VEXT: AN 8-WEEK VIRTUAL EXERCISE AND TEXTING PROGRAM FOR PEDIATRIC SOLID ORGAN TRANSPLANT PATIENTS

by

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Abstract

Introduction: Pediatric solid organ transplant (SOT) recipients report lower physical activity levels, exercise capacity, muscular strength, and quality of life than their healthy peers. Opportunities for structured recreational activity are limited for this population. Virtual exercise programs may reduce barriers to exercise, allow better access to specialized care, and cost less than traditional exercise rehabilitation programs. The aim of this study was to implement an 8-week virtual exercise program for pediatric SOT recipients.

Methods: A circuit-based training program with a primary focus on strength was designed by a clinical exercise physiologist (AD). All participants completed a treadmill exercise stress test prior to starting the exercise program. Self-report surveys were used to assess quality of life (Pediatric Quality of Life Inventory, PedsQL), fatigue (Pediatric Quality of Life Multidimensional Fatigue Scale, PedsQL-Fatigue), and physical activity (Physical Activity Questionnaire for Children and Adolescents, PAQ) at baseline and at completion of the program. The strength subtest of the Bruininks-Oseretsky Test of Motor Proficiency (2nd Edition) was administered virtually pre- and post-intervention. Exercise classes were conducted via Zoom, thrice weekly for 30 minutes. Weekly engagement with the study team was provided through a web-based text messaging platform (WelTel Inc., Vancouver, BC). Participants who could not attend a class were sent a recorded link of the class via email.

Results: Prior to the intervention, the median z-score for strength was -1.00 (-1.65 - -0.60). After the exercise intervention, strength scores improved to a z-score of -0.20 (-1.30 - 0.40); p=0.007. There were no changes in z-scores for the PAQ (-0.53 (-1.60 - -0.01) vs. -0.28 (-1.78 – 0.21) p=0.959, PedsQL -0.83 (-1.79 - -0.02) vs. -0.81 (-1.80 - -0.20); p=0.441, or PedsQL Fatigue [-0.75 (-1.90 - -0.08) vs. -0.74 (-1.49 - -0.16), p=0.314].

Conclusion: Results showed that the delivery of this program was successful amongst participants. Increases in strength were seen following the 8-week exercise program with no changes in total quality of life, daily physical activity levels, and fatigue. These results suggest that a virtual exercise program may be used in future studies involving pediatric SOT patients to promote exercise.

Lay Summary

Solid organ transplantation (SOT) is a lifesaving procedure for those with end-stage heart, lung, kidney, or liver disease. Physical activity levels are low and the ability to exercise is limited in pediatric SOT patients. However, both physical activity and exercise have been shown to address risk factors associated with SOTs and lead to both immediate and long-term physical and mental health benefits. The purpose of this thesis was to determine the feasibility of an 8-week virtual exercise program for pediatric SOT patients. The program was found to be successful and led to increases in strength, however, did not affect quality of life, fatigue levels, or daily levels of physical activity.

Preface

The current research study was designed by Ms. Astrid De Souza, Dr. Jim Potts, Dr. Kathryn Armstrong, and myself, Nikol Grishin. Ethical approval, participant consent/assent, data collection and analysis, testing, result interpretation, and writing was performed by myself. As primary supervisor, Dr. Bill Sheel oversaw and provided guidance for all aspects of work related to this master's thesis. Dr. Kathryn Armstrong, Dr. Jim Potts, and Ms. Astrid De Souza provided guidance, assisted with the data analysis, and results interpretation. Ms. Astrid De Souza assisted me greatly with the creation of the exercise intervention and implementation of the study. Dr. Eli Puterman gave guidance with the study design and results interpretation. All methods executed in this thesis were approved by The University of British Columbia's Children's and Women's Research Ethics Board (H21-00180-A001).

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List of Abbreviations

BCCH	BC Children's Hospital
BMI	Body Mass Index
BOT-2	Bruininks-Oseretrsky of Motor Proficiency (2nd Edition)
DEXA	Dual Energy X-ray Absorptiometry
FITT	Frequency, Intensity, Time, and Type
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HR	Heart Rate
ISHLT	International Society for Heart and Lung Transplantation
LAS	Lung Allocation Score
MET	Metabolic Equivalent Units
MOT	Multi Organ Transplant
PAQ	Physical Activity Questionnaire
PedsQL	Pediatric Quality of Life Inventory
PedsQL-Fatigue	Pediatric Quality of Life Inventory Multidimensional Fatigue Scale
pLAD	Paracorporeal Lung Assist Device
QoL	Quality of Life
REDCap	Research Electronic Data Capture
SOT	Solid Organ Transplantation
UNOS	United Network for Organ Sharing
VE	Minute Ventilation
VO_2peak	Peak Rate of Oxygen Consumption

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Dedication

This work is dedicated to my parents, grandparents, and friends.

To my mom, stepdad, and grandparents, thank you for your unconditional love and support. For pushing me to succeed and for always believing in me, even when I did not. Thank you for being individuals that I could always look up to and depend on. I could not have done this without you.

To my friends, thank-you for your unwavering support. For continuously uplifting me, pushing me, and inspiring me to be better.

In addition, I would like to dedicate this work to the pediatric solid organ transplant patients that participated in this study and made this thesis possible. Thank you for your enthusiasm, engagement, and willingness to share your experiences with me. You have all inspired me with your strength and resilience and have taught me a lot. I will hold this experience and all that I have learned from you close to my heart.

Chapter 1: Introduction

Solid organ transplantation (SOT) is a life-saving intervention for those with end-stage heart, lung, kidney, or liver disease. [1] Children with SOTs typically do not undertake sufficient levels of exercise and physical activity which leads to both immediate and long-term consequences. Exercise is defined as a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.[2] Physical activity on the other hand is defined as any bodily movement produced by skeletal muscles that results in energy expenditure.[2] Immediate consequences of not being active include lack of skill development and physical competency, along with the inability to participate in sports and other activities that involve exercise.[3] These consequences may impact social skill development and ability to build relationships.[4] Long-term consequences include early-onset of cardiovascular disease, musculoskeletal disorders, and post-transplant metabolic syndrome which includes obesity, diabetes, and hypertension.[1,5] Diabetes and obesity are prevalent in SOT patients due to their sedentary lifestyle which impacts the body's metabolism and resistance to insulin.[6-8] Musculoskeletal disorders are also a common comorbidity in SOT patients due to elongated immobility and extensive use of immunosuppressive agents that result in decreased bone density.[9] Osteoporosis has now emerged as a frequent complication of the SOT process.[10]

Exercise rehabilitation programs have been proposed as a countermeasure to some of the complications that accompany SOTs.[11,12] Exercise training, including aerobic, resistance or combined training, has been shown to improve physical function, which is the ability to perform the activities of daily living, as well as quality of life (QoL) in SOT recipients.[1,13] Greater physical function in transplant candidates and recipients is also associated with lower pretransplant mortality and improved posttransplant outcomes.[1] Structured exercise training in transplant recipients may also reduce cardiovascular risk factors, such as hypertension and percent body fat, and increase lumbar bone mineral density. [1,13-16] Increase in bone mineral density is an especially important consideration in pediatric SOT patients who have yet to reach their peak bone mass and are reliant on proper bone growth to prevent osteoporosis.[17]

However, despite knowing the importance of exercise and physical activity, post-operative activity levels and exercise capacity remain low amongst SOT patients.[18] Although each SOT cohort has its own unique characteristics, many factors that contribute to this reduction in capacity are the same. Factors involved with reduced exercise capacity include deconditioning of skeletal muscles, immunosuppressive agents, and prolonged stay in the hospital.[1,19] Evidence shows that administration of immunosuppressive medications can lead to myopathy, resulting in myalgia and muscle weakness, and can affect mitochondrial respiration and muscle regeneration/remodelling.[19,20] Prolonged stays in the hospital prevent SOT patients from being physically active or able to participate in structured exercise.[1]

Current clinical guidelines recommend exercise training as a standard of care for pediatric SOT patients.[12] However, there are few transplant rehabilitation programs available in Canada. Previous exercise rehabilitation programs that have been delivered have typically been either hospital-based and/or home-based programs. Hospital-based programs are expensive and reach a geographically limited population which creates barriers with accessibility. Previous work from the British Columbia Children's Hospital (BCCH) found that a 16-week hospital-based program cost $6,000 per patient and required approximately 3,000 person-hours of time.[21] Hospital-based programs have been shown to have positive impacts on pediatric SOT patients with research showing improvements in exercise capacity and QoL.[22,23] Home-based exercise programs have also been shown to yield significant improvements in endurance time, maximal oxygen uptake, and strength at a much lower cost ($250/person) than the hospital programs as shown in Patel et al's study.[24] Patient compliance with exercise training has remained to be difficult and so a method of engagement outside of the exercise program may facilitate greater interaction.[25,26] Factors related to the disease process itself may have an influence on adherence to exercise, in addition to external factors such as social support, one's perception of competency, self-esteem, and enjoyment of the activity.[25,27,28]

With the advances in technology and digital healthcare, more innovative and engaging ways to deliver exercise and rehabilitation programs have emerged. However, there still lacks specificity (i.e. in structure, type, and difficulty of exercises) and participant engagement which are two essential parts of successful exercise programs. For pediatric SOT patients specifically, exercise programs also need to be safe, affordable, and accessible for families while also addressing the diverse needs of these children who may have additional medical considerations, developmental delays, or motor or sensory disabilities. Creating safe and accessible exercise programs for patients can include virtual programs that individuals can access from any location and providing modifications and adaptations to each exercise so that every patient has a safe option to choose from. A virtual program may also help with the affordability of the program by reducing costs that would normally be spent on space and equipment rentals.

Overall, the goal for children with SOTs is to regain function, improve their QoL, and to promote confidence for safely participating in activities, which can be accomplished by introducing exercise and participating in it regularly.[12] Most exercise programs that have been conducted in this population have been focused on cardiovascular training with no known programs targeting strength. However, in healthy children, strength programs have been shown to have a positive influence on cardiorespiratory fitness, bone mineral density, blood lipids, and selected psychological measures.[29-34] There is evidence to suggest that strength training may be an effective stimulus for bone mineralization in children and adolescents which is especially important in the pediatric SOT population who have shown to have low bone mineral density.[35,36] Strength training has also been shown to lead to increased self-confidence in a child's ability to do exercise and also in their self-image.[29] All these components tie into one's physical literacy which is described as the motivation, confidence, physical competence, knowledge and understanding to value and engage in a physically active lifestyle.[37] By increasing physical literacy through strength training (i.e. increasing physical strength, confidence and, in turn, their motivation to exercise) these patients are more likely to obtain health benefits offered by habitual physical activity.[37]

At this time, few studies have evaluated the effects of exercise training, specifically strength training, in children and adolescents with SOTs as most of the research is focused on adults.[24,38] Although some comparisons may be drawn between adults and the pediatric population, the experiences of children and adolescents are unique. Considering that musculoskeletal disorders have become more prevalent in these patients, strength training as a form of rehabilitation should be better considered due to its potential impact on bone mineralization and bone density. By improving musculoskeletal health, we can increase the patient's confidence in exercising and cause a change in behaviour in relation to exercise and being active. To promote engagement and accessibility for exercise rehabilitation programs, consideration of a virtual platform may be of benefit.

In conclusion, based on the available literature, pediatric SOT patients display low levels of physical activity and exercise which leads to both short-term and long-term consequences. Despite knowing the important role that physical activity and exercise play, there are limited rehabilitation programs offered to SOT patients. No study to our knowledge has used a virtual platform to administer exercise to pediatric SOT patients. This thesis aims to examine the feasibility and functional impact of a virtual exercise training program in pediatric SOT patients.

