobin, platelets, and white blood cells will be seen mostly among children having a bone marrow transplant [54].

Anemia

Anemia is a decrease below normal values of blood hemoglobin, affecting a person's ability to carry oxygen in their body [54]. Typical signs and symptoms of anemia include:

- ✓ Drowsiness, weakness, increased need for sleep
- ✓ Shortness of breath on exertion
- ✓ Headache, irritability, poor mental concentration (can impact school performance)
- ✓ Poor appetite
- ✓ Being unusually pale **(pallor)**
- ✓ Increased resting heart rate (tachycardia)

"Symptoms must drive PA prescription! Keep safety precautions in mind as a guideline, but exercise will be modified for the child and his/her situation.

PA recommendation for a person with anemia depends on whether or not they have symptoms. Research tells us that it is safe to do PA, so long as a person does not show any symptoms, and usually a blood transfusion will be enough to remove the symptoms when necessary .

Table 5.8. Areas of emphasis and caution in patients and survivors with anemia.

Emphasize:
✓ Encourage PA starting from a low intensity and gradually building up, ✓ Provide encouragement as exercise done regularly will improve a person's endurance, ✓ Use rated perceived effort (RPE) scales (*Appendix E*), or the talk rule (see box below) to assess intensity of PA. ✓ Balance between rest and activity.
Caution:
✓ If hemoglobin < 80 g/L, and showing symptoms of lightheadedness, dizziness, nausea, being generally unwell, or experiencing a sudden change in alertness: Wait for blood transfusion prior to resuming physical activities (usually only applies to children in hospital who are involved in PA or an exercise program during hospitalization) ✓ Hemoglobin < 80 g/L, and asymptomatic: Do PA with caution, at low-intensity, and monitor for symptoms. ✓ A child who regularly exercises will find it easier to get involved with PA. A child who rarely exercises will need a slower, more progressive approach.

Note. Compiled from [54-59].

"Talk rule"

It is used to understand PA intensity. In simple terms, how easy is it to talk during exercise?

Light intensity: you would be able to carry out a normal conversation, or even sing during exercise.

Moderate intensity means you are able to talk during exercise, but would struggle with a full conversation. You would not be able to sing.

Vigorous intensity: means being unable to say more than a few words while exercising.

Thrombocytopenia

Thrombocytopenia is defined by a platelet count below the lower limit of 150 x 10^9/L [54]. Typical signs and symptoms include:

- ✓ increased frequency and severity of bruising
- ✓ signs of bleeding from small blood vessels under the skin (spotted bruising for no apparent reason)
- ✓ spontaneous bleeding (can be from the mouth, anus, or unusually long nosebleed)
- ✓ bleeding that seems to last longer, or be far worse, than expected

Generally, the risk of severe spontaneous bleeding is rare, unless the platelet count is really low or the platelets are not functioning normally [60]. *Table 5.9* highlights the areas of emphasis and caution [54].

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

Emphasize:
✓ Supervised progressive resistance training.
✓ Proper form and technique with exercises.
✓ Minimize the risk of bleeding or unnecessary bruising (e.g., having a "spotter" during balance or strengthening activities, and avoiding high impact sports).
✓ Extra padding on hard surfaces.

Caution:
✓ Platelets < 50 x 10^9/L - Avoid high risk activities (e.g., contact sports). ✓ Platelets 10-20 x 10^9/L - Might need platelet transfusion. Can still exercise at low intensity. Extra care to avoid injury. ✓ Platelets < 10 x 10^9/L- Requires transfusion. Higher risk of spontaneous bleeding. Do not perform PA until after transfusion.

Note. Compiled from [54,55,57,58,60].

Leukopenia or Neutropenia

Leukopenia, also known as neutropenia, refers to a white blood cell count below normal range for your age (and is often referred to as immune system suppression) [54]. To identify those at a higher risk of infection, it is more useful to look at their **absolute neutrophil count**, as neutrophils are considered the "first responders" of our immune system and are crucial in fighting off infection [61,62]. Neutropenia is considered mild, moderate, or severe when absolute neutrophil count is below 1.5 x 10^9/L, 1.0 x 10^9/L and 0.5 x 10^9/L, respectively [63]. Neutropenia accompanied by fever is a medical emergency for children undergoing treatment for cancer, due to a decreased ability to fight infection [63]. PA is usually avoided if a child has a temperature greater than 38 degrees Celsius, because exercise will sometimes increase a person's body temperature more. For additional areas of emphasis and caution refer to *Table 5.10.*

Safety Precautions when Working with Immunocompromised Patients:

- ✓ Focus on individualized sessions
- ✓ 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

Research looking at the effects of PA with a low immune system have shown that PA (both resistance and aerobic training) is safe, so long as there is no fever present [55,57,58].

Table 5.10. Areas of emphasis and caution in patients and survivors with leukopenia.

Emphasize:
✓ Aerobic training- low to moderate intensity. Use the talk rule.
✓ Progressive resistance training.
✓ Reduce risk of infections (proper hygiene, hand-washing, and equipment cleaning).
Caution:
✓ Neutrophil count < 0.5 x 10^9/L, indicates severe neutropenia. Follow safety precautions to prevent avoidable infection.
✓ In some cases, avoid aquatic sports and high intensity exercise.
✓ Avoid exercise if fever >38 degree Celsius.

Note. Compiled from [64-67]. If in doubt, consult your child's oncologist, as neutropenia is not the only factor involved in risk of infection.

viii) Bone tumor effects: Post-surgical considerations in osteosarcoma

Osteosarcomas are the most common malignant bone tumors and derive directly from the bone-tissue. Please refer to *Chapter 9* for more details. Surgical options vary based on which bones are involved, but lower extremity **amputations,** or **limb-sparing surgery,** are used to offer the best possible functional outcomes [68-70].

Several types of cancer can grow in bones. Some start in other tissues, but can then grow into nearby bony structures, as in Ewing's sarcoma or rhabdomyosarcoma [71]. Metastatic disease can also spread and cause pathological fractures, or fractures from disease [71]. By following the same guidelines for osteoporotic patients, as outlined in the osteopenia and osteoporosis sections, one can exercise safely depending on the bone involvement. For other PA recommendations and precautions see *Table 5.11.* These precautions might change depending on the surgical procedure. Please consult your orthopedic surgeon for specific limitations [69,70,72].

Bone healing will be slowed by cancer therapies: bones that would usually take 6-8 weeks to heal will need more time. The risk of infection is higher due to low white blood cell counts. Excellent communication with surgical and oncology teams is necessary, especially if wanting to participate in a community program or sport. If uncertain, consult the primary physician.

Table 5.11. Areas of emphasis in patients and survivors with osteosarcoma.

Emphasize:
✓ Improving flexibility under the guidance of the surgeon or supervising therapist. ✓ Progressive resistance training using motions that are part of day-to-day life (e.g., practicing stairs). ✓ Gradual weaning-off of ambulatory aids (e.g., walker, crutches, cane) to encourage muscles to relearn normal movement patterns. ✓ Symmetry during walking (Note: asymmetry can be a hint for issues of weakness or lack of flexibility). ✓ Balance and coordination training. ✓ Progressive return to sport or work with physician clearance.
Caution:
✓ Avoid extreme range of motion during first few months of healing. ✓ In total hip replacement, avoid hip flexion past 90 degrees. ✓ Weight-bearing is commonly discouraged during first few weeks after surgery. ✓ High impact activities should be introduced slowly under guidance of surgeon. ✓ If your surgeon recommends using a brace to protect a joint (e.g. a knee), learn how to use it properly and what it's limitations might be.

Note. Compiled from [68,70,73,74]

ix) Sensory impairments

Refer to *Table 5.12* for areas of emphasis and caution if a patient or survivor is experiencing sensory impairments.

Skin sensation

Surgeries carry a risk of damaging nerves, which can affect how much (if at all) a person might feel over their skin at or near the surgical site. Chemotherapy-induced peripheral neuropathy may also cause a loss of sensation.

Depending on the extent of nerve injury, this may include changes or loss in [75,76]:

- ✓ Sensation of hot/cold (can be dangerous if not aware that an area is freezing or burning)
- ✓ Being able to feel if touch is deep, light, or pinprick sensation
- ✓ Joint proprioception (knowing where a limb is without looking at it), which might make a child seem or feel uncoordinated or clumsy

- ✓ Sensation of different kinds of pain

Nerve injury can also make your body feel pain without any external source of pain. Sensation plays a role in protecting a joint or limb during activities in healthy individuals. A cancer survivor with sensory impairment due to chemotherapy-induced peripheral neuropathy or major surgery may be unable to feel what their body is doing. Therefore, early re-introduction into PA and sports should be closely supervised.

Ototoxicity

Ototoxicity refers to the damage to the cells within the inner ear responsible for hearing and balance, and is a moderately common side effect of the platinum-based chemotherapy (e.g. cisplatin, carboplatin, most drugs ending with -platin) typically used to treat osteosarcoma [75] and medulloblastoma (a form of brain tumor) [77]. These drugs can cause hearing loss in the high frequency ranges and, rarely, within ranges related to speech among cancer patients and survivors [75]. Hearing loss typically happens on both sides. It rarely occurs at doses less than 260mg/m^2 of cisplatin, but has been reported to cause hearing impairment in almost one in four children who receive more than 400mg/m^2 [77]. It is important to be aware of the potential for hearing impairment, because this may affect safe participation in PA.

If a person cannot rely on their inner ear to give them information useful for balance and hearing, they will become more dependent on the information that their joints and eyes provide them to keep their balance. As a consequence, a child's balance might seem worse at night or when lights are dim, which could lead to a fall. Small changes, such as having a night-light available in a hallway on the way to the bathroom, might help avoid a fall and injury [78]

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

Emphasize:
✓ Education regarding risks of loss of sensation; frequent skin checks particularly in hard-to-see areas. ✓ Learn proper alignment of joints during PA. ✓ Progressive balance training if necessary.
Caution:
✓ Careful when applying hot or cold to a limb with impaired sensation, due to risk of burn/ frostbite. ✓ 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. ✓ If unable to learn proper alignment through activity, consider bracing for additional support and prevention of injury. ✓ When training over uneven terrain during return to sport, gradual progressive drills are important to avoid injury.

Note. Compiled from [77,78]

x) Graft-versus-host disease

Graft-versus-host disease (**GVHD**) can be acute or chronic (refer to *Chapter 8*). **Chronic GVHD** is a frequent cause of health complications, for a person after having had an allogeneic hematopoietic stem cell transplant. Chronic GVHD usually begins between three months to two years after transplantation. Generally the signs and symptoms of chronic GVHD do not differ significantly between children and adults [79,80]. The text box below describes symptoms that might affect PA participation.

It is worth noting that chronic GVHD often impacts a few, and not all, of the organ systems listed below. One area might be more severely affected than another. The prevention of chronic GVHD is usually done through the use of steroids [79,81]

Children with chronic GVHD must have a slow, gradual re-introduction into PA. Often these children have been ill for long periods of time and parents are reasonably afraid to “push too hard”. Early sessions with a child with chronic GVHD 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. Generally, chronic GVHD will not directly pose a danger to the child in terms of PA, but might limit their ability to participate (e.g., shortness of breath because of lung tissue damage) [79]. Because of the

complex nature of this condition, experts in this area recommend that patients with chronic GVHD seek services from a specialized center familiar with GVHD after a bone marrow transplantation [79] . Areas of emphasis and caution are explained in *Table 5.13* and *5.14*.

Common organs affected by chronic GVHD:

- ✓ **Skin:** Can evolve from a rash to deeper skin changes that can tighten up like a severe burn
- ✓ **Oral mucosa:** Ulcers, gingivitis and destruction of salivary glands
- ✓ **Gastrointestinal tract**: Nausea and vomiting, chronic diarrhea, and lack of nutrient absorption
- ✓ **Lung:** Progressive, irreversible lung damage, and increased risk of severe infections
- ✓ **Joints:** Potentially limiting movement in large joints; rheumatic-like symptoms in the joints (swelling, stiffness, pain)

Table 5.13. Physical activity recommendations based on chronic GVHD impact.

Organ system affected	Recommendation
Skin and fasciitis: scarring over joints and deep into tissues	Stretching program will help prevent stiffness and loss of range of motion.
Muscle weakness is extremely common, especially in the shoulders and hips	Emphasize strengthening shoulder and hip muscle groups; develop endurance.
Joint pain	Emphasize strengthening muscles around painful joints to improve joint protection.
Damage to lung tissue, in some cases might need to go home with home oxygen	Learn rate of perceived exertion (see *Appendix E*); may need to learn relaxation/ breathing exercises as breathlessness can be very anxiety-provoking and could lead to panic attacks.
Osteoporosis	Strengthening of surrounding muscles. See osteoporosis in this chapter.
Pancytopenia	Refer to pancytopenia in this chapter.

Note. Compiled from [79-83].

Table 5.14. Areas of caution depends of organ affected by chronic GVHD.

Organ system affected	Caution
Joint	Extreme stretching discouraged.
Lungs	A portable oxygen tank does not mean they cannot participate in PA. Refer to the Pulmonary Toxicity section for details on safety for this population.
Osteoporosis	See osteoporosis in this chapter.
Pancytopenia	See pancytopenia in this chapter.

Note. Compiled from [79-83].

Summary

Children treated for cancer are at risk for many side effects; however, every cancer treatment is different and every child responds in their own way. Many will not experience serious symptoms when they perform PA; however, it is important to understand the possible side effects of specific treatments in order to be safe. Children and adolescent 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 be safe, we encourage that the general and specific PA recommendations described in this chapter are followed. Supervision is recommended when starting a PA program, during intense cancer treatment periods, and when making any significant changes to a program. If symptoms are present, refer back to the oncologist for further testing. It is essential to make PA fun and successful so that children will continue to exercise for years to come. Finally, always consult with a physician before starting a PA program.