1.1 Review of Literature

Defining Solid Organ Transplantation

Kidney Transplantation in Children

Kidney transplantation has become the best treatment for patients with end-stage kidney failure. Early pediatric kidney transplantation has been complicated by technical, immunologic and logistical problems, however, over the last 15 years a number of advances have been made that have greatly improved patient and graft survival in pediatric kidney transplant patients.[39] The most common cause of kidney failure in young children include renal dysplasia, obstructive uropathies, or reflux nephropathy.[39] In older children, the most common causes include acquired glomerular diseases such as focal segmental glomerulosclerosis and lupus nephritis.[39]

The allocation of kidneys from their deceased donors is complex and involves considering the degree of anti-HLA sensitization, the blood-group match, and the relative HLA match.[39] Certain kidney transplants can also be done through living donors. In addition, kidney allografts are different than hearts and livers as they are placed in a different location from the failed native organ. Therefore, size and age matching are generally not required in kidney transplantation as it would be for either heart or liver transplants.[39]

Kidney transplants that have occurred in children 5 years of age or younger have shown the greatest improvement. However, adolescents now have the worst long-term graft survival among the pediatric recipient age groups, and it is believed that the main reason for this is poor adherence to medication therapy.[40,41]

Liver Transplantation in Children

Liver transplantation in children has been very successful in treating end-stage liver disease. There are four main reasons for pediatric liver transplantations which include cholestatic liver disease, fulminant hepatic failure, metabolic liver disease, and liver tumours.[42] To determine prioritization for transplantation, all patients receive a pediatric end-stage liver disease score. This score accounts for their bilirubin, international normalized ratio, serum albumin, age > 1 year, and growth failure.[42] There are also multiple different options for transplantations which include deceased donor transplantation with appropriate size donor, split liver transplantation from a young adult donor, and living donor transplantation. [42] Both patient and graft survival following pediatric liver transplantation have improved progressively over the years with current long-term survival rates of greater than 85%.[43] [44] However, there still remain to be risks and considerations with liver transplants. One of these considerations is immunosuppression which is critical in order to minimize the risk of rejection.[44] Depending on the institution, either steroids or IL-2 receptor antagonists or a T-Cell depleting agent is used for this process. Following this immunosuppressive induction, liver transplant recipients are at greater risk of developing malignancies and are more susceptible to infections. However, improvements have been made in surgical techniques along with the immunosuppression regimen to decrease these risks and increase the overall survival rate.[44]

Heart Transplantation in Children

Heart transplantation in children of all ages is now the accepted therapy for end-stage heart failure.[45] This procedure is a treatment option for children with intractable heart failure or congenital heart disease not amenable to surgical palliation.[45] The approach to a pediatric heart transplantation is different than that of adults; indications and expectations are different and decisions regarding the prevention of rejection and complications associated with immunosuppressive medications have a more profound effect on children.[45] Establishing indications for pediatric heart transplantation is a complex process that includes determining the benefits of the procedure, optimizing donor longevity, and ensuring equitable allocation of organs within the society.[46]The pre-transplant assessment allows for the identification of any possible complications or reasons to completely exclude transplantation as a treatment option.[47] The pre-transplant assessment includes a thorough cardiac evaluation, evaluation of other organ systems to ensure no contraindications, and HLA typing as well as a few other tests.[47] Recent data from the International Society for Heart and Lung Transplantation (ISHLT) has shown that the overall 20-year survival for all pediatric heart transplant recipients is 40%, with 1-, 5-, and 10-year survival reported as 80%, 68%, and 58% respectively.[47,48]

Physical Activity in Pediatric Solid Organ Transplant Recipients

Physical activity has been shown to be beneficial for pediatric SOT patients, however, little is known about this relationship. Lower physical activity levels are often seen following transplantation especially in the first 2 to 3 years after transplant, known as the "early years". The early years are composed of several transition points for the child as they move from the hospital to home, they return to physical activity and eventually school.[49] These transition points encompass ongoing challenges that the child may face including physical deconditioning, cognitive effects relating to the transplant procedure, and attaining proper nutrition.[49] Children and their families may expect that they will have an immediate increase in energy, however, recipients often will experience a reduction in exercise tolerance and aerobic capacity along with muscle weakness due to prolonged bed rest, physical inactivity, and immunosuppressant use.[49-51]

In addition to this, recipients will often undergo medically prescribed activity restrictions as well as overprotection from their parents and coaches at times. This in turn promotes physical inactivity and leads to poor exercise tolerance in these children.[49]

Multiple studies have shown that physical activity levels are indeed low in this population. One study assessed physical activity levels and identified baseline and contemporaneous factors in the pediatric SOT population and found that the median Physical Activity Questionnaire (PAQ) score was 2.2 (males: 2.2, females: 2.3) which was low compared to a healthy population (males: 3.00, females: 2.70).[18] Kidney transplants were found to have the lowest PAQ scores (2.1) with heart transplants having the highest (2.3). [18] This study also found that lower PAQ scores were associated with sensory disabilities and age at the time of completion, with older children reporting lower scores.[18] Similar findings were seen when measuring physical activity via accelerometry in pediatric kidney transplant patients.[52] Participants wore an accelerometer over a 3-day period to estimate physical activity, energy expenditure, and number of steps taken a day. The results showed that participants spent more than half of their day taking part in sedentary activity (58.5%), 37% was spent on light activity, and only 4.5% on moderate to vigorous activity. [52] Another study used the Previous Day Physical Activity Recall (PDPAR) and also found that pediatric kidney and liver transplant patients reported only 8% of their after-school time being spent on physical activity.[53] In this study, the average metabolic equivalent unity (MET) level of physical activity was 1.8 and 1.9 for kidney and liver transplant patients, respectively.[53] A MET of 1.0 is equivalent to rest and sedentary behaviour with greater scores being equivalent to more moderate and/or vigorous activity. Thus, a MET level of 1.8 and 1.9 is indicative of a relatively sedentary lifestyle.

Exercise Capacity in Pediatric Solid Organ Transplant Recipients

In addition to reductions in physical activity levels, exercise capacity (VO_2) remains reduced to 40%-70% of predicted in the majority of adult and pediatric SOT patients.[52,54] Research has shown that pediatric heart transplant patients display a lower workload, heart rate (HR), and peak rate of oxygen consumption (VO_2peak) but similar cardiac output relative to controls because of augmented stroke volume.[55,56] However, it still remains unclear as to whether solid organ transplant recipients have a compromised hemodynamic (i.e. stroke volume) or metabolic (VO_2peak) exercise response, or both.[56] It is also reported that heart transplant recipients display smaller left ventricular chambers due to a thicker myocardial wall, preservation of left ventricle diameter and filling as well as ejection as heart rate increases.[56] Although heart rate increases with exercise in pediatric heart transplant patients, the response was attenuated.[56] This blunted heart rate response has been well-described in previous literature as a consequence of denervation of the cardiac nerves.[56]

Exercise capacity may be impacted post-transplant due to reasons such as prolonged hospitalization, low physical activity levels, side effects of immunosuppressant medications, ongoing skeletal muscle atrophy and weakness, and episodic illnesses (infections, rejection). [12,57] Research has shown that exercise training improves the exercise capacity in this population by increasing factors such as (VO_2peak), minute ventilation (VE), and workload with no documented risks to the patient.[58] Such results were found in a 12-week at-home exercise program for pediatric heart transplant patients.[24] The exercise program consisted of three days a week of either running or using a provided bike, as well as strength training twice a week. For the strength training component, participants were given a handout that demonstrated the exercises and were provided with a live demonstration as well.[24] Metabolic measurements were collected with a VO_2max test prior to and after the exercise program. The results of this program demonstrated a statistically significant increase in endurance time and VO_2peak; however, there was no difference in peak HR or systolic blood pressure.[24]

Unfortunately, all other studies measuring exercise capacity have been conducted using adult SOT patients. However, these studies still show positive results of exercise training and should be understood when planning an exercise training program for the pediatric population. Such a study includes a randomized controlled trial in kidney transplant recipients where an exercise training program was introduced in half of the participants and continued for 12 months[59]. The exercise protocol was an independent home-based exercise program and included aerobic exercise (walking or cycling) with a frequency of at least four times a week [59]. Participants in this study were asked to keep exercise logs which were checked by the research team every two weeks. Cardiorespiratory fitness was measured by performing a VO_2max test, body composition was determined with the use of dual-energy X-ray absorptiometry (DEXA), and health-related QoL was measured with the Short-Form 36 Health Survey Questionnaire.[59] The results of this study showed that participants in the exercise group increased their peak systolic and diastolic blood pressure and peak VE [59] In addition, the exercise group had significantly greater increases in VO_2peak and muscle strength in comparison to the standard of care group.

Strength in Pediatric Solid Organ Transplant Recipients

There is previous evidence that has shown that exercise capacity is not solely determined by cardiac factors alone but also on the interplay between cardiopulmonary and muscular factors. [60] Research has suggested that the diminished exercise capacity may be due to peripheral muscle dysfunction which is known to be caused by detraining or immunosuppressive therapy.[61] Immunosuppressive therapy has been shown to lead to the inhibition of glucose uptake in skeletal muscles which contributes to the breakdown of muscle proteins.[62,63] Immunosuppressive agents, such as glucocorticoids, also directly affect muscle protein content, both by stimulating protein degradation and inhibiting protein synthesis.[62,63] Transplanted heart and lung patients have also been shown to have higher resting serum potassium levels and a higher slope of increase of potassium levels during exercise which suggests the presence of muscle deconditioning post-transplantation.[61] Potassium plays an important role in maintaining cell function, particularly in muscles and nerves, and low levels can weaken muscle contractions and in turn decrease one's muscle mass.[64] Although most research supports cardiovascular delivery of oxygen to be the central component of exercise capacity, the importance of skeletal muscle function should not be diminished, especially in SOT patients who receive immunosuppressive medication which is known to induce skeletal muscle dysfunction.[65] Research has shown that cardiac output of transplanted individuals is appropriate for their oxygen consumption, suggesting that the bulk oxygen delivery to the musculature is not impaired, but rather it is the inability to increase oxygen consumption which relates to altered muscle metabolism that limits their exercise capacity[66]. This could be due to loss of oxidative enzymatic capability, [67] decreased muscle capillarization, and inability to recruit muscle vascular beds [68], which are all factors associated with deconditioning.[66]

Exercise training has been shown to improve the functional capacity of solid organ transplant recipients due to the adaptations in their peripheral muscles.[69] Peripheral muscles are a key factor in exercise tolerance as they facilitate oxygen consumption and delivery. Strength in peripheral muscles, or strength in general, is a topic that is understudied in the solid organ transplant population, especially in children. Only one study, to our knowledge, has conducted an exercise in pediatric transplant patients where a three-month physiotherapy exercise program was introduced to pediatric heart and lung transplant patients.[38] Participants in this study were separated into two groups, home-based and institution-based exercise training. The programs included both aerobic and resistance training, as well as gross motor skill development. The outcomes of this study included strength and flexibility. A dynamometer was used to measure strength whereas popliteal angle, goniometric measurements of gastrocnemius/soleus, and "hand behind back" were used to measure flexibility.[38] The results showed that there were no differences between the two groups as both saw increases in right shoulder abduction, elbow extension, right hip abduction and extension, as well as left hip flexion. Improvements in hamstring, shoulder, and lower back flexibility were seen in both groups as well.[38] This study also showed the important finding of home-based exercise interventions being just as effective as institution-based programs.[38]

Quality of Life in Pediatric Solid Organ Transplant Recipients

The World Health Organization defines health as the state of "physical, mental, and social well-being" and not solely the absence of a disease.[70,71] Thus, when considering one's health-related QoL, it is important to consider all three of these factors from the patient's perspective. Physical factors may include energy level and health status, mental factors may include emotional status and self-esteem, and social factors may include social support and social health, and more.[70] Health-related QoL is especially important in pediatric SOT patients who are living with a chronic condition which is associated with its own unique comorbidities.

Kidney Transplants

Kidney transplant recipients have been shown to experience better overall health-related QoL after transplantation, however, many physical and psychosocial issues remain after the transplant.[70,72,73] This includes issues such as headaches, fatigue as well weight gain, and increased emotional problems. Health-related QoL has been shown to be significantly different in the dimensions of friends, schools, and hobbies when compared to healthy peers.[72] It is believed that chronic illnesses may impose certain restrictions on social activities which in turn can negatively impact one's social development.[72] In addition, other research has similarly shown that there is significant difficulty with returning to school after a prolonged absence due to the transplantation. This leads to lower self-concept and self-esteem and difficulty in sustaining peer relationships.[70,74] Four areas of concern have been identified from previous research for pediatric SOT patients; 1) physical symptoms such as fatigue, 2) body image and weight concern, 3) school disruption due to medical follow-up, and 4) strained relationships with family and peers.[70,75]

Liver Transplants

Pediatric liver transplant patients have been found to have decreased QoL compared to their health peers, specifically in the physical, psychological, social, and family functioning domains. [70,76] Health-related QoL improves with time since transplantation in liver transplant patients as well as age at transplantation along with maternal education predicted psychosocial functioning.[76] Similar findings were seen when Ng and colleagues conducted qualitative 1-to-1 interviews with children and adolescents with liver transplants and identified a range of common experiences following a pediatric liver transplant.[77] Such experiences include physical health restrictions, bullying and teasing, fears and worries about future health, sadness because of the knowledge of their parents worrying about them, difficulty in concentrating, and more.[77]

Heart Transplants

To date, there remains to be little literature available on quality of life amongst pediatric heart transplant recipients. Unlike kidney and liver transplants, studies have shown that quality of life after a heart transplant improves physical status and that children were active and could generally return to age-appropriate developmental, educational, social, and recreational activities.[70,78-80] DeMaso and colleagues found that the majority of 23 pediatric heart transplant patients they were examining showed improved psychological functioning after the transplant.[70,81] Improvements in psychological functioning have been shown to be maintained for over a decade with improvements in both emotional and psychological functioning in a previous longitudinal study.[70,82] Similar results were found in Pollock-BarZiv's study where self-perceived QoL and psychological well-being were found to be excellent in this population. [70,83] However, studies still show that patients may experience psychological difficulties at some point after transplantation and that heart transplant recipients are at an increased risk of psychological distress such as anxiety and depression, as well as poor self-concept.[70,78,79,84]

Fatigue in Pediatric Solid Organ Transplant Recipients

Literature has shown that fatigue is one factor that is frequently reported to have a large impact on the health-related QoL in patients with chronic conditions, such as a transplant. Fatigue can be defined as a persistent, subjective experience of weakness, lack of energy, and a sense of physical, emotional, and/or cognitive tiredness.[85-87] There is limited research on fatigue in pediatric solid organ transplant patients, with only one study, by Petersen, that was found to directly examine this topic.