Additional Resources:

- ✓ Chamorro Viña C, Keats M and Culos-Reed SN. Pediatric Oncology Exercise Manual - Professional Version. Health and Wellness Lab, Faculty of Kinesiology, University of Calgary. 2014. Download: http://ucalgary.ca/poem

Take Home Message

It is generally safe and beneficial for patients and survivors of pediatric cancer to perform physical activity, as long as they are aware of a few precautions based on their treatment and side effects. Awareness of the areas of emphasis and caution for physical activity will assist families in optimizing a child's success in a physical activity program.

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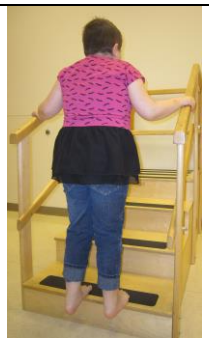
Appendix 5.A

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 Gastrocnemius-Soleus Stretch	Children less than 7 years or unable to do independent stretching		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 sec.
Gastrocnemius-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.
Gastrocnemius-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 without stepping off. Increase difficulty with 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 hold for >10 sec; 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:

- ✓ …practical steps that can be taken to integrate your child back into physical activity taking into account the impact of cardiotoxicities.

Introduction

The National Cancer Institute defines cardiotoxicity, in general terms, as toxicity that affects the heart (www.cancer.gov/dictionary). Cardiotoxicity is one of the most serious long-term complications of pediatric cancer therapy and may appear as **cardiomyopathy, pericarditis, congestive heart failure or valvular heart disease**.

Cardiomyopathy refers to diseases of the heart muscle. These diseases have many causes, signs, symptoms, and treatments. In cardiomyopathy, the heart muscle becomes enlarged, thick, or rigid.

Pericarditis happens when the sac surrounding the heart becomes irritated. This can cause chest pain.

Congestive heart failure happens when the heart cannot pump blood normally. This makes it hard for blood to get to other parts of the body.

Valvular heart disease occurs when one or more of the heart valves do not open fully or close completely. This makes it hard for the heart to pump blood.

Research on cancer survivorship has shown that cardiovascular problems caused by **chemotherapy** (such as coronary artery disease, stroke, and especially congestive heart failure) have become one of the main long term effects, and causes of death in **long-term survivors** of childhood cancer [1]. In fact, childhood cancer survivors are 15 times as likely to develop congestive heart failure, and have 7 times the risk of premature death due to cardiac causes [2] when compared with the general population. Treatments that are used in adults and children with cancer that have been associated with cardiotoxicity are [3,4]:

i) Chemotherapeutic agents that include but are not limited to anthracycline, cyclophosphamide, cytarabine, cisplatin, and isofosfamide;

ii) **Radiotherapy** around the heart (chest).

i) Chemotherapeutic Agents

Chemotheraputic agents have been associated with negative cardiovascular effects that could decrease a child's well-being and limit his or her future treatment options. Anthracycline antibiotics are the best-known class of chemotherapeutic drugs associated with cardiotoxicity. These agents, especially doxorubicin, have been a key part of the therapy for blood cancer and solid tumors in children, and are still used in treating nearly 60% of childhood cancers. Anthracycline–induced cardiotoxicity can manifest as either asymptomatic, or clinical congestive heart failure. The incidence of congestive heart failure increases with greater doses of anthracyclines exposures, exceeding 30% for children exposed to doses >600 mg/m² [5]. This risk is higher in females, those who are treated at a younger age (<5 years of age), exposed to chest radiation, and those who develop cardiovascular risk factors, such as hypertension and diabetes after completion of therapy (*Table 6.1*) [1].

A PEER participant working on balance

ii) Radiotherapy

Radiotherapy that includes the heart in the area of treatment can cause many long-term complications, including constrictive pericarditis**,** cardiomyopathy**,** valvular heart disease**,** coronary artery disease, and conduction abnormalities [5].

These survivors have shown to be at a high risk for preventable heart disease [5]. This means that heart disease may be prevented through changes in the children's health habits, such as more **physical activity (PA),** and managing high blood pressure, high cholesterol, and diabetes. The period of time expected between the cardiotoxic exposure of your child and the manifestation of cardiac disease can be more than 10 years [4,6].

Those children exposed to doses ≥250 mg/m^2 of anthracycline are at the highest risk to develop cardiotoxicity.

Rales is defined as, an abnormal rattling sound heard when examining unhealthy lungs with a stethoscope.

Table 6.1. Clinical signs and symptoms and risk factors associated with congestive heart failure.

Signs and Symptoms	Therapeutic Exposures Associated with Increased Risk	Other Risk Factors
Signs: ✓ Swelling ✓ **Rales** Symptoms: ✓ **Dyspnea** ✓ Fatigue	Anthracycline chemotherapy (e.g., doxorubicin, danorubycin). Dose-dependent increase in risk (lifetime cumulative incidence, %). ✓ <250 mg/m^2 (<5%) ✓ 250-600 mg/m² (5-30%) ✓ >600 mg/m² (>30%) Chest radiation exposure in which the heart is in the area of treatment.	✓ Younger age at treatment (<5 years old). ✓ Female sex. ✓ Cardiovascular risk factors (ie., hypertension, diabetes).

Note. The definition for symptomatic congestive heart failure is taken from [7]. Risk classifications taken from [1,8,9]. Refer to *Appendix 6.A to see anthracycline conversion factors*.

Because cardiac disease can be asymptomatic, it is important to detect it early. This is why the Children's Oncology Group, as well as other international organizations [10-13], have created guidelines that recommend all survivors who have been treated with cardiotoxic therapies, to get yearly detailed history and physical examinations. Physicians should pay close

attention to signs and symptoms of cardiac disease. In addition, echocardiograms should be performed, ranging from every year to every 5 years, depending on the risk of congestive heart failure (*Table 6.2*).

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

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/m^2	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/m^2	Every 2 years
		≥300 mg/m^2	Every year
Any age with decrease in serial function			Every year

Note. From the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancers [10]. †Age at time of first cardiotoxic therapy. ††Based on equivalent mg of doxorubicin/daunomycin.

Given up to 50% of childhood cancer survivors treated with cardiotoxic therapies may have asymptomatic disease, it is important that the above mentioned screening (i.e., MUGA scans) occurs prior to PA involvement. However, PA might be helpful for preventing future heart disease. The following sections provide specific guidelines for different patient populations according to cardiac function risk factors.

Physical Activity after Cardiotoxic Therapy Exposure

Patients with normal cardiac function at risk of cardiotoxicity

There is good evidence supporting the benefits of regular, moderate PA in pediatric cancer survivors [14,15]. Literature shows that survivors can have improvements in muscle strength, flexibility, **cardiorespiratory fitness**, and overall physical function when engaged in PA [16] (see *Chapter 2* for more details). The American Heart Association and the American College of Sports Medicine for adults, recommend 30 to 40 minutes of aerobic exercise, 5 times per week, and strength training 2 times per week, for the general population [15]. Recommendations for PA in childhood cancer patients and survivors exposed to cardiotoxic therapies exist, however, these were created by centers that describe their own experiences, or by researchers and clinicians through agreement and support among those present [5,10,17]. Regular PA is recommended for survivors treated with anthracyclines, and/or chest radiation, who have normal left ventricular systolic function [5,7,18-20].

A sibling in the PEER program

The Children's Oncology Group – Long Term Follow up Guideline has offered a few conditional recommendations for children undergoing cardiotoxic therapies [10] (refer to *Table 6.3* and *Table 6.4*). If your child is at risk of developing cardiotoxicity, always ask your physician before engaging in PA. Each child might be different. The best person to let you know what your child can or cannot do is your child's physician.

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

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

Recommendations
✓ Patients and survivors beginning regular PA for the first time should tell their physicians if they feel tired or have difficulty breathing, that does not go away with rest.
✓ **Aerobic exercise** is generally safe and should be encouraged. No limit in PA intensity is prescribed if the child has normal cardiac function [19,20].
✓ Repeatedly lifting lighter weights is generally safe. The child should only do as many repetitions as they are comfortable with.

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

Contraindications
✓ Patients and survivors who choose to engage in demanding PA (e.g., **weight lifting, wrestling**), or team sports should discuss appropriate guidelines and a plan for ongoing monitoring with a cardiologist. This especially applies to patients and survivors defined in *Table 6.2* as those who need screening every one or two years.

Patients with asymptomatic cardiac disease

No specific guidelines for children with cancer and asymptomatic cardiac disease currently exist. It is recommended that survivors with asymptomatic cardiomyopathy talk to a cardiologist to define their own limits and precautions for PA (i.e., limited, or no participation in high intensity competitive sports, such as body building, rock climbing, windsurfing, ice hockey) [17]. For children with asymptomatic cardiac dysfunction (not affected by cancer), there are specific recommendations about permitted activities (high,

Isometric exercises involve an intense, focused, muscle contraction, with no real movement. This would be like pushing against a wall without either you or the wall moving, just a contraction without movement.

moderate, and low-intensity) that are based on the severity of the existing cardiac condition [19]. The American Heart Association and the European Society of Cardiology recommend consultation with a cardiologist if a childhood cancer survivor is at a high risk to develop cardiotoxicity, and is planning to engage in intensive **isometric** exercises[19,20]. It is important to note that more studies are needed to create better PA recommendations for children with cardiac conditions.

Additional Resources:

- ✓ Okada M, Meeske KA, Menteer J, Freyer DR. Exercise recommendations for childhood cancer survivors exposed to cardiotoxic therapies: an institutional clinical practice initiative. Journal of Pediatric Oncology Nursing. 2012; 29(5): 246-252.
- ✓ Maron BJ, Chaitman BR, Ackerman MJ, et al. Recommendations for physical activity and recreational sports participation for young patients with genetic cardiovascular diseases. Circulation. Jun 8 2004; 109(22): 2807-2816.

Take Home Message

Cardiovascular complications, such as congestive heart failure, are a serious side effect of cancer therapies. 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 well-being.

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Chapter 7

Physical Activity and Leukemia

Alejandro San Juan, PhD; Carolina Chamorro-Viña, PhD;

& Julia Beulertz, PhD candidate

Learning Objectives

After completing this chapter you will know:

- ✓ …the potential side effects of leukemia treatment.
- ✓ …the role of physical activity during the leukemia journey.
- ✓ …precautions for childhood leukemia cancer patients and survivors to safely participate in physical activity.

Introduction

Leukemia is when the bone marrow produces abnormal white blood cells. These abnormal blood cells make it difficult for the healthy blood cells to do their job. There are different types of leukemia:

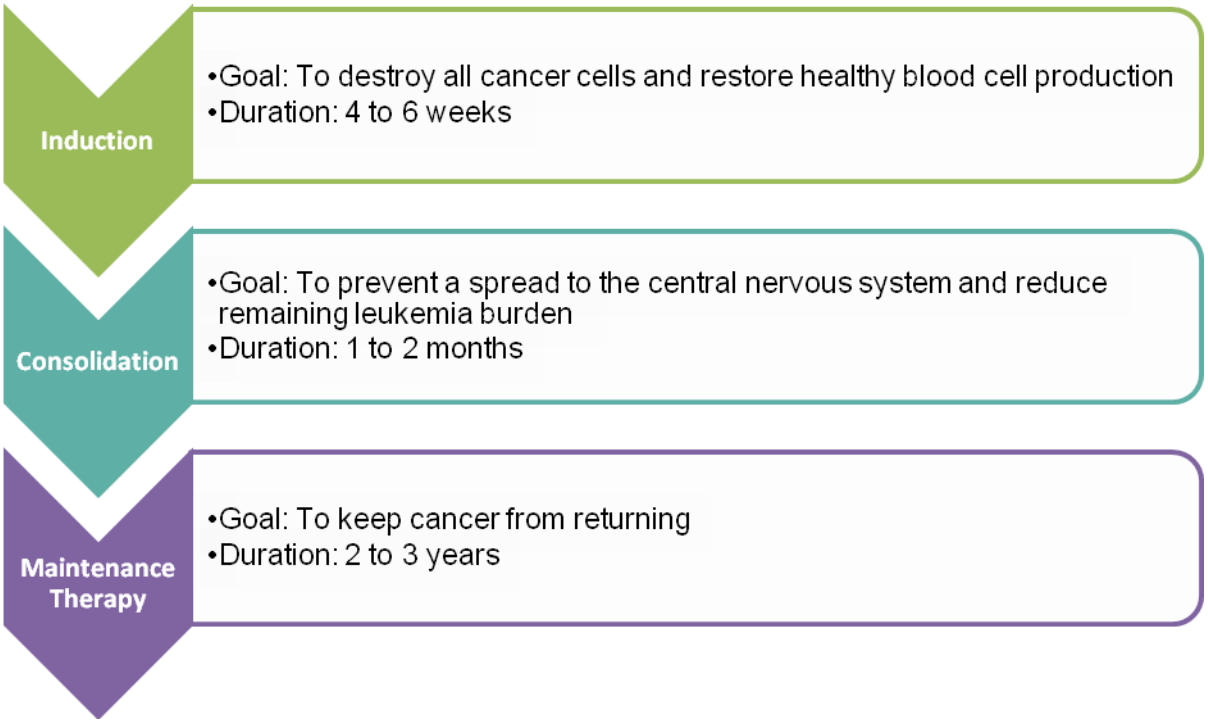
- ✓ **Acute lymphocytic leukemia (ALL)** is the most common cancer among children, approximately 25% of all cancers in children < 15 years of age [1].
- ✓ **Acute myeloid leukemia (AML):** 4% of all cancers among children < 15 years of age [1].
- ✓ Chronic lymphocytic leukemia
- ✓ Chronic myeloid leukemia

White blood cells are cells that help your body fight infection, and are made in your bone marrow.

Leukemia can progress quickly (acute leukemia) or slowly (chronic leukemia). Children will usually have an acute type of leukemia, while adults can have either type.

Common Treatments and Phases

Acute lymphoblastic leukemia treatment phases



Note. Compiled from [2,3].

Acute myeloid leukemia treatment phases

Acute myeloid leukemia treatment phases are similar to ALL, except it does not usually have the additional maintenance therapy phase [4].