Petersen and colleagues investigated the occurrence of fatigue in 100 pediatric liver patients between the ages of 2 and 18, and its impact on health-related QoL.[88] They administered the Pediatric Quality of Life Inventory Multidimensional Fatigue Scale (PedsQL-Fatigue) and the Pediatric Quality of Life 4.0 Generic Core Scales (PedsQL). The study reported that the PedsQL total scores of patients were significantly lower in the child-report survey with the most impaired domain being school functioning. [88] Strong relationships were found between fatigue and the PedsQL scales with correlations between the domains of health-related QoL and different fatigue scales all being significant. [88] With regards to specific subscales, cognitive fatigue was highly correlated with social functioning and school functioning.[88] Cognitive functioning in childhood is believed to be an underlying prerequisite for successful school achievement and is highly predictive for educational achievement.[89]

Besides this study conducted by Petersen, other studies that have looked at fatigue in children with chronic medical conditions have found similar outcomes. Children with chronic pain along with their caregivers, have been shown to have many significant problems with comorbid fatigue.[90] Specifically, it has been found that both the caregiver and the child themselves demonstrate moderate to severe impairments in total fatigue, general fatigue, and sleep/rest fatigue compared with the population-based normative samples.[90,91] These children state that they need to rest during the day, that their attention and memory have been impacted, and that they are too tired to participate in any activities.[90] Another study investigating the prevalence of fatigue in children and adolescents with chronic disease also found higher fatigue levels amongst children and adolescents with chronic diseases in comparison to the general population.[92] Chronic disease in this study included cystic fibrosis, autoimmune disease, and/or post-cancer treatment patients.[92] Amongst these patients in this study, total fatigue, general fatigue, and sleep/rest fatigue were found to be greater than the healthy control group.[92]

Digital Health in Clinical Pediatric Populations

Over the last few years, digital health has emerged as a promising area through which to deliver health care through. With research showing that over 95% of teens own a smartphone and access the internet daily, this has become the most accessible and barrier-free platform for clinical populations to use. [93] Digital health interventions and services reduce barriers that in-person services are associated with, including geographic distance, long wait times, high economic costs for travel and accommodation, and more. Both randomized and nonrandomized studies of digital health interventions in children with special health care needs have shown improved clinical, economic, and QoL outcomes. [94-97] Synchronous digital health technologies have also been shown to improve parental caregiver outcomes such as QoL, psychological health, satisfaction with care, and social support.

Despite knowing the success of digital health, information on tele-exercise or delivering an exercise training program online for pediatric clinical populations is limited. Only one study was found to conduct a similar program amongst children with type 1 diabetes. Calcaterra and colleagues explored physical activity levels in children with type 1 diabetes and then consulted with sport scientists to create an online training program.[98] The online training program was delivered through a platform called "LAMAJunior" where participants were encouraged to participate in exercise five times a week for a total of eight weeks.[98] The program itself consisted of two types of training, full training and active breaks. Full training consisted of 50-minute-long sessions with a combination of aerobic and resistance exercises adapted to the young age of participants whereas the active breaks were 3-5 minutes long and were aimed to cut off prolonged sedentary activities during the day.[98] The results of this study focused mainly on insulin levels but they also showed that there was an increase in physical activity levels, however, participants were still not meeting the physical activity guidelines set by the World Health Organization.

All other studies that have used digital health, to our knowledge, have used virtual reality, videogames, and online games such as *Dance Dance Revolution* to "administer" exercise.[99,100]. No study has used a digital health platform to conduct an exercise training program for pediatric SOT patients. However, a digital health platform, WelTel, has been used and shown to improve communication between the SOT team and the patient at BCCH.[101] WelTel is a two-way texting and mobile communications platform that was created by Dr. Richard Lester who pioneered WelTel in health care over 15 years ago in response to the HIV/AIDS crisis in Africa.[102] At that time, Dr. Lester found that patients who received WelTel support had significantly improved antiretroviral therapy adherence and rates of viral suppression compared with the control individuals.[102] Today, WelTel is being used in a variety of settings, from connecting physicians with pediatric cardiology patients and their families, to supporting primary health care and specialty services in urban and remote communities.

1.2 Conclusion

It is known that exercise and physical activity are beneficial and lead to positive outcomes in the pediatric SOT population. This includes physical benefits such as muscle strength and improved graft survival, as well as mental health benefits such as improved QoL, especially in areas of school and social functioning.[18,103,104] Although exercise training programs have posed certain barriers and challenges, the emergence in tele-exercise and digital health can now act as a bridge between these gaps. Despite knowing about this growth in digital health, no studies to our knowledge have conducted a virtual exercise program in pediatric SOT patients.

1.3 Purpose

To determine the feasibility of an 8-week virtual exercise training program in pediatric solid organ transplant recipients.

1.4 Objectives

1. To deliver a live stream exercise program to participants for 8-week (3 classes per week; 30 minutes each).
2. To evaluate muscular strength before and after implementation of an 8-week exercise program, through virtual delivery of the Bruininks-Oseretsky Test (BOT-2) of Motor Proficiency (2nd Edition).
3. To assess compliance through class attendance throughout the 8-week virtual exercise program.
4. To assess engagement and acceptability using a text-messaging platform during the 8-week exercise program.

Chapter 2: Methods

2.1 Participants

Children between the ages of 8 to 18 who had received either a heart, lung, liver, or kidney transplant and were current patients at the Multi Organ Transplant (MOT) Clinic at BCCH were recruited. E-consent was obtained from a parent or guardian, and e-assent was obtained from the child, prior to participation. Ethics approval for this investigation was received from the University of British Columbia Children's and Women's Research Ethics Board (H21-00180-A002).

Inclusion Criteria:

1. Female or male SOT patients between the ages of 8-18 years who had access to a cell phone or use of a parent's phone under their supervision.
2. Participants must have completed a clinical exercise stress test within 12 months of starting the program.
3. Participants had to speak and understand English.
4. The participants and their guardian(s) needed to assent/consent to participating in the study.

Exclusion Criteria:

1. Female or male SOT patients younger than 8 years of age or older than 18 years of age.
2. SOT patients who did not have access to a cellular device or were unable to use their parents' phone.
3. SOT patients who were unable to speak and understand English.
4. Those who did not provide consent/assent to participate in the study.

5. Patients who were excluded by their transplant physician due to medical reasons or other concerns.

2.1.1 Recruitment

Recruitment started on July 20th, 2021 and finished on September 8th, 2021. A total of 89 eligible participants were identified from the Multi-Organ Transplant (MOT) patient registry at BCCH. Recruitment was done via email, phone, MOT clinic, or monthly SOT Zoom meetings with a social worker. A letter of invitation, assent and consent forms were sent to all eligible participants via email. These same forms were also provided to eligible patients who came to the MOT clinic for their annual visit. Recruitment was also conducted through one of the monthly Zoom meetings held by the social worker who works with SOT patients at BCCH. These monthly meetings are held for certain patient populations at BCCH which allows them to connect with one another and provides them with a support system. During this meeting, the study was explained to the patients and any questions that they had were answered. Patients who were interested in participating in the study were provided with contact information of the research team, who then sent out information about the study including the letter of invitation, assent, and consent form.

Eligible participants were given a week to decide if they were interested in the study. E-consent and assent was provided via phone or through Research Electronic Data Capture (REDCap). REDCap, which is hosted at the BCCH Research Institute, is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.[105] Those who expressed interest in participating in MOT clinic were e-consented and e-assented in person.

2.2 Study Overview

An 8-week virtual exercise program was tailored to the specific needs of the SOT participants and was live-streamed across the province through Zoom. The intervention started on the 13th of September 2021 and ended on the 4th of November 2021. Pre-assessments were held within a week of consenting. Post-assessments were held 1 to 2 weeks after the completion of the intervention. However, participants were still scheduled for a post-assessment even if they were unable to make it within the designated time frame

2.3 Demographic Data

Demographic and clinical characteristics were extracted from clinical charts and entered into REDCap. Demographic data that was collected included age, sex, race, weight, height, and body mass index (BMI). Clinical data including medical history (i.e. age at transplant, age at transplant, additional medical considerations, etc.) and exercise stress test results were also recorded.

2.4 Exercise Stress Tests

All participants completed a stress test on a treadmill to ensure that it was safe for them to exercise. The BCCH protocol [106] was used in the majority of participants, except in those who could not safely complete the protocol or those who completed their stress test off-site. The BCCH protocol follows a constant incline of 1% grade and an increase in speed by 0.5mph with a starting speed of 2.0 miles per hour until volitional fatigue or other criteria including safety concerns are met.[106] Modifications to the BCCH protocol were made by maintaining both the incline and speed of the treadmill before reaching a stage that participants would not be able to complete safely. Those who completed their stress test off-site at an adult hospital completed the Bruce protocol.[107] Our participant's exercise data was age- and sex-matched with historical healthy control data.[106]

2.5 Exercise Program

Exercise content was designed and scripted based on the initial assessment with participants as well the strength subtest of the BOT-2. The exercise program was designed to improve strength with exercises focused on whole-body movements that incorporated the upper body, lower body and core. Elements of cardiovascular and balance exercises were also included. Each class was composed of 3 different circuits, each consisting of 3 to 4 different exercises (Appendix A). All exercises were equipment free and had varying degrees of difficulty. The program was originally designed to be a periodized model with increases in time spent in each exercise for weeks 1-3 and an unloading week at week 4. Modifications to the periodized model needed to be made at week 3 as the duration of the exercises were unmanageable for the study participants.

Classes were held thrice weekly and were delivered online through Zoom on Mondays, Wednesdays, and Thursdays at 5:00pm. Class schedule was only changed if a class fell on a statutory holiday. Participants obtained the link for each class through a broadcasted message on WelTel and via email. The Zoom link remained the same for the entirety of the program which allowed participants the opportunity to also save the link on their device.

2.6 Measurements

2.6.1 Feasibility Measurements

Attendance and Engagement

Attendance was taken at each class. Data on recruitment, retention, and reasons for withdrawal or missing class was also collected. To ensure compliance, participants who missed classes were asked to text message a picture or video of them doing any of the live stream classes that they missed.

Participant engagement was maintained through WelTel, a digital health platform that sent a weekly text message to maintain communication between participants and the study team. The weekly text message asked "How are you?" and responses were categorized by the WelTel platform as "OK", "Not OK", or "Unrecognized". The unrecognized responses were questions, comments or concerns posed by the participant. Messages of "Not OK" or "unrecognized" were responded to with a follow-up text message within 48 hours. Participants were aware that WelTel was not to be used as an emergency service and if they required immediate medical attention, they should call 911 or visit the nearest hospital's emergency department.

The WelTel platform collects metrics such as number of SMS messages sent/received, response rates, and number of interactions/conversations between participants and the study team. These metrics were recorded as a surrogate for patient engagement and platform acceptability.

Cost and Person's Hours

The total cost of the program was calculated based on the cost of WelTel subscriptions, honorariums, and the salaries for the exercise class leader, exercise physiologist and study coordinator. Total hours spent on the study were also found by summating the time that was allocated to the exercise leader, exercise physiologist, and study coordinator.

Exit Interview

An exit interview was conducted with participants to determine feasibility of the program (Appendix A). The interview incorporated questions around the class structure, enjoyment, and acceptability of the program.

2.6.2 Strength Measure

The Bruininks-Oseretsky Test (BOT-2) of Motor Proficiency (2^{nd} Edition), which has been proven to be a reliable and consistent tool, was delivered virtually and used to measure strength. Participants were told which tools (i.e. measuring tape) and how much space they would need for the BOT-2 prior to the assessment.[108-110] The BOT-2 measures fine and gross motor proficiency, with subtests that focus on stability, mobility, strength, coordination, and object manipulation. The test is tailored to school-aged children and young adults between the ages of 4-21 years. [109,111] Only the strength subtest was used in this study.[109,111] The strength subtest consists of 5 exercises; push-ups, sit-ups, wall sits, v-ups, and a standing long jump. For push-ups and sit-ups, participants were given 30 seconds to complete as many repetitions with proper form as possible. For the v-ups and wall sits, participants were instructed to hold the position for 60 seconds. Time was stopped as soon as form was compromised. A raw score was generated for each exercise and converted to a total point score. The total point score was then converted into a scale score according to sex and age standard tables provided in the BOT-2 manuals.[109]

2.6.3 Physical Activity Levels

The PAQ for Children (-C) and Adolescents (-A) was used to assess physical activity in study participants pre- and post-assessment. The PAQ is a valid and reliable self-administered, 7-day recall instrument tool that assesses general levels of physical activity throughout the school year for students (Appendix A).[112,113] The PAQ was completed online, both pre- and post-assessment. The questionnaire is derived from a series of items on sport participation, activity during and after school, and evening/weekend activity.[112,113] A summary physical activity score is derived from nine items, each scored on a 5-point scale, with 5 indicating the greatest level of physical activity. The PAQ was completed online, at both pre-and post-assessment. Participants were sent a link to REDCap where they would complete the questionnaire. Participants were sent 3 reminder emails following the initial email requesting that they complete the PAQ-C/A.

2.6.4 Quality of Life Measure

The Pediatric Quality of Life Inventory (PedsQL) generic module is a self-report tool that measures health-related QoL and is easily understood by children and adolescents.[114] QoL is measured across 5 different domains: physical functioning, emotional functioning, school functioning, social functioning and psychological functioning.[114] This measure was completed by the participant (self-report) and their parent/guardian (proxy report). Lower scores on the PedsQL indicate lower levels of QoL. The PedsQL was administered prior to and after the 8-week intervention with a link to REDCap where the questionnaire could be completed online. Participants were sent 3 reminder emails following the initial email sent to complete the PedsQL.

2.6.5 Fatigue Measure

The PedsQL-Fatigue Scale is a symptom specific instrument to measure fatigue in pediatric patients.[115]There are three domains in this scale including general fatigue, sleep/rest fatigue, and cognitive fatigue. The PedsQL-Fatigue questionnaire was completed by the participant (self-report) and their parent/guardian (proxy report) before and after the 8-week intervention. Lower scores on the PedsQL-Fatigue Scale indicate greater levels of fatigue. Similar to the PedsQL, a link to REDCap was sent to participants and their parents/guardian to complete the questionnaire online. Three reminder emails were sent following the initial email.

2.7 Statistics

Frequency distributions were used to determine normality for PAQ, PedsQL, PedsQL-Fatigue and BOT-2 scores. Median and interquartile ranges are reported for all continuous data. Attendance (number of classes attended) and engagement (response rate) through WelTel are also reported. A Wilcoxon-Signed Rank Test was used to determine differences in scores between pre- and post- exercise intervention. Spearman Correlation Tests were performed to analyze correlations between attendance and PedsQL, PedsQL-Fatigue, PAQ, and BOT-2 scores. Z-scores were calculated for the PAQ-C/A, PedsQL, and PedsQL-Fatigue scores.[112,114,115] Significance was set at $p \leq 0.05$ for all tests. All statistical analyses were run using SPSS Version 28.0.0.0 (IBM Corporation, Armonk, NY).

Chapter 3: Results

3.1 Participants

Of the 89 eligible participants, 18 consented to participate in the study, 11 completed the exercise program (Figure 1). Nine completed all pre-and post-intervention assessments (5 females, 4 males), 2 participants partially completed the assessments (1 male, 1 female). Demographics are shown in Table 1. Participant medications are shown in Table 2.

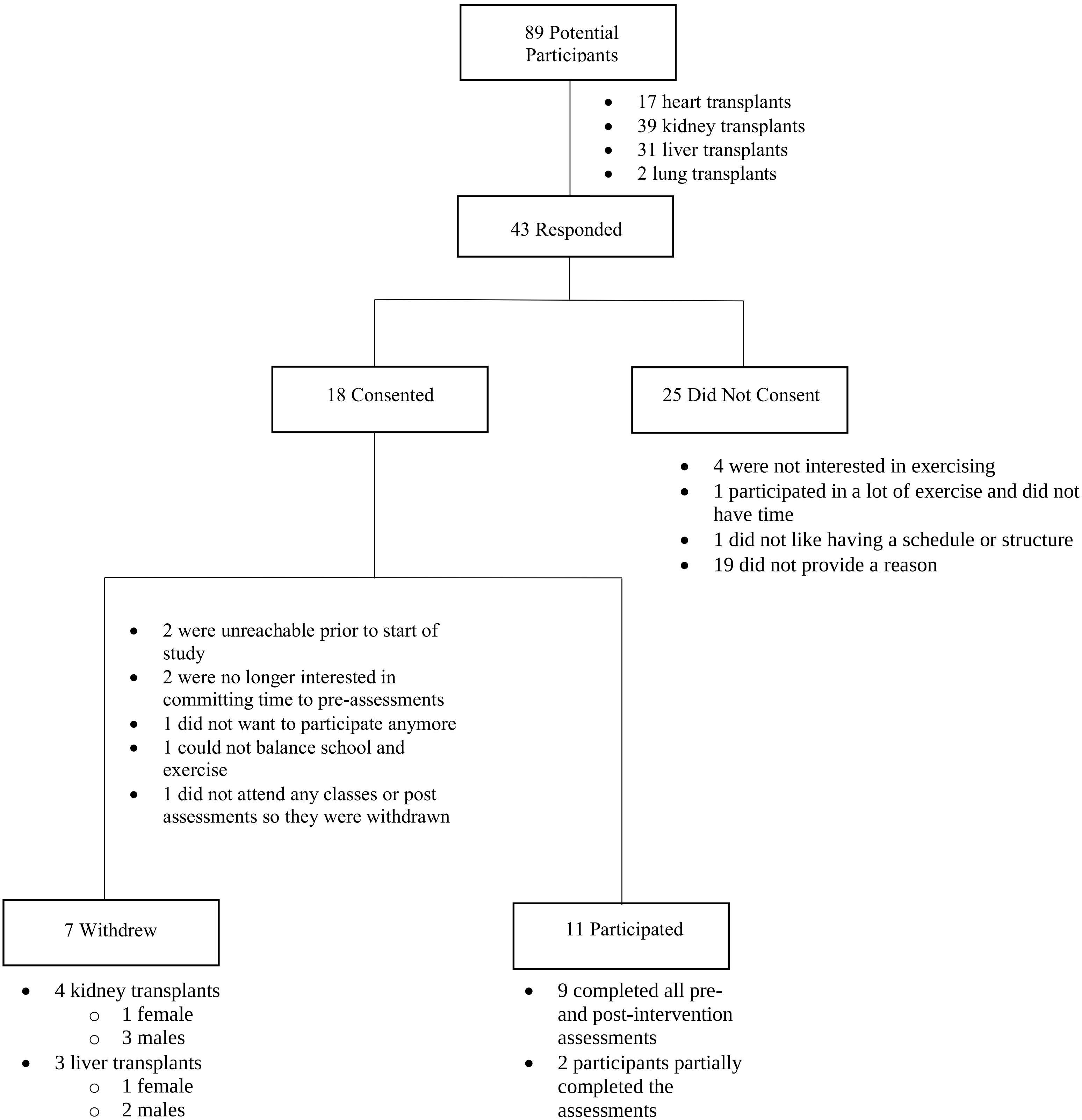

Figure 1. Breakdown of Recruitment

Table 1. Participant Demographics. The number (%) or median (IQR) are reported.

Demographics	Females (n=6)	Males (n=5)
Age (years)	12.00 (9.75 – 14.50)	11 (10 – 15)
Height (m)	1.57 (1.45 – 1.64)	1.41 (1.27 – 1.62)
Weight (kg)	48.8 (44.0 – 55.9)	53.0 (33.7 – 54.3)
BMI (kg/m^2)	19.51 (17.82 – 24.48)	20.34 (17.05 – 28.10)
Race:		
Caucasian	2 (32%)	2 (40%)
Asian: Oriental/Caucasian	1 (17%)	-
Asian: Southeast, Far East, India, Philippines	1 (17%)	3 (60%)
Caucasian/North American Indian	1 (17%)	-
Race is not reported	1 (17%)	-
Time Since Transplant (years)	10.00 (3.5 – 11.0)	4.0 (2.5 – 9.5)
Age at Transplant (years)	4.5 (0.0 – 7.8)	8.0 (5.0 – 10.5)
Type of Transplant:		
Heart	3 (50%)	1 (20%)
Kidney	1 (17%)	4 (80%)
Liver	2 (33%)	-
Distance Between Home and Hospital (km)	42.50 (21.25 – 123.75)	45 (25 – 85)
Additional Medical Conditions:		
Obesity	1 (17%)	2 (40%)
Cerebral Palsy	1 (17%)	-
Eagle Barret Syndrome*	-	1 (20%)
Diabetes	1 (17%)	-

Anxiety and/or Depression	2 (33%)	-
Epilepsy	1 (17%)	-
Additional Considerations:		
Developmental Delay/Learning Disability	3 (50%)	2 (40%)
Sensory Disability	1 (17%)	-
Reason For:		
Heart Transplant	Underlying non-compaction cardiomyopathy,	Underlying complex congenital heart disease with failed Fontan palliation
Kidney Transplant	End stage renal disease from bilateral multi-cystic dysplasia	End stage renal disease secondary to focal segmental glomerulosclerosis, End stage urethral atresia, and End stage glomerulonephritis
Liver Transplant	Argininosuccinic lyase deficiency, Post-fulminant liver failure secondary to Wilson's Disease, and Biliary atresia	

**Eagle Barret Syndrome is defined as a rare disorder characterized by partial or complete absence of the stomach (abdominal) muscles, failure of both testes to descend into the scrotum (bilateral cryptorchidism), and/or urinary tract malformations.*[116]

Table 2. List of Participant Medications

Participant ID	Transplant Type	Transplant Regimen (including immunosuppression and anti-rejection medication)	Other Medications	Supplements
1001	Liver	Tacrolimus	Fluoxetine	Vitamin D
1004	Heart	Tacrolimus, Mycophenolate Mofetil	Atorvastatin	Vitamin D
1005	Kidney	Tacrolimus, Mycophenolate Mofetil	Prednisone, Salbutamol	Vitamin D, Iron Supplement
1008	Kidney	Leflunomide, Tacrolimus, Prednisone	IVIG, Fludrocortisone, Magnesium Oxide	Vitamin D
1009	Kidney	Mycophenolate Mofetil, Tacrolimus, Prednisone		Vitamin D
1010	Kidney	Tacrolimus, Mycophenolate Mofetil, Prednisone	Potassium Chloride, Amlodipine, Septra, Darbepoetin	Vitamin D, Iron Supplement
1014	Kidney	Mycophenolate Mofetil, Tacrolimus Topical, Tacrolimus Sandoz, Prednisone	Calcium Carbonate, Darbepoetin, Hydrocortisone, Somatropin, Testosterone Intramuscular Injection	Alfacalcidol, Vitamin D, Replavite, Iron Supplement
1016	Liver	Tacrolimus	Amlodipine, Ethosuximide, Levetiracetam, Insulin Levemir, Metformin	Vitamin D, Iron Supplement
1017	Heart	Mycophenolate Mofetil, Tacrolimus, Prednisone	Fludrocortisone	Vitamin D
1018	Heart	Mycophenolate Mofetil, Tacrolimus	Ramipril, Atorvastatin	Vitamin D
1019	Liver	Tacrolimus	Keflex, Sertraline, Visanne, Ondansetron, Ursodiol	Vitamin D, Folic Acid, Iron Supplement, B12

3.2 Exercise Stress Tests

Out of the 11 participants, 8 completed the BCCH protocol, or a modified version of it (n=2), and 1 participant completed the Bruce protocol. The average exercise time for the modified protocols was 6.83 minutes (2.16 minutes for the female participant and 11.50 minutes for the male participant). All participants were medically cleared for participation in the program. No participants displayed ECG changes suggestive of an arrhythmia or ischemia with exercise. Heart rate and blood pressure responses were normal with increases in heart rate and systolic blood pressure, and stable diastolic blood pressure, as exercise time increased.[117] Reasons for test termination included: fatigue (n=9) and physical limitations due to ankle foot orthoses (n=2). Exercise test results are summarized in Table 3.