Hematopoietic stem cell transplantation (HSCT)

HSCT is another treatment option for certain types of AML and ALL, which involves putting in new **hematopoietic stem cells** to rebuild the bone marrow. See *Chapter 8* for more information.

Hematopoietic stem cells are immature cells that can develop into all types of blood cells.

Potential treatment side effects and implications for physical activity

Cancer treatments can affect physiological systems that, in turn, might impact PA participation. Refer to *Table 7.1* and *Chapter 5* for more detailed information.

Table 7.1. Main late-effects in pediatric cancer.

System	Example of late side effects	Implications for PA
Heart and Blood Vessels	Decreased heart function and efficiency, irregular heartbeat, high blood pressure, and heart valve problems.	Diminished fitness levels that might affect their ability to perform moderate to high intensity or prolonged PA.
Lungs	Difficulties breathing and shortness of breath.	Decreased ability to move oxygen and blood to working muscles and other body tissues, which reduces their fitness (50-70% lower than healthy children), and causes fatigue during normal activities of daily living.
Muscles and Bones	Increased risk of fracture, reduced/uneven growth, reduced function/mobility, curved spine, muscle weakness and fatigue.	Decreased muscle and bone strength, and flexibility that may impact the type of PA the child can tolerate and perform safely.
Immune and Blood	Decreased ability to fight infection, decreased ability to stop bleeding and anemia.	See *Chapter 5* for detailed information.
Brain	Decreased attention, memory, and learning speed, and increased fatigue.	Children might need extra time to learn and understand an activity. May affect how they relate with others.
Nerves	Numbness or tingling in feet or hands, decreased ability to feel and muscle weakness.	See *Chapter 5* for detailed information.
Psychosocial	Social withdrawal, depression, anxiety, stress and fatigue.	Children may need extra time to get comfortable in a group.

Note. Translated from San Juan [5].

Specifically, impaired lung function, decreased blood oxygen transport capacity, diminished blood volume being pumped by the heart to the body's tissues (e.g., exercising muscles), and reduced cardiorespiratory fitness. As a consequence, fatigue symptoms are developed during normal **activities of daily living** such as playing with peers or climbing stairs. These side effects, as well as other factors, may be related to or promote a sedentary lifestyle.

Is Physical Activity Beneficial During the Leukemia Journey?

From the literature, we know that PA is feasible, safe, and beneficial for pediatric leukemia patients and survivors [6-11]. The evidence suggests PA increases muscular mass and strength, makes bones stronger, and increases the capacity of the muscles, heart and lungs to transport oxygen [7,12-18]. In other words, PA increases the ability to play or climb stairs with less fatigue. PA also seems to be beneficial for improving self-confidence and relationships with others and overall well-being.

Austin, age 8

Physical Activity Recommendations

Consult your child's physician before starting a PA program, because their treatment and overall health status may impact what activities they are able to participate in safely. Refer to *Table 7.2* for an example of objectives and PA recommendations. It is important to note, certain precautions must be taken when participating in PA. For example, if your child develops specific conditions, such as osteoporosis, peripheral neuropathy, anemia, immunosuppression, or is at a

high risk to develop cardiotoxicity, PA modifications should be made. See *Chapter 5* and *6* for specific recommendations and precautions for PA.

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

Phase of Treatment	Objective	Physical Activity Recommendation
Induction	Managing the side effects of cancer and its treatments. The goal is to prevent decreases in muscle strength and endurance.	In-hospital physiotherapy (also known as, **physical therapy**) and supervised PA.
Consolidation	Continue managing side effects of cancer and its treatments. The goal is to continue to prevent decreases in muscle strength and endurance.	In-hospital physical therapy and supervised PA.
Maintenance	Continue managing the side effects of cancer and its treatments. The goals are, to continue to prevent decreases in muscle strength and endurance, and start the recovery process (restore to healthy levels).	In-hospital or community-based supervised PA to rebuild physical fitness levels. Physical therapy if needed.
Survivorship	Health promotion. The goal is to optimize health.	Community-based PA programs. Physical therapy, if needed.

Note. Based on Courneya and Friedenreich [19], as well as the authors' own experiences.

Additional Resources:

- ✓ Summary of PA interventions in leukemia populations in *Appendix 7.A.*
- ✓ Wolin KY, Ruiz JR, Tuchman H, Lucia A. Exercise in adult and pediatric hematological cancer survivors: an intervention review. Leukemia. 2010; 24(6): 1113-1120.

Take Home Message

Physical activity programs are safe and necessary for this population. Physical activity has positive effects on muscle strength, fitness, and quality of life. Physical activity during induction and consolidation phases of treatment should be supervised and preferably performed in a hospital. In later phases of treatment (e.g., maintenance), home-based and community physical activity programs are recommended. If the child is experiencing extreme fatigue, nausea or pain, decrease the intensity or duration of physical activity and consult a physician. Once recovered, the child should be encouraged to have an active lifestyle and slowly begin community and school-based physical activity.

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Appendix 7.A

Clinical physical activity interventions with pediatric leukemia patients.

Authors	Study cohort	Setting/Duration/Form of exercise	Outcomes
Yeh et al. [8]	**IG:** n=12 (ALL) **CG:** n=10 (ALL) *maintenance therapy*	**Home-based.** **IG:** 6wk; 3/wk, 30min; at mild to moderate intensity; endurance. **CG:** standard care.	**Adherence:** 67-83%. **Fatigue:** fatigue score ↑ in IG vs. CG.
Gohar et al. [6]	n=9 (ALL) *intensive medical treatment*	**Supervised, in-hospital and home-based.** ~ 6-7 mo; 5/wk; physical therapy program (mixed exercises).	**Adherence:** 98%. **Physical functioning:** increased coordination. **Fatigue:** improved fatigue (15%).
San Juan et al. [14] **Ruiz et al.** [10]	n=7 (ALL) *maintenance therapy*	**Supervised, in-hospital and 20-wk detraining.** 16wk + 20wk detraining; 3/wk, 90-120 min. Endurance: 30min. at mild to moderate intensity. Strength: one set, 8-15 repetitions, 11 exercises.	**Immune status**: PA does not alter the immune system, therefore, it can be safely performed. **Adherence:** > 85%. **Physical functioning:** improved flexibility, ability of muscles, heart, and lungs to transport oxygen, muscular strength, flexibility, and the ability of the children to perform activities of daily living. **Well-being:** no differences.
Hartman et al. [16]	**IG:** n=20 (ALL) **CG:** n=21 (ALL) *completed medical treatment*	**Supervised, in-hospital (every 6wks) and home-based** **IG:** 2yr exercise program (mixed exercises). **CG:** standard care.	**Physical functioning:** the IG ↑ physical fitness, ↑ strength of the bones, and ↑ ankle flexibility. BMI ↓ in IG during intervention and ↑ at follow up; body fat ↑ in IG during intervention and ↓ at follow up. **Unsatisfactory adherence.**

Moyer-Mileur et al. [17]	**IG:** n=6 (ALL) **CG:** n=7 (ALL) *maintenance therapy*	**Home-based.** **IG:** 12mo; >3/wk, 15-20 min. physical activity (mixed) and educational sessions. **CG:** standard care.	**Physical functioning:** IG ↑ endurance in an aerobic test. The children increase the amount of steps (~140%).
Takken et al. [7]	n=9 (ALL) *survivorship*	**Supervised, community-based and home-based.** 12wk; 4/wk, 45-min, at moderate to vigorous intensity (mixed exercises).	**Adherence:** 60%. **Physical functioning:** no significant changes, but adherence to the program was low.
San Juan et al. [12]	**IG:** n=8 (leukemia) **CG:** n=8 (healthy matched controls) *~8.9 ± 4.5 mo post HSCT*	**Supervised, in-hospital.** 8wk; 3/wk, 90-120min. Endurance: 10-30min. at mild to moderate intensity. Strength: 1 set, 8-15 repetitions, 11 exercises.	**Adherence:** 70%. **Physical functioning:** the ability to perform activities of daily living ↑ in IG; strength ↑ in IG; endurance ↑ in IG vs. CG. **Well-being:** ↑ in IG vs. CG.
Ladha et al. [9]	**IG:** n=4 (ALL) **CG:** n=6 (healthy matched controls) *maintenance therapy*	**Acute, supervised intervention.** 30min., intermittent run-walk on a treadmill at moderate to vigorous PA.	**Immune system:** no negative response.
Marchese et al. [18]	**IG:** n=13 (ALL) **CG:** n=15 (ALL) *maintenance therapy*	**Supervised (5 sessions) and home-based.** **IG:** 4mo exercise program (physical therapy; mixed exercises). **CG:** no exercise recommendations.	**Physical functioning:** ankle flexibility ↑ in IG vs. CG; knee extension strength ↑ in IG vs. CG.

Note. ↑: improved/ better; ↓: deteriorate/ worse; n: sample size; IG: intervention group; CG: control group; ALL: acute lymphoblastic leukemia; min: minute(s); d: day(s); wk: week(s); mo: month(s); yr: year(s); BMI: body mass index; HSCT: Hematopoietic stem cell transplant.

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Chapter 8

Physical Activity in Children Treated with Hematopoietic Stem Cell Transplantation

Carolina Chamorro-Viña, PhD & Antonio Pérez Martínez, MD, PhD

Learning Objectives

After completing this chapter you will know:

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

Introduction

Hematopoietic stem cell transplant (HSCT), formerly referred to as a bone marrow transplant, is a procedure that involves the infusion of hematopoietic **stem cells** to rebuild the bone marrow function (i.e., patient's blood forming system) in patients [1]. HSCT is used to treat a wide variety of diseases, both cancerous and non-cancerous, including acute and chronic leukemia and lymphomas, immunologic and hematologic disorders (e.g., severe combined immunodeficiency syndrome), and bone marrow failure syndromes [2]. In the diseases mentioned here, the stem cells or the bone marrow of the patient are damaged and are no longer able to produce healthy blood cells. HSCT is associated with countless side effects, such as muscle wasting, fatigue, diminished cardiovascular functioning, immunosuppression, and **graft versus host disease (GVHD)** [3,4]. Fortunately, due to less toxic

Stem cells are young, immature cells that will become mature (through a process called **differentiation)** to become different types of specialized cells. They can copy (replicate) themselves to replace or rebuild tissues in the body. Some stem cells mature into blood cells. Blood-forming stem cells develop into different types of blood cells in the bone marrow. When blood cells are mature, they move from the bone marrow into the bloodstream [1].

conditioning regimens, improved viral surveillance, and better treatment of infectious complications, these outcomes are improving [5].

Physical activity (PA) has recently been studied as a complementary tool to boost the recovery of children and adults with cancer [3,6,7]. Although the evidence is scarce, especially in children, the results are promising and no side effects due to PA have been reported [3,7-11]. To successfully and safely prescribe or engage in PA, it is important to understand the basics of the disease processes and the complications frequently encountered in this population.

Common Types and Phases of HSCT

Common types of HSCT

When the donor and the recipient (patient) for the HSCT are the same, it is called an **autologous HSCT**. In these cases **hematopoietic stem cells** are removed from the patient and frozen. Typically, after intensive conditioning regimens that promote death of bone marrow (i.e., myeloablative conditioning regimen), the hematopoietic stem cells are put back in the patients' body to regenerate normal blood cells. This is also known as a rescue transplant.

When the donor and the recipient are not the same, the transplant is called **allogeneic HSCT.** These donors could be a family member (related) or a non-family person (unrelated). The **major histocompatibiity complex,** also called **human leukocyte antigen** typing, is used to match the donor with the recipient. If the sibling is an identical twin, this transplant is called a **syngeneic HSCT.** Haploidentical donors are the parents of the patients and half of their siblings; these donors share 50% of the human leukocyte antigen with the patient.

Human leukocyte antigen are cell surface receptors and is what the immune system uses to distinguish between self and non-self. Differences in the HLA, between donor and recipient, will initiatiate an immune response. This phenomenon is called alloreactivity.

Sources of hematopoietic stem cells

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

Table 8.1. Sources of hematopoietic stem cells.

Sources used in the HSCT	Known As	Procedure
Cord blood	Hematopoietic stem cell transplantation	Collect hematopoietic stem cells from the cord blood at birth.
Peripheral blood	Peripheral stem cell transplantation	The hematopoietic stem cells are obtained from the peripheral blood by a sophisticate system called leukapheresis.
Bone marrow	Bone marrow transplantation	Bone marrow aspirated from the iliac crest has traditionally been the primary source of HSCT.

Note. Compiled from [13-15]. HSCT: Hematopoietic stem cell transplantation.

Phases of HSCT

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.

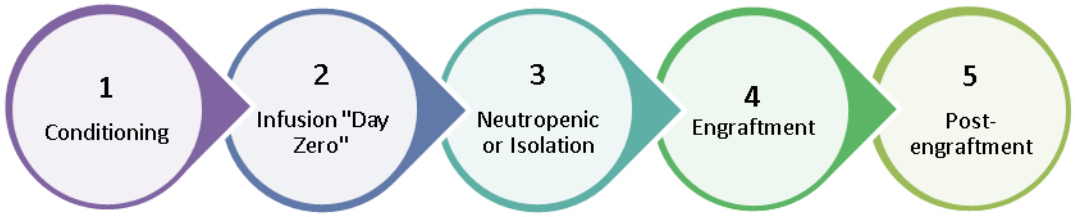
1) The **conditioning** phase lasts approximately 1 week. Chemotherapy, and/or radiotherapy are given to eliminate any existing disease, prevent graft rejection, and create space for the hematopoietic stem cells.

2) During the **infusion** phase (also known as **Day Zero),** hematopoietic stem cells are put into the patient. In order to eliminate all the cytotoxic agents from the patient's body, a day of rest is given between conditioning and infusion. The volumes are infused through a central venous catheter, and vary depending on the stem cell source, processing, and size of the recipient.