Table 3. Exercise stress test results. Median (IQR) are reported.

	Female Participants n = 6	Male Participant n = 5	Historical BCCH Controls Females	Historical BCCH Controls Males	p-value for Females	p-value for Males
Time (minutes)	8.00 (6.18 - 9.26)	11.50 (6.08 - 12.00)	15.03 (14.10 - 15.40)	14.00 (11.14 - 16.15)	0.028*	0.138
Rest						
Heart Rate (bpm)	89 (85 - 95)	87 (82 - 94)	76 (67 - 80)	84 (76 - 96)	0.058	0.684
Systolic Blood Pressure (mmHg)	108 (102 - 119)	110 (102 - 123)	113 (107 - 118)	113 (103 - 121)	0.916	0.345
Diastolic Blood Pressure (mmHg)	66 (60 - 72)	66 (62 - 83)	72 (63 - 76)	70 (69 - 78)	0.833	0.684
Peak						

Heart Rate (bpm)	180 (169 - 188)	162 (144 - 189)	194 (187 - 206)	198 (190 - 205)	0.028*	0.043*
Systolic Blood Pressure (mmHg)	147 (130 - 162)	140 (136 - 146)	159 (153 - 167)	143 (135 - 170)	0.172	0.500
Diastolic Blood Pressure (mmHg)	70 (60 - 73)	76 (65 - 78)	74 (65 - 76)	68 (55 - 75)	0.172	0.104

**Significant p-values*

3.3. Feasibility

3.3.1. Attendance

Table 4 shows the attendance of participants over the course of the 8-week program. Half of the study population attended more than 60% of classes while the other half attended less than 25% of the time. Reasons for missed classes can be found in Table 4. There were no correlations between attendance (number of classes attended) and post-intervention PedsQL, PedsQL Fatigue, BOT-2, and PAQ Scores (Table 5).

Table 4. Class Attendance Over the 8-Week Intervention (Days vs. Participant)

Study ID	Number of Classes Attended (% out of 24 classes)	Reasons for Not Attending*
1001	20 (83%)	Wasn't feeling up for it (1 class)
1004	20 (83%)	On family vacation (4 classes)
1005	15 (63%)	Play date with a friend (1 class), Bloodwork (1 class), Feeling tired or sick (2 classes), Scheduling conflict (1 class)
1007	0 (0%)	No reason provided
1008	23 (96%)	No reason provided
1009	21 (88%)	No reason provided

1010	15 (63%)	No reason provided
1014	1 (4%)	No reason provided
1016	3 (13%)	No reason provided
1017	4 (17%)	Hospitalized (3 classes), Forgot charger (1 class)
1018	6 (25%)	No reason provided
1019	11 (46%)	Hospitalized (5 classes)
Median	**13 (54%)**	
IQR	**3 – 20 (13% - 83%)**	

**Not all participants provided reasoning behind missed classes. Only reasons that were given are reported in this table.*

Table 5. Pearson correlation coefficients between outcome measures and attendance (n=9).

Outcome Measure	Pearson Correlation	Significance
Attendance vs. Self-Report PedsQL Total	r=0.333	p=0.381
Attendance vs. Self-Report PedsQL Fatigue Total	r=0.143	p=0.714
Attendance vs. PAQ	r=0.382	p=0.276
Attendance vs. BOT-2	r=0.357	p=0.311

3.3.2. Cost and Person's Hours

This program cost $1,900 per participant and required a total of 580 staff hours of time. The breakdown of costs and time spent on the study can be found in Table 6.

Table 6. Total Cost and Hourly Breakdown

	Cost Total N=11	Total Hours Spent on Study
WelTel Subscription	$660	-
Exercise Class Leader	$600	24
Exercise Physiologist	$9,000	72
Participant Honorarium	$500	-
Study Coordinator	$10,156	484
Total	$20,196	580

3.3.3. Engagement through WelTel

Text messages were sent to and received by all participants throughout the program (1 message per week over a total of 9 weeks which includes the 8-week intervention and 1 reminder prior to starting the program). All text messages were delivered. Out of the 99 messages that were sent (9 weeks x 11 participants), the response rate was 40 (40%). Out the 40 messages received, 3 messages were medically related while the rest were social messages (i.e. telling us how they were feeling or asking questions about the program). The median number of responses between participant and the study team was 2.5 (1.0-6.3). Participants who were clinically diagnosed with a depression and/or anxiety (n=2) were more responsive with a mean of 6.5 messages sent to the study team with 2 of the messages related to a medical issue while the others were related to how they were feeling.

3.3.4. Exit Interview

An exit interview was conducted with 10/11 participants. Exit interview themes focused on feasibility, structure, and enjoyment of the program. Results from the interview are displayed in Table 7.

Table 7. Exit Interview Following Intervention

	N = 10 (%)
Found the virtual exercise to be enjoyable	10 (100%)
Would recommend this program to others.	10 (100%)
Found it useful to be able to text their health care team.	9 (90%)
Had problems receiving the text messages.	0 (0%)
Had problems sending the text messages.	0 (0%)
Had problems accessing the Zoom link.	0 (0%)
Participating in this program increased their daily PA levels.	
Strongly Agreed	4 (40%)
Agreed	4 (40%)
Neutral	2 (20%)
Participating in the program increased their overall wellbeing.	
Strongly Agreed	4 (40%)
Agreed	3 (30%)
Neutral	3 (30%)
Participating in the program increased their confidence with exercise.	
Strongly Agreed	3 (30%)
Agreed	7 (70%)

Neutral	0 (0%)
The frequency of classes were:	
Just Right	8 (80%)
Too Frequent	0 (0%)
Not Frequent Enough	2 (20%)
How did you feel about the duration of each class?	
Just Right	7 (70%)
Too Long	2 (20%)
Too Short	1 (10%)
How did you feel about the difficulty of the classes?	
Just Right	10 (100%)
Too Difficult	0 (0%)
Too Easy	0 (0%)

All participants found the program enjoyable and would recommend it to others. Positive feedback included that this gave them something to do after school, they made friends through the program, and it helped them get stronger and fit. Participants found it useful that they could text the health care team noting that it provided them with “constant access”, “easy communication with the team”, and made participants feel “less lonely”. Additional positive feedback included that they planned on continuing to do the exercises, they wanted to be more active during recess and lunch, and that they looked forward to exercising. Reasons for improvement in wellbeing included: feeling more energetic, happier, independent, and more confident in their own body. Participants who felt an increase in their confidence with exercise felt like they could do as much exercise as other kids around them because they were taught how to do exercises properly. Before the program, these participants felt like all exercises were difficult and that they could not keep up.

The structure of the program, including frequency, duration, and difficulty, were all appropriate according to responses. One participant stated that they would have liked to have this class 5 times a week while another said 4 times a week. Two other participants stated that they would have liked the classes to be between 15 to 20 minutes long, and 1 participant stated that they would have liked the class to be 60 minutes. The difficulty of the classes was found to be a good balance between easy and hard exercises. "Easy" exercises included jumping jacks, diamond hops, and lunges while difficult exercises included supermans, push-ups, and crunches.

When asked what the greatest challenge of the program was, participants stated that it was getting themselves to the class because they were often tired from school (n=6). Additionally, core exercises were thought to be the most difficult (n=6). The greatest benefits were feeling stronger and more confident with exercise (n=4) as well has having fun and enjoying seeing other kids doing the exercises (n=7). Additional comments from participants included that they felt like they were going to be doing something "great" on the days that they had class (n=1) and that they felt encouraged to exercise (n=2).

3.4 Strength

After 8 weeks of training, the median z-score for strength improved from baseline [-1.0 (-1.65 to -0.60) to -0.2 (-1.30 - 0.40); p=0.007]. Specifically, there was a significant increase in the number of push-ups, sit-ups and wall sit duration with no changes in V-ups and standing long jump (Table 8). Raw scores for the baseline BOT-2 are displayed in Appendix A.

Table 8. Median (IQR) Scores for BOT-2 Exercises Pre and Post Intervention (n=10)

	Pre	Post	p-value
Push-Ups (number completed)	9.00 (5.25 -12.00)	17.00 (13.25 - 23.5)	0.009*
V-Ups (seconds)	28.00 (16.25 - 35.50)	17.00 (13.00 - 45.00)	0.540
Wall Sits (seconds)	34.00 (21.25 - 41.50)	47.00 (32.00 - 60.00)	0.008*
Sit-Ups (number completed)	12.00 (8.00 - 14.75)	19.50 (13.25 - 23.50)	0.012*
Standing Long Jump (inches)	42.00 (31.10 - 53.25)	37.85 (29.25 - 49.50	0.960
Total Point Score (out of a possible 42)	19.50 (15.75 - 22.00)	24.00 (16.00 - 28.50)	0.007*

**Significant p-values*

3.5 Daily Physical Activity Levels

Baseline PAQ scores for this group was 2.49 (1.75 - 2.73) [Males: 2.87 (2.57 – 3.25) vs. Females: 1.89 (1.30 – 2.25); p=0.066], representing a z-score of -0.53 (-1.60 to -0.01). After the intervention, PAQ scores remained unchanged from baseline with a median of 2.69 (1.77 - 2.91), [Males: 2.74 (2.20 – 3.25) vs. Females 2.00 (1.75 – 2.88), p=0.345] and z-score of 0.28 (-1.78 – 0.21) (p=0.959).

3.6 Quality of Life

At baseline, the z-score for QoL was -0.83 (-1.79 - -0.02) and was unchanged post-intervention [-0.81 (-1.80 - -0.20), p=0.441] (Table 9). At baseline, parent proxy-reports were significantly lower than the self-reported scores across all domains except school and emotional functioning (Table 9). Proxy reports also remained unchanged prior to [z-score= -1.68 (-2.03 - -0.86)] and post-intervention [z-score= -1.49, (-2.31 - -0.79)] (p=0.779). There were no significant changes pre-and post-intervention scores for self-report or proxy-report questionnaires (Table 9)

Table 9. Pre and Post-Intervention Self-Report and Proxy-Report Scores for PedsQL

		Self (n=9)*	Proxy (n=9)*	p-values for self vs. self	p-values for proxy vs. proxy	p-value self vs. proxy
Physical	Pre	75.00 (59.38 - 87.50)	53.13 (46.88 -71.88)	-	-	0.044*
	Post	68.75 (51.57 - 85.94)	59.38 (50.00 -75.00)	0.933	0.726	0.123
Emotional	Pre	65.00 (50.00 - 80.00)	55.00 (50.00 - 65.00)	-	-	0.136
	Post	65.00 (47.50 -75.00)	60.00 (45.00 - 67.50)	0.776	0.892	0.621
Social	Pre	75.00 (70.00 - 90.00)	60.00 (50.00 - 75.00)	-	-	0.017*
	Post	70.00 (42.50 - 92.50)	65.00 (32.50 - 80.00)	0.932	0.496	0.055
School	Pre	60.00 (25.00 - 75.00)	55.00 (35.00 - 60.00)	-	-	0.121
	Post	55.00 (37.50 - 77.50)	50.00 (35.00 -72.50)	0.953	0.553	0.102
Psychological	Pre	68.33 (48.33 - 80.00)	58.33 (46.67- 66.07)	-	-	0.025*
	Post	65.00 (45.84 - 77.50)	58.33 (42.50 - 68.33)	0.859	0.611	0.084
Total	Pre	68.33 (51.09 - 82.61)	55.43 (46.74 - 53.04)	-	-	0.047*

	Post	66.30 (45.66 - 78.81)	58.70 (42.94 - 72.28)	0.859	0.484	0.465

**One participant did not complete their self-report following the intervention and one participant's parent/guardian did not complete the proxy report prior to the intervention resulting in an n=9.*

3.7 Fatigue

At baseline, participants report a total PedsQL-Fatigue z-score of -0.75 (-1.90 to -0.08) which remained unchanged after the intervention with a z-score of -0.74 (-1.49 to -0.16); p=0.314. At baseline, proxy-reports were lower than self-report scores for the general fatigue domain but remained the same across all other domains (Table 10). The proxy z-scores remained unchanged throughout the intervention [Pre: -1.52 (-1.73 to -0.72) vs. Post: -1.80 (-2.60 to -1.42); p=0.930]. Following the intervention, proxy-report scores were significantly lower amongst the general fatigue domain and the cognitive domain when compared to the self-report scores (Table 10).

Table 10. Pre and Post Intervention Self-Report and Proxy-Report PedsQL Fatigue Scale questionnaires.