3) **Neutropenia (isolation phase)** typically lasts 2-4 weeks. At this point, the patient's ability to produce white blood cells is reduced. The white blood cells are responsible for fighting infections; therefore, patients are at a high risk of infection. In this phase, the patient might be

isolated in their hospital room, and any health care professionals or allied health care professionals entering their rooms might have to follow special precautions. During this phase, medication will be given to prevent infection and GVHD**.** Nutrition deficiency is another common problem of this phase and parental nutrition is often administrated. Finally, platelet and hemoglobin transfusion may be needed.

Figure 8.1. Phases of hematopoietic stem cell transplant.



Note. Data taken from [12].

4) **Engraftment** occurs after several weeks when the new blood-forming cells (e.g., hematopoietic stem cells) begin to grow and make sufficient number of healthy blood stem cells to normalize the blood cell counts (platelets and red blood cells), and improve the immune system function (white blood cells). It is an important milestone in the transplant recovery. Neutrophils recover faster at that point and are an important measure of engraftment, due to their ability to fight bacteria. However, the lymphocyte function (e.g., T cells and B cells) remains compromised at this time, due to immunosuppressive medications and the delayed process of immune rebuilding. Thus, patients are at an increased risk for viral and fungal infections at this time. **Prophylactic** strategies must be implemented to try to prevent morbidity from these infections. It is during this stage that the patient may develop acute GVHD.

- ✓ An **absolute neutrophil count (ANC)** of 500 or more for 3 days in a row is a sign of engraftment.
- ✓ Platelet count of 20,000 to 50,000 is a sign of platelet engraftment.

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5) The post-engraftment is the longest phase in which the immunological recovery and immune reconstitution tolerance will happen. The immune system reconstitution can take 1 to 2 years. Lymphocyte function remains poor until 8-10 months after transplantation. This may be further delayed by the presence of chronic GVHD, in which case it may never fully reconstitute.

Types of conditioning regimens

The goal of HSCT is ensure engraftment with low toxicity and high antitumor effect. There are two types of conditioning regimens: Myeloablative (classical) and non-myeloablative (mini or reduced intensity) transplant [16,17]. In the myeloablative conditioning regimen, the treatment is based on high doses of chemotherapy and radiotherapy that destroy the bone marrow of patients and their capacity to produce blood cells. The goals of the myeloablative treatment are to destroy 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 [16,18].

The non-myeloablative transplant aims to suppress the patient's immune system sufficiently to allow engraftment of the donor cells. Eradication of cancer cells occurs, due to **graft versus tumor** effect [19]. The graft versus tumor also known as graft versus leukemia is a really positive reaction. The donor's immune cells may recognize residual leukemia, lymphoma, or cancer cells as being different and destroy them.

Immune Cell Alloreactivity as a Basis of Allo-HSCT

Alloreactivity only occurs in the setting of allogeneic HSCT. This process is initiated because differences in the HLA exist between donor and patients. These differences promote complex interactions between the patients and donors immune system cells that lead to three different results [20]:

- ✓ Graft versus host disease: A complication where the transplanted immune cells attack the patient's body. Prevalence of acute GVHD is directly related to the degree of mismatch between HLA of patient and donor. This reaction promotes a general inflammation in the patient's body. There are two types of GVHD: acute and chronic [23]. In children, the incidence is lower than adults and chronic GVHD ranges between 25-50% [24]. Symptoms in both acute and chronic GVHD range from mild to severe [23]. 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. This is the major drawback of HSCT.

- ✓ Graft rejection: The patient's immune system recognizes the hematopoietic stem cells of the donor as foreign, and destroys them. The more similar the HLA are between the donor and recipient, the less likely that the hematopoietic stem cells will be rejected.
- ✓ Graft versus leukemia or graft versus tumor: The donor's immune cells may recognize residual leukemia, lymphoma, or cancer cells as being different and destroy them.

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.

- ✓ 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, contributing to inadequate nutrition and low energy, which further decreases the ability of a child to do PA [3]. 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 fitness [3]. Pain is also common at this time. Pain should never be ignored. A pain rating scale (refer to *Appendix D*) should be used to monitor pain during PA. If pain increases during PA, immediately stop and consult with the oncologist

- ✓ Graft versus host disease

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 has an inflammatory effect, children with GVHD present an increased systematic inflammation that may reduce their ability of skeletal muscle to produce energy [3]. This may contribute to decreased PA, and therefore, to a poor fitness condition. An extend treatment with corticosteroid must be needed and is associated with the

development of osteoporosis. See *Chapter 5* to see more recommendations about chronic GVHD and PA.

✓ Immune recovery delayed – increased risk of infections

Infections remain a main cause of morbidity and mortality in patients undergoing HSCT [26]. From conditioning to engraftment, neutropenia and disruption of anatomical barriers are the most important risk factors [27]. In autologous HSCT, the risk of infection decreases significantly after neutrophil engraftment. Refer to *Chapter 5* for recommendations and precautions for PA in immunocompromised patients.

✓ Cardiac and pulmonary damage

Cardiotoxicity is common side effect of the administration of anthracyclines, a common chemotherapeutic agent administered as part of the conditioning regimen. The use of this agent 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, and sometimes may lead to early myocardial damage in children [3].

Pulmonary toxicity is common in children after HSCT, and usually presents as increased **pulmonary 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.

✓ Anemia

Anemia is a decrease in the red blood cells that impacts the ability to transport oxygen, thereby, leading 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.

Lessons Learned From Research

Physical activity and graft versus host disease

Acute GVHD can lead to damage of the skin, lungs, and the gastrointestinal tract; while, with chronic GVHD, all organs are vulnerable to damage [30]. GVHD can be extremely debilitating and lead to a poor health state, decreasing QOL and physical functioning [30]. Regular PA at a

moderate intensity may decrease systematic inflammation and improve immune function [31]. Specifically, PA increased survival rate, diminished total clinical severity scores, and improved physical fitness in mice models. This result must be carefully interpreted, but suggests that PA may be an important non-pharmacological therapy to improve the disease course and QOL in these patients, without altering an already depressed immune system [30].

Physical activity as cancer prevention

In adult populations, the incidence of several types of cancer may be reduced by regular PA [32]. Research suggests PA has a therapeutic effect in cancer patients, by reducing cancer recurrence, enhancing health outcomes, and increasing survival [32,33]. There is a hypothesis in adult populations affected by cancer that, PA-mediated changes in immunity may contribute to a faster immune system recovery after HSCT [34-36]. A faster immune system recovery might be a key factor in order to decrease risk of infection after HSCT.

When is a child able to start physical activity during the HSCT?

PA is recognized as being beneficial during treatment, since prolonged bed rest leads to lost of muscle and strength, and aggravates the already low **aerobic capacity** induced by the immunosuppressive therapy given to children treated with HSCT [38].

Performing mild to moderate PA from the conditioning phase to engraftment phase was hypothesized to be beneficial. To test this, Chamorro et al., [8] performed a study during the conditioning and neutropenic phase of HSCT in children. This study showed that a moderate and individualized PA program was feasible, safe, and did not alter immunological recovery. The authors also found the intervention group was able to increase the time spent in the aerobic training, and the amount of resistance used in the strength training by the end of the intervention. That means, in some way, children maintain or improve their fitness condition during HSCT hospitalization period. That is very important, because during hospitalization, children tend to display a decrease in their fitness condition. Rosenhagen et al.,[10] conducted a similar study and corroborated these findings. Refer to *Table 8.2* for a summary of the interventions.

Table 8.2. Physical activity interventions performed in children undergoing HSCT.

Author/Study Design	Population	Intervention	Result
San Juan et al. [9]	HSCT post-transplant phase of treatment	• **Duration:** 8 wk. Supervised in-hospital intervention. • **Frequency:** 3/wk; 90 min. • **PRT:** 1 set, 8-15 repetitions, of 11 types of exercise engaging the major muscle groups). 1-2 minute 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 low intensity (50% of age predicted HRmax), to 30 min at moderate intensity (≥70 % HR max).	Aerobic capacity was lower in HSCT patients than in CG. IG: ↑ aerobic capacity and strength.
Chamorro-Viña et al. [8]	HSCT in neutropenic phase	• **Duration:** From the beginning of conditioning regimen until neutrophil engraftment (~30 days). Supervised in-hospital intervention. • **Frequency:** 5/wk; 50 min (5/wk aerobic training + 2/wk strength training). • **PRT:** 1 set, 8-15 repetitions, of 6-10 types of exercise engaging the major muscle groups. 1-2 min rest period between exercises, with stretching of the muscles involved in the last exercise**.** • **Aerobic training:** Ranged from 10 to 40 min, depending on child status. Intensity controlled by heart rate monitor between low to moderate (50%- 70% of age predicted HR max).	IG: ↑ BMI and weight. ↑ muscle mass and body fat. ↑ Aerobic fitness and strength. CG: ↔ BMI, body fat, and weight with a trend to decrease.
Rosenhagen et al. [10]	HSCT in neutropenic phase of treatment	• **Duration:** Approximately 34 days supervised intervention during the isolation phase of HSCT. In –hospital intervention. • **Frequency:** 3/wk; approximately 50 min. • **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 with a minimal resistance of 6 watts for a minimum of 10 min. The resistance of the bicycle was increased in the next class only if participant reached 10 min. Intensity of training: Heart rate should not exceed age predicted maximum HR [180- patient age]; and breathing frequency has to be below 35 breaths per minute. Participant trained for a median of 18 minutes.	IG: 10% ↑ in the time spent on the bicycle. ↔ Strength assessed by grip strength. CG: not reported. Regular PA during isolation phase of HSCT is feasible, safe, and counteracts the side effects of immobilization, such as muscle mass lost.

Note. PRT: progressive resistance training; N: number of participant; IG: intervention group; CG: control group; BMI: body mass index; HSCT: hematopoietic stem cell transplantation; yr: year(s); wk: week(s); min: minute(s); ↔: maintain/ no change; ↓: decrease; ↑: increase/improve.

Physical activity improves health related 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 of the patients after the PA intervention. Chamorro et al., [8] have shown that training induces gains in body mass and body mass index over the hospitalization period [8]. During the neutropenic phase, a decrease in body mass index is a common side effect, and is associated with a negative HSCT outcome. Maintenance of skeletal muscle proteins is crucial in immunocompromised children [39]. Avoiding losses in body mass during pediatric HSCT is important, because children undergoing this treatment are a particular risk of malnutrition [40].

This evidence, with the extrapolated results from the adult population studies, suggests that recipients of HSCT may benefit from PA [11]. No harmful effects were reported from the PA interventions [6,11,33,41]. However, due to small sample size and other limitations, more research is needed to generalize the benefits of PA in pediatric HSCT patients.

Balance training at the PEER program.

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 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 [18]. Wearing a heart rate monitor or using rating perceived exertion scale (RPE) scales (refer *to Appendix E*) may help allied health care professionals control the intensity of aerobic training better.

- ✓ **Early post-transplant phase**: is the time between infusion up to 100 days post-transplant.
- ✓ **Later post-transplant phase**: is the time over 100 days post-transplant.

Table 8.3. Physical activity recommendations for children undergoing HSCT.

	Recommendations
Objectives of PA	**Conditioning, neutropenic, or early post-transplant phase**: Maintain the patient's capacity to perform activities of daily living. **Later post-transplant phase**: Enhance the patient's health-related fitness enabling him/her to engage in PA with his/her healthy peers, without undue fatigue [16].
Aerobic capacity	**Frequency:** At least 3 days/week. Preferably most days of the week. **Intensity:** • Conditioning and neutropenic phase: Low to moderate in order to avoid fatigue and compromised immune system. If use HR to control intensity, HR should be between 50-70% of age predicted maximum HR. • Post-transplant phase: Start with low to moderate. If patient is not immunocompromised, he/she can slowly progress to vigorous. **Time:** 10-40 min, as tolerable without fatigue. **Type:** Any activity that your child enjoys. Dancing, riding a bike, playing sports, or active video games. If a child is immunocompromised, some activities might be discouraged by his/her physician, such as swimming or sports in groups. Also, some precautions should be taken if child has other comorbid conditions, such as graft versus host disease, anemia, thrombocytopenia, osteoporosis, and/or risk of cardiotoxicity. Refer to *Chapter 5* to find some recommendations and precautions to PA in those cases.
Progressive resistance training	**Frequency:** At least 2 days/week. **Intensity:**

	• 1-2 sets, 8-15 repetitions. • 1-2 min rest between exercises, stretching the muscles worked. **Type:** Perform 6-10 exercises engaging the major muscle groups. Alternate between upper and lower body muscles groups and core.
Fundamental skills	It 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 designed for their healthy peers.
Considerations	• Due to large variability of comorbid conditions associated with HSCT, PA has to be individualized for each child undergoing HSCT. • 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's preferences. • Physician clearance is always needed. • A supervised PA program is preferable when starting.

Note. PA: physical activity; min: minutes; HR: heart rate.

In summary, although research in this field is scarce, it has been demonstrated that PA is both safe and feasible in immunocompromised patients undergoing HSCT. 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.

Take Home Message

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

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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 treatments of solid tumors in children.
- ✓ …potential side effects of these treatments, and their implications for physical activity.
- ✓ …physical activity is almost always possible; however, modifications and creativity are necessary for individual adoption.

Introduction

Solid tumor is a term used to describe an abnormal mass of tissue found in different areas of the body. Solid tumors may be benign (not cancer), or malignant (cancer). Different types of solid tumors are named for the type of cells that form them. This chapter will discuss the most common types of malignant solid tumors in children.

- ✓ **Brain and other central nervous system tumors:** the most common type of solid tumor, accounting for 23% of cancerous tumors in children up to the age of 15. See *Chapter 10* for more information.
- ✓ **Neuroblastomas:** come from undeveloped nerve cells, and are mainly located in the abdomen and the adrenal medulla above the kidneys [1].
- ✓ **Nephroblastoma (Wilms tumor):** located in the kidneys [2].
- ✓ **Soft tissue sarcomas:** form in muscles, vessels, and nerves. For example, rhabdomyosarcoma arises from muscle, and is the most common soft tissue sarcoma in childhood [3].
- ✓ **Malignant** bone tumors: Osteosarcoma and Ewing's sarcoma are the two main types of bone cancers in the pediatric population.

  i) Osteosarcomas*:* are the most common malignant bone tumors, usually they occur in areas of the bone that grow quickly. Most commonly, they are found around the knee [4,5].

ii) Ewing's sarcomas*:* start from premature nerve cells within bone or soft tissue. Ewing's sarcoma usually appears in the large bones of the arms and legs, and the flat bones of the pelvis, spine and ribs [5,6].