Domain		**Self (n=9)***	**Proxy (n=9)***	**p-values for self vs. self**	**p-values for proxy vs. proxy**	**p-value self vs. proxy**
General	Pre	68.75 (54.17 - 83.33)	55.00 (33.33 - 66.67)	-	-	0.035*
	Post	66.67 (50.00 - 79.19)	54.17 (50.00 - 62.50)	0.726	0.271	0.018*
Sleep/Rest	Pre	65.00 (45.83 - 79.17)	54.17 (37.50 - 79.17)	-	-	0.833
	Post	75.00 (47.92 - 79.17	66.67 (47.92 - 89.59)	0.574	0.344	0.435

Cognitive	Pre	54.17 (29.17 - 38.55)	45.83 (33.33 - 79.17)	-	-	0.190
	Post	58.33 (45.84 -79.17)	45.83 (27.09 - 64.58)	0.398	0.715	0.028*
Total Fatigue	Pre	66.67 (43.06 - 80.56)	65.28 (47.92 - 78.47)	-	-	0.121
	Post	65.28 (47.92 - 78.47)	57.61 (44.51 - 63.89)	0.398	0.465	0.102

**One participant did not complete their self-report following the intervention and one participant's parent/guardian did not complete the proxy report prior to the intervention resulting in an n=9.*

Chapter 4: Discussion

The purpose of this study was to evaluate the feasibility of a virtual exercise training program for pediatric SOT patients. Participants took part in an 8-week exercise program that incorporated upper body, lower body, and core exercises. Each class was 30 minutes long and occurred thrice weekly. QoL, fatigue, daily physical activity levels, and strength were measured prior to and after the training program. The main findings are two-fold. Firstly, we were able to successfully deliver an 8-week virtual exercise program. Secondly, we showed improvements in strength as measured by the BOT-2 with no associated improvements in QoL, fatigue, or daily physical activity levels following the intervention.

4.1 Participants

Out of the 89 eligible participants, only 11 consented and participated in our study, displaying low recruitment. Some reasons that may have attributed to low recruitment include not understanding the value or importance of exercise, being fatigued (with Zoom, school, and daily life activities), and not enjoying having a structure in their schedules. Prior to participation in the exercise program, all participants underwent baseline exercise testing to ensure that it was safe for them to exercise. Treadmill protocols had to be adjusted for 2 participants due to physical limitations. Endurance time was low in these participants compared to healthy children which aligns with previous studies conducted in pediatric SOT patients.[12,52,54] Exercise capacity (VO_2) has been shown to improve following transplantation but remains at 44-70% of that of normal, healthy children.[54] Some factors that may impact exercise capacity in these patients include deconditioning, anemia, allograft dysfunction, and medications (i.e. corticosteroids). [54] In our participants, specific considerations for exercise included sensory disabilities, usage of ankle foot orthosis, potential seizures (i.e. a diagnosis of epilepsy), and lack of abdominal and core strength (i.e. Eagle Barret Syndrome).

Forty-two percent of our participants had an intellectual disability diagnosis which needed to be considered in our program design. This percentage is lower than what has been previously reported with Wightman showing that 7%-9% of pediatric heart, liver, and kidney transplant patients in their study were living with an intellectual disability.[118] Children with intellectual disabilities report lower levels of physical fitness, aerobic endurance, and strength at all stages of their life.[119,120] This may be related to mental inability and short attention span, limitations and impediment in motor development, sedentary lifestyle, and the lack of motivation to try one's best.[119,121-126] Circuits were designed to be short, easy to follow and with varying degrees of difficulty to counter the short attention span and to be inclusive of potential limitations related to motor development.

4.2 Feasibility

4.2.1 Compliance and Engagement

Despite us designing a program that was as barrier-free and accessible as possible, we still saw low compliance (number of classes attended) from our participants when compared to what has been reported in other studies.[127-133] Compliance to exercise interventions has been shown to differ between prepubertal children (91% to 100%), early pubertal children (60% to 93%), and pubertal children (65% to 73%).[127-133] Some factors that may reflect greater compliance to exercise programs seen in previous studies include shorter duration of classes (i.e. 10 to 12 minutes), repeating the same set of exercises throughout the entire program, and integrating the classes into the participants school gym class.[127-133] Reasons for our participants not attending class included being too tired after school, having play dates, being hospitalized, forgetting to charge their device, and being away on vacation with family. It is key to note that research has shown that despite compliance for exercise programs being low (less than 10% at times) these programs are integral in promoting general health and wellbeing of a patient.[134,135] This is an important consideration for our study where we saw that despite low compliance amongst our participants they also displayed increases in strength, feelings of self-confidence, and independence.

Studies have shown that self-efficacy and self-confidence, which are components of QoL, are predictors for motivation and adherence to exercise in children.[136] In our participants, QoL is lower than that of healthy children and therefore may be a reflection as to why adherence was low. Furthermore, parental involvement has been shown to be important for lifestyle-changes to occur and is associated with persistent reduction of body mass index (BMI) in overweight children.[137,138] In our study, children were encouraged to participate in the program on their own with minimal parental involvement which may have also contributed to their adherence. Parental involvement was minimal in our study to prevent any extraneous variables impacting our outcome measures. Another reason for low compliance may be due to the levels of fatigue in our participants. To our knowledge no studies have studied the direct impact of fatigue on adherence to exercise programs in youth, however, participants in our study stated that one of the biggest challenges of participating in this program was being too fatigued after school (n=6).

Engagement through WelTel was assessed by evaluating response rate to weekly text messages. Thirty nine percent of all automated messages sent over the intervention period received a response from participants. Previous research using WelTel technology in adults with HIV, tuberculosis, and asthma has shown that the average number of responses to the automated messages were 57%, 68%, and 76%, respectively.[101,102,139-141] Our findings also show a lower response rate than what has been previously reported in a group of SOT adolescents in our institution (68%).[101] Lower response rates in our participants may be due to the fact that they were seeing us (the exercise leader and exercise physiologist) on multiple occasions throughout the week and did not feel the need to respond. Of note participants who were diagnosed with depression and/or anxiety had a greater response rate than other participants which suggests that WelTel may serve as a means of support. The majority of participants stated that they found it useful to be able to text their health care team. Potentially, having access and communication with the health care team when needed may be viewed as a benefit. Families who lived further away expressed the importance given that the hospital was not easily accessible for them.

4.2.2 Acceptability and Practicality

Acceptability of the program was an important outcome to consider. We considered the following to determine acceptability of the exercise program; satisfaction, intent to continue and perceived appropriateness.[142] Our exit interview found that participants were satisfied with the exercise program and would recommend it to others. One participant commented that the program was tailored to a younger demographic and wanted it to be more inclusive towards adolescents. Change to some of the exercises and methods to engage adolescent participants may include increasing interaction between exercise leader and participants or between participants themselves, using music throughout the class, creating themed classes, and including challenges throughout the circuits as motivators.

Intent to continue to be a part of the program was reflected in several responses from parents/guardians of the participants. Parents felt the program was beneficial both physically and socially and that they would like to enrol their child into another program like ours if one was available in the future. We had one parent specifically who, prior to this program, indicated that they had a negative relationship with the hospital and viewed it as a place of trauma. Following this program, this parent described that their interactions with our team throughout the study had been very positive. They also stated that they saw the benefits that the program had on their child and would enrol their child into a similar program if it were to be offered.

The practicality of the program was also evaluated. The program was created with an appropriate intensity, frequency, and duration.[142] The majority of participants found the program to be of appropriate difficulty, duration, and frequency, with only a couple suggesting that changes should be made to the program. Exercises that participants found to be difficult included supermans and sit-ups whereas the easier exercises included high knees, jumping jacks, and push-ups. Participants may have found certain exercises to be more difficult over others due to their history with exercise, where exercises that they were more familiar with were deemed to be easier (i.e. jumping jacks) and exercises that they were less familiar with (i.e. supermans) were more difficult. Our study design, as a whole, had to be modified during the program. Originally, the program was designed to using a periodization model, with each week displaying an increase in time spent on exercising up until the 4th week where we would unload. When trying to periodize the program, it was found that certain exercises were too rushed making the transitions less seamless. This in turn made the classes feel as though they were less enjoyable and more challenging for our participants. Due to the difficulty of the periodized model, we adjusted workloads more gradually and were more mindful of choosing impactful exercises being taught. We also decreased the number of different exercises that were introduced each class to simplify the lesson plan (i.e. decreasing total from 4 exercises per circuit to 3).

Cost per patient is another important component to consider when deciding on whether the program was practical.[142] This exercise program cost $1,836 per participant and required 580 hours of persons' time which included the exercise leader, exercise physiologist and study coordinator. When compared to a previous 16-week exercise program run at BCCH that cost $6,000 per patient and required 3,000 hours of persons time, this 8-week virtual exercise program can be considered a cost-efficient method of delivery.[21] These results are similar to that of Patel's study that showed home-based exercise programs yielding significant improvements in endurance time, maximal oxygen uptake, and strength at a much lower cost ($250/person) than the hospital programs.[24] This difference in cost can be attributed to having less involvement of different members of the health care team and delivering this program fully online without the need of additional equipment or space. Therefore, due to the acceptance and practicality of this program, we can deem this program to be feasible.

4.3 Strength Measures

Strength is an important consideration in SOT patients. SOT patients are at risk of osteoporosis due to muscle wasting from the immunosuppression therapy as well as the long periods of inactivity prior to transplantation.[10] Studies have shown that diminished exercise capacity has also been associated with peripheral muscle dysfunction and muscle deconditioning post-transplant.[61] Given the low bone mineral density of this population strength training can provide a safe and effective stimulus for increased bone mineralization.[1,17,19] In addition, strength training has been shown to lead to psychosocial benefits such as increased self-efficacy, self-esteem, and social skills.[29,143-145]

The current study evaluated strength through virtual administration of the BOT-2. Our virtual delivery of the BOT-2 was the first of its kind and was done to reduce barriers of participation which was especially important in the middle of the COVID-19 global pandemic. Although virtual administration of the BOT-2 was successful, some challenges that came with it included ensuring that there was proper set-up of the camera in order to see the participants entire body and ensuring that participants had proper measuring tools (i.e. a tape measure for the standing long jump).

Participants increased their strength over the 8-week exercise intervention with significant improvements in the number of push-ups, sit ups and wall sit duration. V-ups were noted to be the most difficult exercise and there was no significant improvement in scores for this specific exercise after the program. Our findings are similar to a previous study led by Deliva and colleagues who showed an improvement in strength following a 3 month physiotherapy program in heart and lung transplant patients.[38] Strength was measured through the use of a dynamometer rather than the BOT-2.

4.4 Questionnaire Findings

4.4.1 PAQ Scores

Physical activity has been shown to have numerous benefits, including improving QoL, fatigue levels, and strength, all of which are outcome measures in this study.[146-150] Pediatric SOT patients report lower levels of physical activity than healthy children (2.87).[112] Previous small reports have measured physical activity by organ transplant type. Hamiwka et al reported that pediatric kidney transplant patients (n=20) had a mean PAQ score of 2.8 +/- 0.8while Patterson et al reported with a median PAQ score of 3.1 in pediatric liver transplant patients (n=9).[151,152] Lui et al reported no differences in PAQ scores for SOT adolescents, with scores of 2.3 (1.9 – 3.2) for heart transplant patients (n=16), 2.1 (1.6 – 2.8) for kidney transplant patients (n=29), and 2.2 (1.9 – 3.0) for liver transplant patients (n=13).[18] Due to small numbers in our study, we cannot conclude with certainty that there were no differences between transplant specific PAQ scores or that there were no correlations between PAQ scores and total QoL or total fatigue scores. Unlike other studies that have showed lower PAQ levels with increased age, there were no correlations between age and PAQ scores in our participants.[18,153] This lack of correlation may have also been due to our small sample size.

PAQ scores in our participants were unchanged following the intervention even though participants were taking part in a thrice weekly exercise class which would be an addition to whatever exercise and physical activity they were doing before. Despite participants stating that the program increased their daily physical activity, encouraged them to do exercise on their own and be more active during recess and lunch, this was not reflected in their PAQ score. The PAQ reflects physical activity completed within the previous 7 days. Thus, participants who completed their post-assessment PAQ more than a week after the end of the program would not have the program reflected in their scores. Challenges in 7-day recall may also result in inaccurate reporting of activities which in turn may skew the results.[154] Future studies could use accelerometers to objectively measure physical activity .