Potential Treatment Side Effects and Implications for Physical Activity

Apart from side effects resulting from chemotherapy and radiotherapy, side effects from surgeries are expected. These additional side effects can further influence your child's ability to do **physical activities (PA)** and **activities of daily living.**

In most cases, muscle tissue has been removed, and some nerves may be damaged or removed. This can result in several limitations including, loss of muscle strength, reduced range of motion, decreased coordination, and gait abnormalities [7-10]. Because of these limitations, PA will be more exhausting for a child affected by a solid tumor than for healthy peers. For example, walking with **prosthesis** requires greater exertion [11] than walking without it. Also, the resection of some muscle tissue will impact the control of certain movements.

PA for patients with solid tumors is also more challenging because immediately after surgery survivors might have instructions to i) use aids like crutches or a wheelchair for several weeks, and ii) limit weight bearing in order to promote healing of the area affected by surgery. This may limit the options they have to participate in PA, and requires PA to be adapted.

Tips to perform PA in patients with solid tumors:

- ✓ Reduced risk of falls
- ✓ Being familiar with surgical procedure
- ✓ Adapt PA to special needs of participants

Physical Activity and Bone Tumor Research Summary

In the limited research to date, PA has positive effects on sleep, upper body muscle strength, and flexibility [13,14]. Also, PA may benefit heart and lung health, physical functioning, well-being, and fatigue [14-17]. Benefits have been seen from both supervised and home-based PA programs, but supervised programs appear to have a greater effect [18,19] [15].

Physical Activity Recommendations

In general, PA is possible for every child with a solid tumor during almost every stage of treatment. PA should be tailored to the child's well-being and any possible restrictions from treatment. *Table 9.1* summarizes PA recommendations for children affected by a solid tumor.

Muscular endurance: the ability of a muscle or group of muscles to work continuously/for a long time without tiring. To increase your muscular endurance, we recommend working with light weight and doing 15-30 repetitions.

Table 9.1. *Physical activity recommendations for children affected by a solid tumor.*

Physical Activity Recommendation	
Warm up	✓ Every PA session should start with 10-15 min of warm up in order to prepare the body. ✓ The intensity of the warm up should be low at the beginning, and slowly progress to a moderate intensity. ✓ Walking, cross trainer/elliptical. ✓ Cycling* or hand bikes for children with reduced range of motion in their knee joint.
Aerobic Training	✓ Start with 10-15 min and slowly build up to 30 min. ✓ This training will help your child improve the health of his/her heart, lungs and vascular system, and might help decrease fatigue when exercising. ✓ Whatever activities the child enjoys and performs well during warm up, can be done as part of the aerobic training part of the session. ✓ Think of activities that a child can incorporate in their everyday routine, such as walking and cycling. These are good options for a home-based PA program. ✓ Water programs are good options for children with a bone tumor, because body weight is reduced and limbs can move easier. ✓ Precautions should be taken if your child is immunocompromised, or the wound is not completely healed.

Progressive Resistance Training	✓ Will aid your child in regaining muscle size, strength, function, joint range of motion, as well as bone mass [20,21]. ✓ Perform a whole body program including the most important muscle groups. ✓ Do 8-10 exercises, twice a week. ✓ Intensity (**loads and repetitions**) should be decided individually according to your child's needs. ✓ Back and abdominal exercises are important to prevent deformities of the spine, such as **scoliosis,** that might happen from leg length discrepancies in patients affected with tumors in the lower extremities [22]. ✓ Can either be done on resistance machines, with dumbbells, elastic bands, or using only bodyweight itself.
Coordination training	✓ Might help your child to function confidently in their limbs again, which might feel completely different from before treatment. ✓ Helps muscles and joints work smoothly and accurately. ✓ Include in daily PA. ✓ Wobble boards and active balance computer games may be effective, because they distract the child from the feeling of putting too much weight on the limb.
Flexibility training	✓ An individually adapted stretching program helps to reduce range of motion limitations [23 24]. ✓ Include in daily PA.
Cool down	✓ The objective of the cool down will be returning your child's body and mind to resting levels. ✓ Different options can be explored to discover what works best. ✓ Some options include playing quiet games, relaxation, or reading a story.

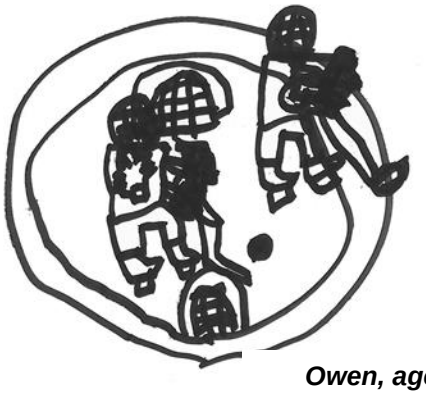
Note. *Cycling might be difficult due to limited range of motion in the knee joint in those children affected by osteosarcoma. Check with your child's physician or surgeon before doing it. Min: minutes.

When starting PA, it may be best for the session to be supervised by an exercise or rehab specialist. Once comfortable, the child can participate in a home–based or community-based program. It is very important to continue to check 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.

Patients and survivors of solid tumors ideally will participate in 60 minutes of PA each day; however, they should start with shorter bouts of activity and build up their endurance. See *Chapter 5* for more recommendations and precautions when participating in PA.

Additional Resources:

- ✓ Punzalan M, Hyden G. The role of physical therapy and occupational therapy in the rehabilitation of pediatric and adolescent patients with osteosarcoma. Cancer treatment and research. 2009; 152: 367-384.
- ✓ Winter CC, Muller C, Hardes J, Gosheger G, Boos J, Rosenbaum D. The effect of individualized exercise interventions during treatment in pediatric patients with a malignant bone tumor. Support Care Cancer. Jun 2013; 21(6): 1629-1636.



Owen, age 5

Take Home Message

Patients and survivors with cancerous solid tumors have unique needs. They have to be looked after with special attention and patience. Some forms of physical activity will almost always be possible in this group. The greatest limitations result from the effects of surgery. Physical activity programs should be adapted after speaking to the surgeons and physiotherapist who care for the child. 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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Chapter 10

Physical Activity and Late Effects of Treatment for Childhood Brain Cancer

Iman Sahnoune, PhD Student & J. Leigh Leasure, PhD

Learning Objectives

After completing this chapter you will know about:

- ✓ …childhood brain cancer and the long-term effects of treatments.
- ✓ …childhood brain cancer survivors' brain function, sense of self-confidence, and well-being.
- ✓ …the role of physical activity in enhancing brain function.

Introduction

Cancer in the central nervous system is the most common solid tumor in children and the second most common childhood cancer after leukemia [1,2]. A **central nervous system tumor** is a mass that is formed when normal cells in the brain or spinal cord change, and grow uncontrollably. Brain tumors can be low grade (generally noncancerous and slower growing) or high grade (likely to grow and spread quickly). In general, tumors that begin growing in the brain (i.e., primary brain tumor) do not spread outside of the central nervous system.

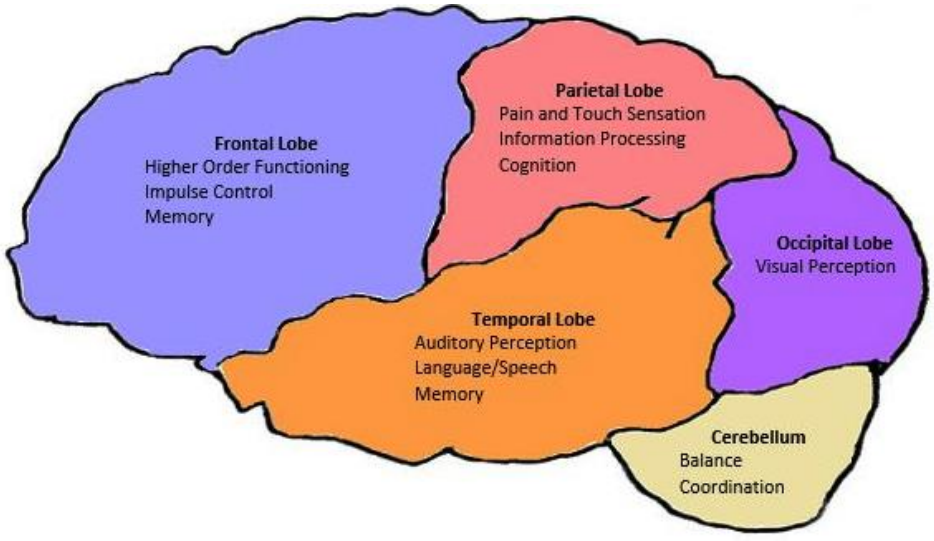
Cognitive function is the ability (or lack of) to think, learn, and memorize.

Fortunately, with the advancement of novel technologies and treatment methods, survival rates exceed 70% across children and young adults [1-3]. Although survival rates are increasing, a child's sense of self-confidence, well-being, and social life can be detrimentally affected. It is

reported that 40 to 100% of childhood brain tumor survivors experience a myriad of cognitive side effects, such as decreased attention and memory, along with difficulties learning and making decisions. These effects can emerge months after treatment [1,4,5], but more frequently 3-5 years after treatment [5], in which case they are called late-effects.

The impact of a tumor is based on its type, location in the brain, size, stage of development, and amount and type of treatment received. Because of the vulnerability of the developing brain, the younger the child, the greater the long-term damage [1,4,5]. Also, girls are more affected than boys [6,7]. Tumor size and location are major factors to determine the extent of these side effects [2,8]. For example, tumors in the left hemisphere are the most likely to result in cognitive impairment (refer to *Figure 10.1* for a visual representation of the brain) [4]. Finally, the amount of radiation given to your child has a major impact on cognitive function [4].

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, chemotherapy, or a combination of these. Because of several problems associated with cranial radiotherapy, it is generally used for, but not limited to, tumors that cannot be surgically removed. Cranial radiotherapy works by killing cells that divide quickly, including tumor cells. Nerve cells (i.e., neurons) are not damaged, because they do not divide, but cranial radiotherapy attacks the cells responsible for supporting nerve health and function [9-11]. Cranial radiotherapy also affects the process by which new nerve cells are generated in the hippocampus (i.e., hippocampal neurogenesis). After cancer treatment, hippocampal neurogenesis is severely decreased, which likely contributes to the cognitive impairment seen in survivors [9,12,13].

The hippocampus is a brain region important for memory, emotion, and spatial navigation. This is represented in blue in the figure below.

Brain tumors and treatments also affect a wide range of cognitive functions, including memory, problem solving, thought processing, attention, ability to read, speak and understand, and **visuo-spatial abilities** [8,9]. These may contribute to a reduced **intellectual quotient** score, commonly found in children affected by brain cancer [10-14]. The sharp decrease in attention makes children affected by a brain tumor less able to learn at the same pace as their healthy peers. Therefore, the decrease in brain functioning in children recovering from brain tumors is not necessarily because of a loss of knowledge, but rather due to a decreased pace of learning [5,7]. This suggests more time may be required for children recovering from brain tumors to catch up to their peers in the classroom [9].

Examples of **visuo-spatial abilities**:

- ✓ Body awareness
- ✓ Coordination
- ✓ Awareness of surrounding environment

The late-effects of childhood brain tumors are long lasting and can severely impact a child's sense of self-confidence, well-being, and relationships with others after diagnosis. This increases the importance of a treatment that can combat these negative side effects.

To summarize, although childhood brain cancer survival rates are increasing, it is important to remember that these treatments have detrimental side effects. Development of an effective intervention to combat these side effects is absolutely necessary. We will focus on **physical activity (PA)** as a potential intervention to improve, or diminish treatment side effects.

Treatment Effects and Their Implications for Physical Activity

The brain functions include:

- ✓ Thought
- ✓ Regulate actions
- ✓ Regulate basic vital functions (e.g., blood pressure, breathing)
- ✓ Regulate and coordinate movement
- ✓ Balance
- ✓ Posture

Most of the benefits presented in this chapter have been extrapolated from research conducted in animal models (in which scientists model in animals what happens in the brains of children affected by cancer), or children without cancer, as we do not yet have sufficient information regarding the benefits of PA in children affected by cancer. It is known that PA increases hippocampal neurogenesis and blood irrigation of the brain [15-19], therefore, this effect might directly counteract the negative side effects of cancer treatment [15-19]. Additionally, PA enhances brain functions associated with neuroplasticity [20,21] and executive function [22], which are usually damaged in children affected by a brain tumor.

- ✓ **Neuroplasticity** is the brain's ability to reorganize itself by forming new neural connections throughout life. Neuroplasticity allows the neurons in the brain to compensate for injury and disease.
- ✓ **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.

Strong research evidence shows that PA, especially aerobic activities, have a positive impact on a child's academic achievement [23]. Importantly, the greatest benefits from PA are seen in the elementary-age kids, and then benefits decrease as they get older. PA can be introduced to school-age children as a therapy, and the program should be adapted as the children get older to enhance the potential benefits. Children lowest in working memory and cognitive function tend to

gain more from PA than higher functioning children and youth [24]. PA may alleviate the harmful effects of brain cancer and its treatment; however, more research is needed to confirm all these benefits in children affected by a brain tumor. Additionally, PA can counteract other side effects, such as muscular weakness and shortness of breath, and improve heart and lung function [25]. PA may also help to decrease depression, anxiety, and other emotional problems. Unfortunately, survivors of pediatric cancer are more prone to be inactive through childhood and into adulthood, due to treatment related side effects [26-28]. We need to double our efforts in order to motivate these children to be active.

Working memory is the part of short-term memory that is concerned with immediate conscious, perceptual, and linguistic processing.

Additional Resources:

- ✓ Rodgers SP, Trevino M, Zawaski JA, Gaber MW, Leasure JL. Neurogenesis, exercise, and cognitive late effects of pediatric radiotherapy. *Neural Plast.* 2013; 2013: 698528.
- ✓ Fedewa AL, Ahn S. The effects of physical activity and physical fitness on children's achievement and cognitive outcomes: A meta-analysis. *Res Q Exerc Sport*. 2011; 82(3): 521-535.

Take Home Message

The long-term effects of treatment for childhood brain tumors can be devastating. There are no effective therapies to combat these effects as well as, lowered sense of self-confidence, well-being, and social life. Physical activity is a promising, inexpensive, and accessible option to promote brain health and reduce the late-effects of treatment.

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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:

- ✓ …the many terms used when discussing non-curative cancer care.
- ✓ …the specific benefits of physical activity for this group.
- ✓ …what to consider when participating in physical activity.

Introduction

Non-curative cancer, also known as **advanced cancer or terminal cancer**, is a type of cancer that cannot yet be cured [1,2]. Terms referring to different stages in non-curative cancer are, **survival length** (e.g., time of diagnosis until death), or **end-of-life** (last and final stage of the cancer continuum) [3,4]. During these stages of treatment, there are medical professionals that help manage pain and symptoms. This type of care is known as palliative cancer care. The World Health Organization describes **palliative care** as, the treatment of pain and any physical, mental, and emotional factors experienced by both the child and family to improve their **quality of life (QOL)** [2].

Quality of life (QOL) is a person's sense of how his or her life is, when compared to his or her goals and expectations.
What affects someone's QOL?

- Physical health
- Emotional and mental state
- Independence
- Family, friends, and other social relationships

The absence of disease does not relate to a high QOL. With the right steps, children and teenagers can have a high QOL, even with the impact of the symptoms of the disease.

Rationale for Physical Activity and Non-Curative Cancer Care

As there is a lack of information on the effects of **physical activity (PA)** for the children, **adolescents and young-adults (AYA)** with non-curative cancer, we have based the recommendations made in this chapter on information that is emerging from the adult population.

Medical advancements have extended the life of those diagnosed with non-curable cancer [4]. PA has helped adults diagnosed with non-curative cancer to maintain their ability to do **activities of daily living** for longer. PA lessens symptoms related to the disease (e.g., nausea, fatigue, shortness of breath, muscle wasting), and improves QOL [5,6]. We want children to benefit from PA and experience similar symptom relief. PA could help them reach a fitness level that will give them energy to enjoy daily activities, such as playing sports with their friends.
The following sections of this chapter will highlight: the benefits of PA for non-curative cancer patients, what types of PA are useful for non-curative cancer patients, and suggestions as to how PA programs can be delivered.

Benefits of Physical Activity for Non-Curative Cancers

Patients diagnosed with non-curative cancer can participate in PA. It is both safe and beneficial. See a summary of the benefits in *Table 11.1.*

Table 11.1. Benefits of adult non-curative cancer patient's participation in physical activity.

Physical Benefits	Psychosocial Benefits
✓ Reduces nausea ✓ Improves sleep ✓ Reduces the sensation of shortness of breath ✓ Reduces tiredness associated with **cancer-related fatigue** ✓ Reduces pain ✓ Maintains the capacity to do activities of daily living ✓ Stimulates appetite	✓ Maintains self-esteem and independence ✓ Provides sense of wellness ✓ Gives sense of body control ✓ Provides distraction from disease ✓ Decreases sense of burden on family ✓ Maintains cognitive (i.e., thinking ability) and social functioning ✓ Increases positive mood ✓ Improves QOL

Note. Compiled from [4,6-10]. QOL: Quality of life.

Types of Physical Activities for Non-Curative Cancer

The table below provides a list of PA preferences of cancer patients of different ages.

Table 11.2. Preferred types of physical activity.

Adults	Adolescents and Young Adults	Children
✓ Walking ✓ Cycling ✓ Yoga	✓ Activities that provide social interaction ✓ Offer support from friends ✓ Technology based	✓ Still unknown

Note. Compiled from [11-13].

Physical Activity Recommendations for Non-Curative Cancer

The overall objective of incorporating PA into this population's lifestyle is to maintain, and improve QOL. *The best PA for people with non-curative cancer is one that is designed specifically for them.* It needs to consider their treatment and their fatigue levels. Researchers have not yet learned exactly how often they should be physically active each week, and how hard and how long they should work to see the maximal benefits. For this reason, we recommend that all PA programs are started slowly and fatigue levels are watched closely, because we do know that safe and tolerable PA is better than none at all. We want these children and AYA to maintain a fitness level that will allow them to do activities of daily living for as long as possible, and bring normalcy into their life [12].

PA for children, teenagers, and young adults needs to be designed for their ages and maturity levels. We also recommend activities that can be done at home, because:

- ✓ Home is a familiar and comfortable space.
- ✓ It is a chance to do something fun with their friends and family.
- ✓ It reduces costs and travel time, and therefore, barriers to being active.

Additional Resources:

- ✓ Lowe SS, Watanabe SM, Courneya KS. Physical activity as a supportive care intervention in palliative cancer patients: a systematic review. J Support Oncol 2009; 7(1): 27-34 [11].
- ✓ Woodside HM, Keats MR. Exploring the role of physical activity during palliative care for adolescent and young adult cancer patients. JAYAO, 2013, 2(1):35-37 [14].

Take Home Message

Because physical activity has been shown to be a beneficial therapy with positive results for adults with non-curative cancer, we think it is very important to explore this further with children and teenagers. Adults, role models, and parents need to encourage children and adolescents and young adults to be active, because they might feel similar benefits.

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Chapter 12

Yoga in Childhood Cancer

Amanda Wurz, PhD candidate; Robyn Long, BA/MA; Tyla Arnason, Yoga Instructor; Carolina Chamorro-Viña, PhD & S. Nicole Culos-Reed, PhD

Learning Objectives

After completing this chapter you will know:

- ✓ …the current literature on yoga for childhood cancer patients and survivors.
- ✓ …the possible benefits of yoga for this population.
- ✓ …what to consider when developing a yoga program for childhood cancer patients and survivors.

Introduction

Modified yoga programs have become popular in adult cancer patients and survivors [1-4]. Yoga is a form of gentle **physical activity** (**PA**) that combines postures (*asana*), breathing exercises (*pranayama*), and meditation (*dhyana*) [4,5]. Research on yoga programs for adults with cancer [1,2], as well as, reviews of yoga programs for children with chronic illnesses [6] draw attention to a range of benefits including physical, mental, emotional, and social. Although the evidence is new, research suggests that yoga may be a beneficial form of PA for childhood cancer patients and survivors.

Sanskrit is the language in which the philosophy of yoga was originally written. In this chapter, the Sanskrit names are italicized in parentheses after the English names.

Yoga Benefits: Research Findings

Table 14.1 gives an overview of the four studies that have researched yoga in pediatric oncology/hematology populations. This body of work overall supports the value of yoga in this population, with improvements seen on physical well-being, engagement in **activities of daily living**, decreased aches, pain and increased energy, and better emotional and social function.

Yoga appears to be a practical intervention that promotes relaxation and may also increase engagement in other types of PA.

Table 12.1. Summary of yoga in pediatric oncology.

Authors	Sample	Intervention	Findings/Conclusions
Geyer et al. [7]	6 children with cancer	1 (BKY) session/week for 5 weeks; (60 minutes/session).	Improved child perception of physical function.
Moody et al. [8]	20 children with cancer or hematological diseases	1-3 individualized yoga sessions (duration not specified).	Improved pain and anxiety scores. Patient quotes suggest yoga was beneficial for relaxation.
Thygeson et al.[9]	16 children with cancer or hematological diseases	1 group yoga session (45 minutes/session).	Improved anxiety. Improved general wellbeing.
Wurz et al. [10]	8 children with cancer	12 week program; 2 group yoga sessions/week (60 minutes/session).	Feasible intervention. Improved children wellbeing as reported by children and their parents. Improved hamstring flexibility. Improved functional mobility. Improved PA levels.

Note. BKY: Bendy Kids Yoga; PA: physical activity.

Currently, these are the only published studies exploring the benefits of yoga for childhood cancer patients and survivors. More research is needed to understand specific benefits offered by yoga for different cancer groups. Research has found improvements in strength, aerobic capacity, physical function, and psychological function in adults with cancer [4], as well as, in other clinical pediatric groups [6,11].

Yoga: Practical Recommendations

Currently, there are no guidelines for creating a yoga program specific to the needs of childhood cancer patients and survivors. However, based on our experience with a 12-week community yoga program [10], individual changes within a structured yoga class can be made, based on the individual's cancer diagnosis and any treatment-related side effects.

Therapeutic modifications

Below is a list of modifications that the authors have found to be appropriate when teaching yoga to childhood cancer patients and survivors through the Yoga Thrive for Youth program (refer to *Appendix 12.A* for more information). An example of a general class plan is in *Appendix 12.B,* and images of the poses described below can be seen in *Appendix 12.C.* Prior to starting in any yoga program, each child should be cleared for PA by their physician, and any concerns that may limit his or her activity should be clearly communicated to the yoga instructor.

- ✓ *Balance:* Children with cancer may experience dizziness, peripheral neuropathy, or a lack of balance due to the cancer and its treatments. Using a wall, chair, or floor to modify poses can help promote stability. For example, if a child feels off-balance, he or she may do Tree Pose (*Vrksasana*) while holding onto the back of a chair, or by placing one hand against the wall for support (refer to *Appendix 12.C* for image).

Tree pose *(Vrksasana)* lifted, externally rotated and their foot resting on the inside of the calf or thigh.

- ✓ *Weight bearing:* Children with bone tumors (pre and post-surgery) may not be able to place weight on one or both legs for long periods of time. Similarly, children who have dorsiflexion-range of motion issues may have difficulty rooting down through both of their feet. In these cases, using 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 pose such as Crescent Moon (*Alanasana*) (high lunge), with the thigh of the affected limb placed on the seat of a chair for support.

- ✓ *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 that children are able to rest throughout a yoga class. For example, they can 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 12.C* for images).

- ✓ *Immobility:* If the range of motion of any joint is affected by peripheral neuropathy or surgery, the yoga instructor should suggest modifications and instruct participants to move within their range of motion without causing pain.
- ✓ *Pain:* Do poses slowly with the breath, and/or hold the poses for a shorter period of time. It is important that yoga and PA does not cause any pain. If the child experiences pain, he or she should stop doing yoga and talk to a doctor.
- ✓ *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 12.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 can provide children with mental, emotional, social, and physical benefits. Children can experience these benefits through a number of group or individual activities. These are a few examples taken from the authors experience in yoga research [10] and the community Yoga Thrive for Youth program.

- ✓ Breathing: Focusing on breathing during yoga poses can help with children's attention and energy during class. Specific breathing exercises may also help participants learn relaxation techniques. For example, in the authors' 12-week yoga intervention, we found Balanced Breath, Elongated Exhalation, and Peace Breath to be helpful breathing exercises (see explanation in boxes below). Breathing exercises should always be tailored to the unique needs of each participant, and they should be taught how to keep a steady and relaxed breath.

Balanced Breath
Inhale and exhale equal counts. Focus on the belly expanding on inhale, and falling back on exhale. Can be performed sitting, laying, or standing.

Elongated Exhalation
Inhale focusing on the belly expanding and exhale longer (than the inhale) with belly contracting. Can be performed sitting, laying, or standing.

Peace Breath
Inhale through the nostrils, and exhale softly saying peace (or any other word). Should be performed seated.

- ✓ *Mindfulness/focus:* Yoga offers participants a chance to focus on the present. This can be helpful, as they may experience distress or anxiety because of their cancer treatments. Ways to promote awareness in yoga include, 1) breathing exercises; 2) guided visualizations; 3) positive affirming meditations; and 4) challenging, yet safe, yoga poses (e.g., standing balances).
- ✓ *Deep relaxation:* Giving participants 10 to 15 minutes to relax at the end of class is important. Relaxation can help slow down their heart rate and breathing, which allows the participants to fully experience the benefits of their practice. Participants should lie flat on their backs in final Relaxation Pose/Savasana and be guided into relaxation or meditation by the instructor. Using props (i.e., bolsters under the knees) to make the pose more comfortable may help with relaxation. Providing participants with blankets will keep them warm and help them feel relaxed. Playing gentle music, and/or encouraging them to focus on their breath during relaxation can also help participants stay focused.
- ✓ *Fun:* As with all PA, children are more likely to participate in yoga if they find it fun. In a group class setting, doing poses with a partner, or in a group circle can create a playful environment.

Areas of Caution

In addition to the PA precautions for patients and survivors experiencing side effects (refer to *Chapter 5*), there are a few precautions to take when doing yoga.

- ✓ *Inversions:* Instructors should use caution with inversions, especially poses that may put extreme pressure on the head. Modifying the pose, such as the Legs Up the Wall (*Viparita Karani*) variation (lying down with legs up the wall), may be better for patients and survivors because there is no pressure directly on the head.
- ✓ *Weight bearing:* Participants at risk of fractures, or who have recently had surgery for a bone tumor diagnosis, should not perform any weight bearing activity that has not been

approved by their treating physician. All weight bearing poses should be modified, for example, by performing poses seated or by using props, such as chairs.

- ✓ *Balancing poses:* Participants at risk of fractures (e.g., children with bone tumors or osteoporosis) should be given the option to place their hands on a chair for support to help with stability, and reduce the chance of falling.
- ✓ *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 or cause dizziness. To decrease the bend, participants can bring their hands to blocks or a chair instead of to the ground.
- ✓ *Pain:* Participants who are experiencing severe pain should not be advised to do yoga, similar to general PA guidelines.
- ✓ *Group size:* When working with a group, classes should be small (e.g., no more than 6 to 8 participants) depending on the physical limitations and needs of the group.