Participants in our study who were clinically diagnosed with obesity displayed greater PAQ scores despite research showing opposing results.[155] Overweight and obese children are found to be less physically active than their peers with normal body weight. [156,157] Participants who were diagnosed with depression and/or anxiety displayed the lowest PAQ scores when compared to other participants. Multiple studies have shown that adolescents who participate in more physical activity at school report lower rate of depressive symptoms than those diagnosed with depression.[158-161]

4.4.2 Quality of Life

Contrary to previous studies that have shown improvements in QoL after exercise training, our exercise intervention did not show similar improvements.[12,162-164] Using the PedsQL as a measure of QoL, we found that the pediatric SOT patients self-report a QoL that is lower than healthy children at baseline and after the exercise intervention. Our findings are similar to other studies that have reported a lower QoL in SOT patients.[75,76,165] Factors that may be contributing to low QoL in SOT patients may be: low self-concept and self-esteem, physical symptoms such as headaches and fatigue, and fears and worry about future health, all components measured in the PedsQL.[77] Chronic illnesses, such as a SOT, also impose restrictions on social activities which can in turn impact social development and lead to poor social competence and lower QoL.[72,78,166,167] Another consideration is that studies that have shown improved QoL following exercise programs have used other measures including the Medical Outcomes Study Short Form Questionnaire and the EuroQol5-Dimension5-Level which may be a contributing factor as to why our results are different.[162-164]

Of note, two participants were hospitalized during this intervention for different reasons. This prevented them from participating in the program and possibly contributed to the low and stable QoL amongst pre- and post-intervention scores. Although scores from the PedsQL show no differences pre- and post-intervention, majority of participants either agreed or strongly agreed that the exercise intervention increased their overall wellbeing. They felt more energetic, independent, and confident with exercise. This may reflect the insensitivity of the PedsQL to detect subtle changes in QoL or may be related to the timing of survey completion as not all participants completed the PedsQL within a week of study completion. Some participants took as long as a month after the end of the program to complete the questionnaire (n=3).

Parent-proxy scores were lower than self-report scores suggesting that the parents/guardians of the participants perceive their child's QoL to be lower than what participants feel themselves. Lower parent-proxy scores have previously been reported. [75]

Childhood illness is a source of stress for the family and exposes family members to a greater risk of developing psychosocial difficulties.[168] This parental stress has been found to be negatively associated with their perceptions of their child's QoL and may provide some explanation for our finding.[169]

4.4.3. Fatigue Levels

Using the PedsQL-Fatigue Scale as a measure of fatigue, participants reported higher levels of fatigue when compared to healthy children but scores were comparable to other chronically ill children (Type 1 Diabetes: 73.46 ± 17.95, Cancer: 68.54 ±17.08, Rheumatology Diseases: 73.82 ± 21.93, and Sickle Cell Disease: 61.10 ± 19.8).[91,115,170,171] Parent proxy-reports also displayed high levels of fatigue, pre- and post-intervention, which is also consistent with previous research conducted in parents/guardians of chronically ill children (Type 1 Diabetes: 73.79 ± 16.91, Cancer: 72.79 ±18.24, Rheumatology Diseases: 72.53 ± 21.11, and Sickle Cell Disease: 67.40 ± 21.50).[91,115,170,171] Fatigue is one of the factors that is most frequently reported in having a large impact on the QoL of patients with chronic medical conditions, such as a transplant.[75,88] There are few studies that examine fatigue specifically in pediatric SOT patients, however, studies that have examined fatigue in chronic medical conditions have showed that both the parent/guardian and the child themselves perceive more fatigued. [91,115,170,171] Fatigue can cause major disruptions in a child's development and social participation, which in turn may also be reflected in their QoL and participation in exercise.[92,172-175] Fatigue might not necessarily be a disease-specific process but something that persists despite low disease activity.[174,176] Our participants all displayed high fatigue levels despite having varying levels of disease activity and additional medical considerations. Previous studies have shown that feelings of tiredness and fatigue are problematic in pediatric SOT patients and that there was acceptance that this was a part of their daily life.[177] Similar thoughts were displayed amongst our participants who stated that the biggest obstacle for them in the program was having the energy to show up to class itself as they often felt very tired after school and would rely on naps to get them through the rest of the day.

4.5 Limitations

Our study was limited by its small sample size. A small sample size may undermine the internal and external validity of the study and raise an issue of generalizability with whether the results seen in this study are representative of the entire pediatric SOT population. All eligible participants were emailed consent and assent forms and were contacted via phone call as well. Only 13% of all eligible participants participated in the study. Many patients simply did not answer (n=46) and those that did were uninterested in exercise, were too busy or felt too fatigued after school to take part in an exercise class or were ‘Zoom fatigued”. Patients in the MOT clinic were more likely to be interested in the study if they were approached in clinic. However, MOT clinic only occurs once a week with most patients having their appointment once every 6 months which limits the ability to reach all patients if recruiting solely from the clinic. There is also some suggestion that the SOT population is over-sampled, meaning that these patients are being frequently asked to participate in different studies, which may also contribute to them not wanting to participate. In addition, exercise training programs often have less uptake as they require more commitment and time than most other studies.

Another limitation in this study is understanding whether a learning effect or a training effect led to an increase in the BOT-2 scale scores. The BOT-2 was administered at the very beginning of the study, prior to the exercise program itself. It is possible that some of the improvements in strength are related to more familiarity with the BOT-2. For future studies, the

BOT-2 can be administered more than once prior to the intervention to tease out any learning effects.

There is an inherent challenge with self-report questionnaires in children which may be reflected in the results seen in all administered questionnaires (PAQ, PedsQL, PedsQL-Fatigue). Participants were encouraged to complete the self-report questionnaires completely on their own and thus, there is a possibility that certain components and/or questions were misunderstood and answered incorrectly. Furthermore, as mentioned previously, children have a desire to please adults, and thus, when answering the questionnaires, participants may have responded in a more positive manner believing that this would lead to a desirable outcome.

4.6 Future Directions

For future programs, dividing the children into two groups based on their age (one group with children below the ages of 13 and another group with children 13 years and older) would perhaps lead to greater engagement because methods of delivering the exercise program may be tailored to specific age categories. In our study, older participants were able to grasp the exercises quicker and were able to easily understand how to complete an exercise with proper form. However, it is also important to note that age does not always correspond to appropriate physical and cognitive development and thus, another way to divide participants would be based off these two factors instead of their age. Developmental differences can be challenging when teaching exercise classes for a wide age-range of children so if participants are split into groups of similar physical and cognitive development, greater engagement may be seen.

Furthermore, instead of altering the time (i.e. changing the amount of time doing the exercise vs. the time resting) and focusing on a periodized model, it would be of more benefit to alter the difficulty of or types of exercises used in a gradual manner. For example, for future studies it would be better to focus on a progression of a plank vs. to focus on the duration that the plank is held for. As mentioned previously, changing the exercise time in our study came with the challenge of participants being unable to do certain exercises while also feeling too fatigued for the next exercise in the circuit. Thus, we found that when the progression was in the type of exercise that was performed, and was small and gradual, participants were better able to understand what was being asked of them and were able to complete majority of the exercises in the circuit back-to-back.

Additional considerations for future exercise programs may include components of socialization with other participants (i.e. allowing participants to keep their microphones on or setting aside time each class for participants to share how their day was) and creating more engaging teaching methods. Many participants stated that they enjoyed meeting other children who had gone through a similar experience but had wished that they had more opportunities to talk to them to get to know each other better. Participants stated that they would prefer exercising to music which we did not use in our study to ensure that participants were able to hear the instructions of the exercise and timer countdown. However, if clear instructions are given in the beginning, and participants understand what the exercises entail, then perhaps playing music throughout the circuit would still create a safe environment while also making it more fun for participants.

The use of qualitative methods to provide feedback for any future studies may also be of benefit. The exit interview conducted at the end of the intervention provided us with feedback about the acceptability and practicality of the program which was not measured elsewhere. Comments made throughout the interview also provided us with a better perspective on how the patient genuinely felt about the program and the impact that the program has had on them outside of the scope of what was asked in the questionnaires.

Lastly, a crossover design may be used for future studies. This would allow for the collection of control data and the ability to compare to results that were found following the intervention. Having a control group would be important in allowing of confirmation that the results of the study are due to the manipulation of the independent variable(s), which in our study would be the presence of exercise, rather than the impact of extraneous variables.[178] This would lead to a better understanding of the impact that that intervention itself has on participants.

4.7 Conclusion

An 8-week virtual exercise program is feasible within pediatric SOT patients. This program was practical and appropriate (i.e. intensity, frequency, and duration). The program was also accepted by participants who stated that they enjoyed the program, would recommend it to others, and participate in similar programs in the future. Increases in strength were seen following participation with no changes in QoL, fatigue, or daily physical activity levels. Despite not seeing changes in QoL or fatigue, participants stated that this program increased their overall wellbeing and made them feel more energetic and confident in themselves and their ability to exercise.

Bibliography

1 Mathur, S. *et al.* Meeting report: consensus recommendations for a research agenda in exercise in solid organ transplantation. *Am J Transplant* **14**, 2235-2245, doi:10.1111/ajt.12874 (2014).

2 Caspersen, C. J., Powell, K. E. & Christenson, G. M. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* **100**, 126-131 (1985).

3 Deliva, R. D. *et al.* The World Transplant Games: an incentive to improve physical fitness and habitual activity in pediatric solid organ transplant recipients. *Pediatr Transplant* **18**, 889-895, doi:10.1111/petr.12370 (2014).

4 Chinnock, R. E. *et al.* Developmental outcomes after pediatric heart transplantation. *J Heart Lung Transplant* **27**, 1079-1084, doi:10.1016/j.healun.2008.07.012 (2008).

5 Patterson, C. *et al.* Physical activity experiences in children post-liver transplant: Developing a foundation for rehabilitation interventions. *Pediatr Transplant* **22**, e13179, doi:10.1111/petr.13179 (2018).

6 Martin-Moreno, P. L., Shin, H. S. & Chandraker, A. Obesity and Post-Transplant Diabetes Mellitus in Kidney Transplantation. *J Clin Med* **10**, doi:10.3390/jcm10112497 (2021).

7 Bondi, B. C. *et al.* Incidence and Risk Factors of Obesity in Childhood Solid-Organ Transplant Recipients. *Transplantation* **104**, 1644-1653, doi:10.1097/TP.0000000000003025 (2020).

8 Garro, R., Warshaw, B. & Felner, E. New-onset diabetes after kidney transplant in children. *Pediatr Nephrol* **30**, 405-416, doi:10.1007/s00467-014-2830-7 (2015).

9 Kulak, C. A., Cochenski Borba, V. Z., Kulak, J. & Ribeiro Custodio, M. Osteoporosis after solid organ transplantation. *Minerva Endocrinol* **37**, 221-231 (2012).

10 Song, L., Xie, X. B., Peng, L. K., Yu, S. J. & Peng, Y. T. Mechanism and Treatment Strategy of Osteoporosis after Transplantation. *Int J Endocrinol* **2015**, 280164, doi:10.1155/2015/280164 (2015).

11 Janaudis-Ferreira, T. *et al.* The effects of exercise training in adult solid organ transplant recipients: A systematic review and meta-analysis. *Transpl Int* **34**, 801-824, doi:10.1111/tri.13848 (2021).

12 Janaudis-Ferreira, T. *et al.* Exercise for Solid Organ Transplant Candidates and Recipients: A Joint Position Statement of the Canadian Society of Transplantation and CAN-RESTORE. *Transplantation* **103**, e220-e238, doi:10.1097/TP.0000000000002806 (2019).

13 Lu, P. W. *et al.* Bone mineral density of total body, spine, and femoral neck in children and young adults: a cross-sectional and longitudinal study. *J Bone Miner Res* **9**, 1451-1458, doi:10.1002/jbmr.5650090918 (1994).

14 Southard, R. N. *et al.* Bone mass in healthy children: measurement with quantitative DXA. *Radiology* **179**, 735-738, doi:10.1148/radiology.179.3.2027984 (1991).

15 Zanchetta, J. R., Plotkin, H. & Alvarez Filgueira, M. L. Bone mass in children: normative values for the 2-20-year-old population. *Bone* **16**, 393S-399S, doi:10.1016/8756-3282(95)00082-o (1995).

16 Braith, R. W., Mills, R. M., Welsch, M. A., Keller, J. W. & Pollock, M. L. Resistance exercise training restores bone mineral density in heart transplant recipients. *J Am Coll Cardiol* **28**, 1471-1477, doi:10.1016/s0735-1097(96)00347-6 (1996).

17 Boot, A. M., de Ridder, M. A., Pols, H. A., Krenning, E. P. & de Muinck Keizer-Schrama, S. M. Bone mineral density in children and adolescents: relation to puberty, calcium intake, and physical activity. *J Clin Endocrinol Metab* **82**, 57-62, doi:10.1210/jcem.82.1.3665 (1997).