What to Look for in a Yoga Instructor

Just like instructors leading PA programs for pediatric cancer patients and survivors, a yoga instructor is part of a team with the child, their parents, and their health care providers. It is important for yoga instructors to have appropriate training and credentials. There are no governing bodies for the certification of yoga instructors. However, there are key qualifications to look for when interviewing potential yoga instructors. The instructor should have at least: a) a 200-hour yoga teaching certificate; b) certification, and/or experience teaching children; and c) certification, and/or experience teaching yoga for cancer survivors. While there are very few certifying programs in yoga for cancer survivors, a yoga instructor may have other qualifications from working with other clinical groups, such as 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 adaptations when teaching yoga to adult cancer patients and survivors (refer to *Appendix 12.A* for more information on the program). Yoga therapy is a new and growing field. Some instructors may identify themselves as yoga therapists if they have completed advanced training, such as one or more programs in addition to their 200-hour teaching certificate. Yoga therapists may have more experience teaching clinical populations than yoga teachers.

Additional Resources:

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

Take Home Message

Yoga is a safe and beneficial form of physical activity for children with cancer, both during, and after treatment. Along with the benefits of physical activity, yoga may help children relax. While more research is needed, research has shown that yoga may help improve how children view their physical function, decrease pain and anxiety, and increase well-being. Future research that explains yoga's effects will help create more specific programs for children with different diagnoses and treatment. More research will also help create better strategies for offering yoga to patients and survivors.

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Appendix 12.A

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 12. 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 12.C

Yoga Poses Described in the Chapter.

Tree Pose (*Vrksasana*) (variations with the lifted foot on the opposite ankle or thigh and back against the wall).

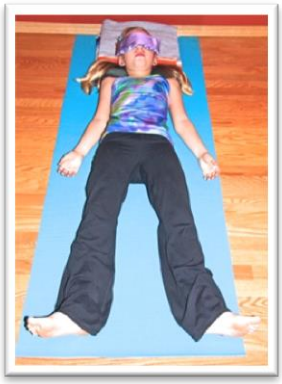

Modified Tree Pose (*Vrksasana*) (holding a chair).

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).



Chapter 13

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 of active video game play in increasing the enjoyment of physical activity, and the motivation it creates to participate in physical activity.
- ✓ …the role of active video game play in reducing inactive screen time and promoting physical activity.
- ✓ …the benefits and limitations of active video game play.

Introduction

Studies have shown that childhood cancer patients and survivors can benefit from physical activity. Therefore, there needs to be more opportunities for **patients** and **survivors** of pediatric cancer to be physically active. What we are still unsure of is *how to promote active lifestyles* in an inactive population [1-3].

Healthy youth often say they have barriers when it comes to being physically active, including not having enough time, and finding inactive activities more fun than being active (e.g., watching television, spending time on the computer, playing inactive video games) [4]. Other barriers to **physical activity (PA)** include social influences (from family, school or peers), accessibility, cost, weather, safety concerns, and the quality of play facilities [4-6]. These barriers can be even bigger for children from low-income households, whose parents might not be able to afford to send their children to organized sports/activities.

Power of Play

Overuse of technological devices has been linked to many health issues and co-morbidities, such as cardiovascular problems [13]. Guidelines say that youth should reduce their

inactive use of technology (i.e., a 2 hour daily maximum) [7]. Instead of trying to get rid of all technology, a new, popular strategy is *replacing* inactive screen time with active screen time. Games that involve being physically active are called **active video games.** These games work well for individual, group, cooperative, and competitive game play. They may also be useful in reducing inactive screen time and promoting more active lifestyles [8-10].

Cardiovascular is a term used to describe the heart and blood vessels.

There are four main reasons why active video games may be useful in promoting PA. The first and most important reason is that *while active video games cannot replace traditional exercise, such as running*, it can still provide light to moderate exercise (similar to brisk walking, skipping, or jogging). Active video games can also increase PA time, and decrease inactive screen time. Second, video games are very popular with youth, and studies show that active video games can increase positive attitudes towards being active. Using a video game to be active makes exercise more fun. This means more youth are likely to continue being active by using the game. The third reason is that many Canadian households have at least one gaming console (e.g., Xbox, PlayStation, Wii etc.). Many youth say they play video games every day. Fourth, using video games as a way to be active makes exercising easier. Those playing the active video games will be comfortable and safe in their own home. This technology might make it easier to be more physically active.

AVG Website Resources

Exergames Unlocked: www.exergamesunlocked.org

Exergame Fitness: www.exergamefitness.com

AVG Practical Recommendations

- ✓ Have a safe space with plenty of room to move while playing a multi-player game; make sure that there is enough room between players so nobody gets hurt.
- ✓ Have different types of games (e.g., dance, sport, fitness, fantasy, adventure) that are age-appropriate and based on the interests and abilities of the player(s).
- ✓ Have multi-player games that are cooperative and/or competitive (create challenges, tournaments, and leaderboards to increase motivation).
- ✓ Be a positive role model; play together (create family events/challenges, challenge physicians/nurses to a game).
- ✓ Active video games are **not** meant to replace traditional PA.

Additional Resources:

- ✓ Barnett A, Cerin E, Baranowski T. Active video games for youth: A systematic review. J Phys Act Health. 2011; 8(5): 724-737 [8].
- ✓ Biddiss E, Irwin J. Active video games to promote physical activity in children and youth: A systematic review. Arch Pediatr Adolesc Med. 2010; 164(7): 664-672 [9].

Take Home Message

Physical activity has many benefits for pediatric cancer patients and survivors. Because this population is often inactive, there needs to be a new take on physical activity. While more games need to be developed, active video games may be able to increase physical activity levels and reduce inactivity.

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Chapter 14

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 your child back into physical activity.

Introduction

The benefits of **physical activity (PA)** for all children are well-known, including positive impacts on both physical and psychosocial outcomes [1]. It is important to realize the potential benefits of PA (refer to *Chapter 2*) when considering the impact of PA on your child.

Integration of children with cancer back into PA programs within their community settings requires considerations at both the medical (i.e., physician), and family levels. 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 contraindications for PA participation, is a crucial aspect to communicate to a family considering a PA program for their child. Weiss-Kelly's article on PA prescription for childhood cancer survivors focuses on using exercise to diminish the long-term side effects of cancer treatment [2]. It is suggested that physicians evaluate the survivor's risk for long-term effects, and prescribe PA to manage and potentially prevent some of these problems. It is crucial that physicians know 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 F and G* for an example of client intake form and physician clearance form.

Information for Fitness and Physical Education Professionals

When working with children 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 help you decide what activities might be most beneficial.

Veronica, 6 years old

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, self-esteem and self-confidence for being active. Finally, encouraging activities with peers will foster social support, enhance the development of social skills, and contribute to a FUN environment for the child. This will likely 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, and between, both health and fitness/education professionals is vital to enhancing your child's PA participation. You are the link between the medical community and the fitness/sport setting your child is in. It is

important to update the fitness/education professionals of any changes in your child's health status that might impact PA participation. 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.* Having 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 patients and survivors. 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.

If you want more information you can read:

- ✓ Kelly AK. Physical activity prescription for childhood cancer survivors. Curr Sports Med Rep. 2011; 10(6): 352-359.

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

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 GI 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, nadolol, 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, isradipine, nicardipine, nifedipine, 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, thromboembolism, thrombophlebitis and vasculitis, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humoral 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, hydrochlorothiazide, 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

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Elitek	Rasburicase	Hyperuricemia secondary to chemotherapy	Nausea, vomiting, diarrhea, headache, fatigue, anxiety, mild rash, fever and swelling in hands and feet	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
Emend	Aprepitant	Nausea/Vomiting management	Nausea, vomiting, heartburn, diarrhea or constipation, loss of appetite, hiccups, hair loss, headache, dizziness, fatigue, mild rash, ringing in ears and insomnia	Passing out, very thirsty/hot, unable to urinate, heavy sweating, fever, chills and bone ache.
Erbitux	Cetuximab	Head and neck cancer	Rash, general weakness, fever and low magnesium levels	Nausea, vomiting, diarrhea, constipation, poor appetite, headache, abdominal pain, mouth sores, insomnia, shortness of breath, wheezing and swelling of facial features.
Erwinaze	Asparginase	Leukemia (ALL)	Mild nausea, vomiting diarrhea and mild stomach pain	Severe pain in upper stomach, thrombosis, hemorrhage, , fever, seizure, weakness, severe headache, pain, hyperglycemia and pancreatitis
Erythrocin	Erythromycin	Infections (Antibiotic)	Upset stomach, diarrhea, nausea, stomach pain, dry mouth, loss of appetite and constipation	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

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
	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 thrombocytopenia
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(Increase 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

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
Neulasta	Pegfilgastrim	Neutropenia associated with chemotherapy	Bone pain, pain in arms or legs, 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	Severe sudden pain in left upper stomach, sever dizziness, skin rash or flushing, rapid BR and signs of infections
Neumega	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
Neupogen	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
Nexium	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

Pantoloc	Pantoprazol	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 myalgia
	Penicillin	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
Platinol	Cisplatin	Refractory solid tumors (Inhibit DNA synthesis)	Severe nausea and vomiting, nephrotoxicity, ototoxicity, mild bone marrow toxicity, anaemia, hypomagnesaemia hypocalcaemia, hypokaliema, hyponatremia, hyperuricemia, muscle irritability, cramps, clonus, tremor and peripheral neuropathies	Vascular toxicities, anaphylactic reactions, hepatotoxicity and ocular toxicity
Rayos	Prednisone	Inflammation, immunosuppression	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	Insomnia, mood changes, personality changes, euphoria, psychotic behaviour and severe depression
Purinethol	Mercaptopurine	Leukemia (inhibit cell division)	Myelosupression, hyperuricemia and intestinal ulceration	Bone marrow toxicity, hepatotoxicity, skin rashes, alopecia, and hyperpigmentation
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

DRUG NAME	ACTIVE INGREDIENT	TARGET	PRIMARY SIDE-EFFECTS	RARE SIDE-EFFECTS
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
Oncovin	Vincristine	Various tumors	Neuropathy, temporary alopecia, decreased weight, jaw pain, bone pain, nausea, vomiting, constipation,	Pallor, easy bruising, numbness, burning, pain and tenderness in stomach, spinning sensation,

			diarrhea, fatigue and weakness	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 for Children & Youth

In this appendix a summary of the physical activity guidelines promoted by three recognize organizations are presented.

Physical Activity Guidelines for Children 5-17 years old	
"Children and adolescents should do 60 minutes (1 hour) or more of physical activity each day" this 60 minutes will have to be 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, physical activity includes play, games, sports, transportation, chores, recreation, physical education, or planned exercise, in the context of family, school, and community activities. This table was created based on the **World Health Organization (WHO)** , **Center for Disease Control and Prevention (CDC)** and **Canadian Society for Exercise Physiology (CSEP)**. See links 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

Appendix C

Infographics

The Importance of Physical Activity for Pediatric Cancer Patients and Survivors

Common Side Effects of Cancer Treatment

Fatigue

You may feel tired a lot. This might make it difficult to do basic activities, like climbing stairs.

Shortness of Breath

Sometimes, it might be hard to take a breath.

Muscle Wasting

Your muscles might seem to be getting smaller and weaker.

Sadness

You might feel alone, unhappy or even angry. You also might not feel good about yourself.

DID YOU KNOW
physical activity can help decrease these side effects.

Reasons Patients and Survivors Don't Exercise


"I don't feel like I fit in."


"My parents and doctors don't think it's a good idea."


"I don't feel supported."


"I'm too tired."

DID YOU KNOW
aerobic and strength training are safe both during and after treatment.

Why is it important to exercise?

Physical activity can help decrease the severity of the side effects of treatment and help you feel better. It can also reduce the chance of developing other conditions later on in life.

Certain treatments, such as chest radiation, drugs called anthracyclines (doxorubicin, daunomycin) and bone surgeries, require discussion with your doctor to make sure your physical activity choices are safe. Get more tips from our Pediatric Oncology Exercise Manual (POEM).

@abletothrive
www.thriveforcancersurvivors.com

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The Benefits of Physical Activity for Pediatric Cancer Patients and Survivors

Do you ever feel tired?

What about gloomy?

Did you know physical activity can help?

Physiological Benefits

- Improved body composition
- Improved heart health
- Stronger bones
- Stronger muscles
- Decreased risk of developing a chronic health condition
- Stronger immune system
- Improved flexibility
- Decreased fatigue and increased energy

DID YOU KNOW
physical activity can help you play without getting tired

Psychosocial Benefits

- Increased motivation
- Increased confidence
- Better relationships with friends
- Improved well-being

DID YOU KNOW
most cancer patients and survivors report feeling happier after exercising

Certain treatments, such as chest radiation, drugs called anthracyclines (doxorubicin, daunomycin) and bone surgeries, require discussion with your doctor to make sure your physical activity choices are safe. Get more tips from our Pediatric Oncology Exercise Manual (POEM).

@ableto thrive

www.thriveforcancersurvivors.com

Types of Exercise for Pediatric Cancer Patients and Surviviros

Aerobic Exercise

Exercises

Playing a light game of soccer, basketball or another sport

Going on a walk with the dog or friends

Tip: Start with a daily small amount of light activity and work your way up by adding time or harder activities.

Benefits

Improved body composition

Decreased fatigue

Healthy heart and lungs!

Strength Training

Exercises

Lift some light weights

Do a some sit ups, squats or push ups!

Tip: Start with 10-12 reps with none or low weight, 2-3 times per week. Work your way up to using more weight.

Benefits

Strong bones and muscles!

Yoga

Exercises

Try to touch your toes

Breath through your nose. Try to make your exhale longer than your inhale

Inhale, reach your arms over to one side, exhale, bring them back down and switch sides

Tip: If your mind starts to wander, focus on your breath!

Benefits

Helps with relaxation

Better balance!

Helps with breathing

WAIT! Only do exercises that you feel comfortable with/your doctor says are okay.

Certain treatments, such as chest radiation, drugs called anthracyclines (doxorubicin, daunomycin) and bone surgeries, require discussion with your doctor to make sure your physical activity choices are safe. Get more tips from our Pediatric Oncology Exercise Manual (POEM).

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Appendix D

Pain Scale

Pain Scale

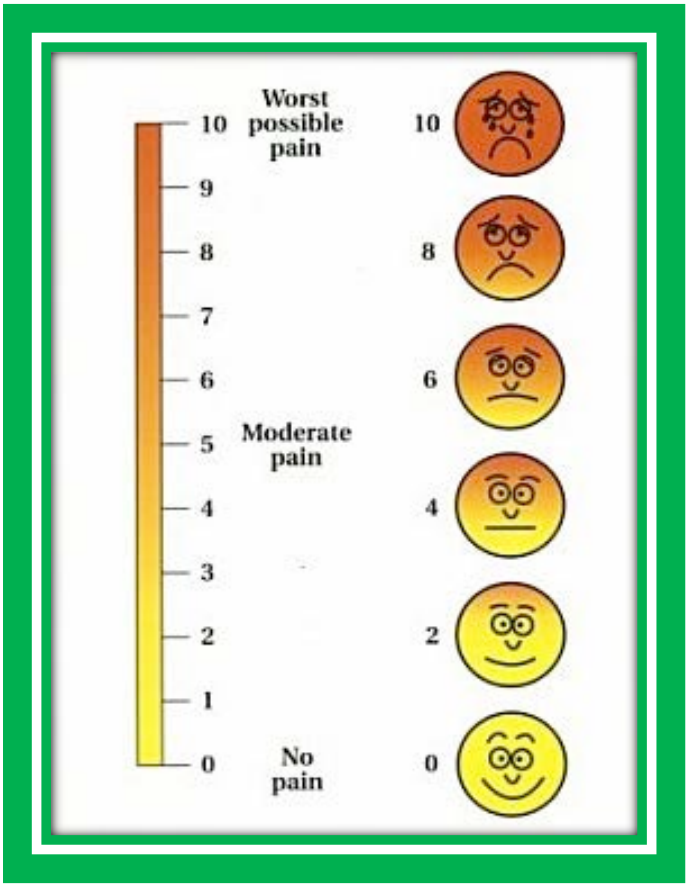
Level 1-2: Pain is present but does not impede activity.

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.

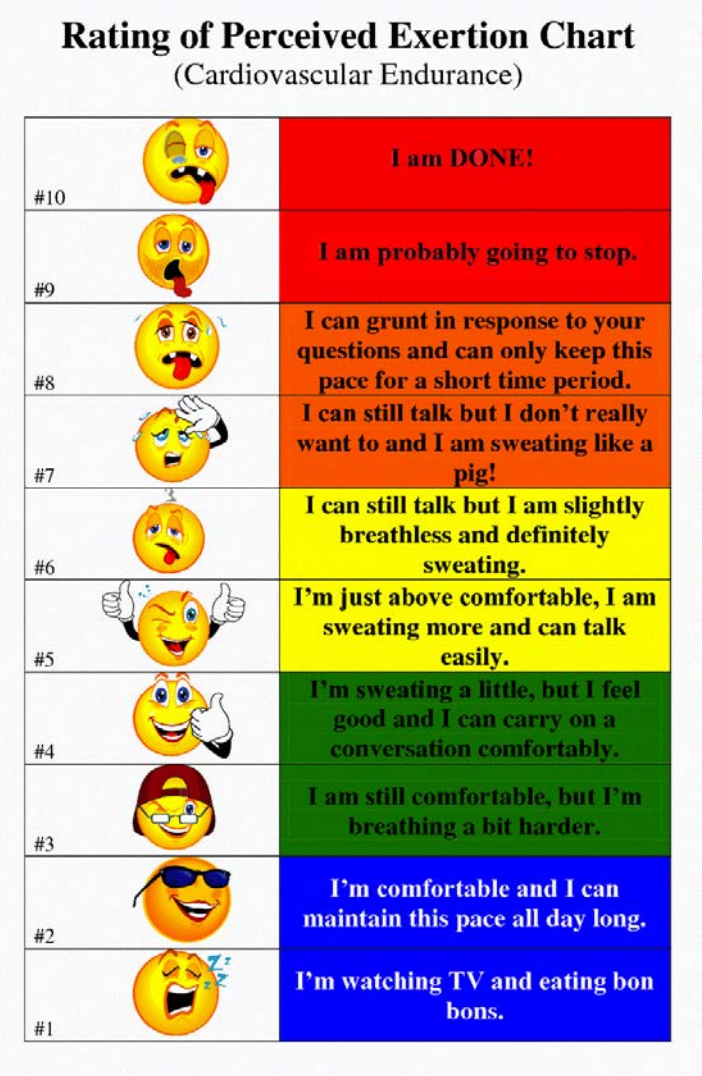
Appendix E

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



Color	Intensity
	Vigorous
	Moderate
	Mild
	Resting

Appendix F

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.

Name of Program:_____

Parents to Complete

Participant Information

Name of Participant: _____

Date of Birth: _____

Gender (select one): Male ☐ Female ☐

Home Telephone: _____

Address: _____

Mothers name: _____

Cell phone: _____

Work phone: _____

Fathers name: _____

Cell phone: _____

Work phone: _____

Medical Information
Name of Family Doctor: _____
Phone Number: _____

Name of Oncologist: _____
Phone Number: _____

Name of Surgeon: _____
Phone Number: _____

Name of Primary Nurse: _____
Phone Number: _____

Diagnosis: _____

Date of Diagnosis (dd/mm/yy): _____

Treatment status: On Treatment ☐ Off Treatment ☐
If OFF treatment, please indicate date treatment completed (dd/mm/yy):
If ON treatment, please indicate anticipated date treatment will end (dd/mm/yy):

Treatment protocol (current and/or completed):

Current side/effects/symptomatology (please tell us if your child has any pulmonary, cardiac,
metabolic, neurologic or other side effects caused or not cased by cancer and/or cancer treatment):

Please list any additional medical concerns:

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 G

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 ___Name of Patient/Survivor__ I recommend:

☐ No physical activity

☐ 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:

☐ Progressive physical activity:

☐ With avoidance of:
_____

☐ 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.

Abbreviation List

Abbreviation List

- **ALL:** acute lymphoblastic leukemia
- **AML:** acute myeloid leukemia
- **ANC:** absolute neutrophil count
- **AYA:** adolescent and young adult
- **CIPN:** chemotherapy induced peripheral neuropathy
- **CNS:** central nervous system
- **Gy:** Gray
- **GVHD:** graft vs host disease
- **HSCT:** hematopoietic stem cell transplant
- **HR:** heart rate
- **PA:** physical activity
- **PEER**: Pediatric cancer patients and survivors Engaging in Exercise for Recovery
- **PRT:** Progressive resistance training
- **QOL:** quality of life
- **RM:** repetition maximum
- **ROM:** range of motion
- **RPE:** rated perceived exertion
- **VO_2 peak:** peak oxygen consumption
- **VO_2 max:** maximal oxygen consumption

Glossary of Terms

Glossary of Terms

Absolute neutrophil count: A measure of the number of neutrophils in the blood. Neutrophils are a type of white blood cell, which help the body to 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.
Activities of daily living: Things done in normal living, including activities performed for self-care (feeding, bathing, dressing, grooming), work, homemaking, and leisure.
Active video games: 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, and 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 defined in several ways. However, there is an 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 activities: See aerobic training
Aerobic training (also known as 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 involves continuous 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 (also known as 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 (also known as maximal aerobic capacity, maximal aerobic power, VO_{2max}, and maximal oxygen uptake): Is the ability to transport and utilize oxygen. It is directly measured by VO_{2max}, which 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.
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 fine-needle aspiration biopsy..

Body composition: It quantifies 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: 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.

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.

Cardiorespiratory fitness: Refer to **maximal oxygen consumption**.

Cardio-Respiratory Endurance: Refer to **maximal oxygen consumption**.

Cardiovascular Fitness: Refer to **maximal oxygen 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 (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 defined as, a patient diagnosed with cancer between 0-18 years old.

Cognition: The mental process of knowing, thinking, learning and judging; the psychological result of perception, learning, and reasoning.

Cognitive function: Pertaining to, or characterized by cognition. The operation of the mind in 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.
Concentric contraction: The overall shortening of the muscle that 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, which 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 cause 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 the 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.
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).
Differentiation: 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.
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.
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 (also known as aerobic training): Activity focused on enhancing cardiorespiratory function.
Engraftment: In the hematopoietic stem cell transplant process; 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 x 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*.

Ewing sarcoma: A type of cancer that forms in bone or soft tissue.

Executive function: Is a set of mental processes that helps to 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**.

Exercise intolerance: Is a condition where the participants unable to do PA at the level, or for the duration, that would be expected of someone in his or her general physical condition; or, after PA experiences unusually severe pain, extreme tiredness or other negative effects

Fatigue: Refer to **cancer related fatigue**.

Flexibility: Is the range of motion around a joint

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 (also known as graft versus tumor): The donor's immune cells may recognize residual leukemia, lymphoma or cancer cells as being different and destroy them.

Graft versus tumor (GvT): See graft versus leukemia

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.

Hematopoietic stem cells: Are immature cells that can develop into all types of blood cells.

Hematopoietic Stem Cell Transplant (HSCT): Also known as a 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.

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 accepted as the best treatment. If it does not 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.
Interval training: Is simply alternating bursts of intense activity with intervals of lighter activity.
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 (also known as side effect)**:** Are those that were not apparent during primary treatment, but become apparent at some later time.
Leukopenia: A condition in which there is a lower-than-normal number of leukocytes (white blood cells) in the blood.
Loads (also known as resistance)**:** Weight lifted in a progressive resistive training.
Long-term effects (toxicities): Refer to **late effects**.
Long-term survivor: Survivors who have been cancer free for at least 5 years.
Limb sparing surgery: Also called limb-salvage surgery and limb biological reconstruction, it 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.
Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop.
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 is 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: 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 **maximal oxygen consumption**.
Maximal oxygen consumption (VO_{2max}): It is the maximum amount of O_2 that can be utilized, typically during an incremental test to exhaustion (although, if the exercise intensity is high enough, VO_{2max} may be eventually attained). VO_{2max} is normally expressed as an absolute

($L \cdot min^{-1}$) or relative ($mL \cdot kg^{-1} \cdot min^{-1}$) rate, and it reflects the cardiorespiratory physical fitness of a person. VO_{2max} 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. VO_{2max} 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.

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.

Moderate aerobic training: Requires some effort, but children can still speak easily while doing it. E.g., fast walking, riding a bike, and active play.

Nephroblastoma: Synonymous with Embryoma, or Wilms’ tumour. It is a 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. These messages are sent by a weak electrical current.

Neuroplasticity: Is the brain's ability to reorganize itself by forming new neural connections throughout life. Neuroplasticity allows the neurons in the brain to compensate for injury and disease.

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: 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 (VO_{2max}), subtract your resting oxygen consumption (found by multiplying 3.5 by your total weight in kilograms) to get your VO_2 reserve. The higher your VO_2 reserve, the more intense the exercise you are capable of doing.
Palliative care (also known as 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
Pancytopenia: Pancytopenia is a medical condition in which there is a reduction in the number of red and white blood cells, as well as platelets.
Patients: Refers to children and adolescents who are receiving active treatment for their malignancy.
Peak oxygen consumption (VO_{2peak}): 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.
Pericarditis: Happens when the sac surrounding the heart becomes irritated. This can cause chest pain.
Peripheral nervous system: Consists of nerves that connect the central nervous system (brain and spinal cord) to different organs in our body, such as the eye, ear, muscles, blood vessels, and glands.
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 (also known as 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 exercises characterized by a resisted eccentric muscle contraction, followed by a rapid concentric contraction. They are designed to increase muscular power and coordination, and are also known as stretch-shortening drills. An example would be box jumping.
Processing speed: The rate at which cognitive functioning occurs.

Progressive resistance training (PRT): An exercise regimen in which the participant progressively increases 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.
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, 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.
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.
Rales: Is defined as, an abnormal rattling sound heard when examining unhealthy lungs with a stethoscope.
Range of motion: Is a measurement of movement around a joint.
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 training, it is the maximum amount of force that can be generated in one maximal contraction.
Restrictive lung disease: A decrease in the total volume of air that the lungs are able to hold; it 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.
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 tissues of the body.
Strength: A health and performance component of physical fitness; it 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.
Survivors: Refers to children and adolescents who have completed treatment for their cancer.
Stem cells: Young, immature cells that will become mature (through a process called differentiation) to become different types of specialized cells. They can copy (replicate) themselves to replace or rebuild tissues in the body. Some stem cells mature into blood cells.

Blood-forming stem cells develop into different types of blood cells in the bone marrow. When blood cells are mature, they move from the bone marrow into the bloodstream

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.

Toxicity: Is defined by the National Cancer Institute as, the extent to which something is poisonous or harmful.

Tumor: An abnormal mass of tissue that can be benign or malignant (cancerous).

Valsalva maneuver: The Valsalva maneuver is performed by attempting to forcibly exhale while keeping the mouth and nose closed.

Vigorous aerobic training: Requires more effort, and makes children breathe harder and faster ('huff and puff').E.g., running, chasing and playing tag, and sports like soccer.

Visuo-spatial abilities: are those related to understanding and conceptualizing visual representations and spatial relationships in learning and performing a task. Visuospatial problems may cause an individual to become disoriented or lost in familiar environments.

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):** M=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% of one's own body weight, but sometime surgeon will specify a specific weight (i.e. "up to 30lbs of pressure). Teaching this is easiest 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 himself or herself. 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 such as jumping and running; or low impact, such as climbing stairs or walking.

White blood cells: Are cells that help your body fight infection, and are made in your bone marrow.

White matter: Is a substance in the brain that coordinates communication between different grey matters areas in the brain. Using a computer network as an analogy, the computers will be the grey matter; meanwhile, the cables to connect them all will be the white matter.

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

PEDIATRIC ONCOLOGY EXERCISE MANUAL