18 Lui, S. *et al.* Physical activity and its correlates in a pediatric solid-organ transplant population. *Pediatr Transplant* **24**, e13745, doi:10.1111/petr.13745 (2020).

19 McKenzie, K. J., McKenzie, D. C. & Yoshida, E. M. Solid organ transplant recipients: clinical considerations in the application of exercise. *Br J Sports Med* **49**, 76-78, doi:10.1136/bjsports-2014-093583 (2015).

20 Diep, J. T., Kerr, L. D., Barton, C. & Emre, S. Musculoskeletal manifestations in liver transplantation recipients. *J Clin Rheumatol* **14**, 257-260, doi:10.1097/RHU.0b013e3181870212 (2008).

21 Potts, J. E. D., H. J.; Potts, M. T.; DeSouza, E.; McKenzie, D. C.; Sandor, G. G. S. The results of a 16-week exercise rehabilitation program in children with post-operative congenital heart disease. *Cardiology Young* (2001).

22 Langer, D. *et al.* Exercise training after lung transplantation improves participation in daily activity: a randomized controlled trial. *Am J Transplant* **12**, 1584-1592, doi:10.1111/j.1600-6143.2012.04000.x (2012).

23 Ihle, F. *et al.* Effect of inpatient rehabilitation on quality of life and exercise capacity in long-term lung transplant survivors: a prospective, randomized study. *J Heart Lung Transplant* **30**, 912-919, doi:10.1016/j.healun.2011.02.006 (2011).

24 Patel, J. N. *et al.* Improved exercise performance in pediatric heart transplant recipients after home exercise training. *Pediatr Transplant* **12**, 336-340, doi:10.1111/j.1399-3046.2007.00806.x (2008).

25 Dew, M. A. *et al.* Meta-analysis of medical regimen adherence outcomes in pediatric solid organ transplantation. *Transplantation* **88**, 736-746, doi:10.1097/TP.0b013e3181b2a0e0 (2009).

26 Martin, J. E. & Dubbert, P. M. Exercise applications and promotion in behavioral medicine: current status and future directions. *J Consult Clin Psychol* **50**, 1004-1017, doi:10.1037//0022-006x.50.6.1004 (1982).

27 Prasad, S. A. C., F. J. . Factors that influence adherence to exercise and their effectiveness: application to cystic fibrosis. . *Pediatric pulmonology* **34**, 66-72 (2002).

28 Weiss, M. R. Motivating kids in physical activity. *President's Council on Physical Fitness and Sports Research Digest.* (2000).

29 Faigenbaum, A. D. Strength training for children and adolescents. *Clinics in sports medicine.* **19**, 593-619 (2000).

30 Weltman, A. J., C.; Rians, C. B.; Strand, K.; Katch, F, I. The effects of hydraulic-resistance strength training on serum lipid levels in prebubertal boys. *American Journal of Diseases of Children.* **141**, 777-780 (1987).

31 Weltman, A. *et al.* The effects of hydraulic resistance strength training in pre-pubertal males. *Med Sci Sports Exerc* **18**, 629-638 (1986).

32 Fripp, R. R. & Hodgson, J. L. Effect of resistive training on plasma lipid and lipoprotein levels in male adolescents. *J Pediatr* **111**, 926-931, doi:10.1016/s0022-3476(87)80221-4 (1987).

33 Morris, F. L. N., G. A.; Gibbs, J. L.; Carlson, J. S.; Wark, J.D. . Prospective ten-month exercise intervention in premenarcheal girls: positive effects of bone and lean mass. *Journal of bone and mineral research.* **12**, 1453-1462 (1997).

34 Holloway, J. B. B., A.; Duda, J. L. Self-efficacy and training in adolescent girls. *Journal of Applied Social Psychology.* **18**, 699-719 (1988).

35 Daniels, M. W., Wilson, D. M., Paguntalan, H. G., Hoffman, A. R. & Bachrach, L. K. Bone mineral density in pediatric transplant recipients. *Transplantation* **76**, 673-678, doi:10.1097/01.TP.0000076627.70050.53 (2003).

36 Terpstra, A. M. *et al.* Bone density and cortical structure after pediatric renal transplantation. *J Am Soc Nephrol* **23**, 715-726, doi:10.1681/ASN.2011050480 (2012).

37 Longmuir, P. E. *et al.* The Canadian Assessment of Physical Literacy: methods for children in grades 4 to 6 (8 to 12 years). *BMC Public Health* **15**, 767, doi:10.1186/s12889-015-2106-6 (2015).

38 Deliva, R. D. *et al.* Effects of an acute, outpatient physiotherapy exercise program following pediatric heart or lung transplantation. *Pediatr Transplant* **16**, 879-886, doi:10.1111/petr.12003 (2012).

39 Dharnidharka, V. R., Fiorina, P. & Harmon, W. E. Kidney transplantation in children. *N Engl J Med* **371**, 549-558, doi:10.1056/NEJMra1314376 (2014).

40 Dobbels, F. *et al.* Adherence to the immunosuppressive regimen in pediatric kidney transplant recipients: a systematic review. *Pediatr Transplant* **14**, 603-613, doi:10.1111/j.1399-3046.2010.01299.x (2010).

41 Hsu, D. T. Biological and psychological differences in the child and adolescent transplant recipient. *Pediatr Transplant* **9**, 416-421, doi:10.1111/j.1399-3046.2005.00352.x (2005).

42 Kamath, B. M. & Olthoff, K. M. Liver transplantation in children: update 2010. *Pediatr Clin North Am* **57**, 401-414, table of contents, doi:10.1016/j.pcl.2010.01.012 (2010).

43 Muiesan, P., Vergani, D. & Mieli-Vergani, G. Liver transplantation in children. *J Hepatol* **46**, 340-348, doi:10.1016/j.jhep.2006.11.006 (2007).

44 Cuenca, A. G., Kim, H. B. & Vakili, K. Pediatric liver transplantation. *Semin Pediatr Surg* **26**, 217-223, doi:10.1053/j.sempedsurg.2017.07.014 (2017).

45 Fricker, F. J. *et al.* Heart transplantation in children: indications. Report of the Ad Hoc Subcommittee of the Pediatric Committee of the American Society of Transplantation (AST). *Pediatr Transplant* **3**, 333-342, doi:10.1034/j.1399-3046.1999.00045.x (1999).

46 Steinman, T. I. *et al.* Guidelines for the referral and management of patients eligible for solid organ transplantation. *Transplantation* **71**, 1189-1204, doi:10.1097/00007890-200105150-00001 (2001).

47 Conway, J. & Dipchand, A. I. Heart transplantation in children. *Pediatr Clin North Am* **57**, 353-373, table of contents, doi:10.1016/j.pcl.2010.01.009 (2010).

48 Kirk, R. *et al.* Registry of the International Society for Heart and Lung Transplantation: Twelfth Official Pediatric Heart Transplantation Report-2009. *J Heart Lung Transplant* **28**, 993-1006, doi:10.1016/j.healun.2009.08.008 (2009).

49 Brosig, C. *et al.* Child and family adjustment following pediatric solid organ transplantation: factors to consider during the early years post-transplant. *Pediatr Transplant* **18**, 559-567, doi:10.1111/petr.12286 (2014).

50 Epstein, S. F., R.; Khayat, A.; Unterborn, J.; Pratt, D.; Kaplan, M. Aerobic capacity is associated with 100-day outcome after hepatic transplantation. *Liver Transplantation* **10**, 418-424 (2004).

51 El-Agroudy, A. E., W; Osama, G; Ahmed, S; Mohamed, G. Weight gain after renal transplantation is a risk factor for patient and graft outcome. . *Transplantation* **77**, 1381-1385 (2004).

52 Clark, C. G., Cantell, M., Crawford, S. & Hamiwka, L. A. Accelerometry-based physical activity and exercise capacity in pediatric kidney transplant patients. *Pediatr Nephrol* **27**, 659-665, doi:10.1007/s00467-011-2054-z (2012).

53 Krasnoff, J. B., Mathias, R., Rosenthal, P. & Painter, P. L. The comprehensive assessment of physical fitness in children following kidney and liver transplantation. *Transplantation* **82**, 211-217, doi:10.1097/01.tp.0000226160.40527.5f (2006).

54 Williams, T. J. & McKenna, M. J. Exercise limitation following transplantation. *Compr Physiol* **2**, 1937-1979, doi:10.1002/cphy.c110021 (2012).

55 Christos, S. C. *et al.* Hemodynamic responses to upright exercise of adolescent cardiac transplant recipients. *J Pediatr* **121**, 312-316, doi:10.1016/s0022-3476(05)81213-2 (1992).

56 Bovard, J. M. *et al.* Physiological Responses to Exercise in Pediatric Heart Transplant Recipients. *Med Sci Sports Exerc* **51**, 850-857, doi:10.1249/MSS.0000000000001889 (2019).

57 Mathur, S., Reid, W. D. & Levy, R. D. Exercise limitation in recipients of lung transplants. *Phys Ther* **84**, 1178-1187 (2004).

58 Singh, T. P., Curran, T. J. & Rhodes, J. Cardiac rehabilitation improves heart rate recovery following peak exercise in children with repaired congenital heart disease. *Pediatr Cardiol* **28**, 276-279, doi:10.1007/s00246-006-0114-0 (2007).

59 Painter, P. L. *et al.* A randomized trial of exercise training after renal transplantation. *Transplantation* **74**, 42-48, doi:10.1097/00007890-200207150-00008 (2002).

60 Baumgartner, H. *et al.* ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J* **31**, 2915-2957, doi:10.1093/eurheartj/ehq249 (2010).

61 Hall, M. J. *et al.* Exercise, potassium, and muscle deconditioning post-thoracic organ transplantation. *J Appl Physiol (1985)* **77**, 2784-2790, doi:10.1152/jappl.1994.77.6.2784 (1994).

62 LaPier, T. K. Glucocorticoid-induced muscle atrophy. The role of exercise in treatment and prevention. *J Cardiopulm Rehabil* **17**, 76-84, doi:10.1097/00008483-199703000-00002 (1997).

63 Hickson, R. C., Czerwinski, S. M., Falduto, M. T. & Young, A. P. Glucocorticoid antagonism by exercise and androgenic-anabolic steroids. *Med Sci Sports Exerc* **22**, 331-340 (1990).

64 Cheng, C. J., Kuo, E. & Huang, C. L. Extracellular potassium homeostasis: insights from hypokalemic periodic paralysis. *Semin Nephrol* **33**, 237-247, doi:10.1016/j.semnephrol.2013.04.004 (2013).

65 Nytroen, K. *et al.* High-intensity interval training improves peak oxygen uptake and muscular exercise capacity in heart transplant recipients. *Am J Transplant* **12**, 3134-3142, doi:10.1111/j.1600-6143.2012.04221.x (2012).

66 Lands, L. C. *et al.* Maximal exercise capacity and peripheral skeletal muscle function following lung transplantation. *J Heart Lung Transplant* **18**, 113-120, doi:10.1016/s1053-2498(98)00027-8 (1999).

67 Chi, M. M. *et al.* Effects of detraining on enzymes of energy metabolism in individual human muscle fibers. *Am J Physiol* **244**, C276-287, doi:10.1152/ajpcell.1983.244.3.C276 (1983).

68 Proctor, D. N., Sinning, W. E., Walro, J. M., Sieck, G. C. & Lemon, P. W. Oxidative capacity of human muscle fiber types: effects of age and training status. *J Appl Physiol (1985)* **78**, 2033-2038, doi:10.1152/jappl.1995.78.6.2033 (1995).

69 Fredriksen, P. M. *et al.* Effect of physical training in children and adolescents with congenital heart disease. *Cardiol Young* **10**, 107-114, doi:10.1017/s1047951100006557 (2000).

70 Anthony, S. J., Pollock Barziv, S. & Ng, V. L. Quality of life after pediatric solid organ transplantation. *Pediatr Clin North Am* **57**, 559-574, table of contents, doi:10.1016/j.pcl.2010.01.006 (2010).

71 PROPOSALS FOR THE CONSTITUTION OF the World Health Organization. *Off Rec World Health Organ* **50**, 69-75 (1948).

72 Qvist, E. *et al.* Psychosocial adjustment and quality of life after renal transplantation in early childhood. *Pediatr Transplant* **8**, 120-125, doi:10.1046/j.1399-3046.2003.00121.x (2004).

73 Overbeck, I. *et al.* Changes in quality of life after renal transplantation. *Transplant Proc* **37**, 1618-1621, doi:10.1016/j.transproceed.2004.09.019 (2005).

74 Davis, I. D. Pediatric renal transplantation: back to school issues. *Transplant Proc* **31**, 61S-62S, doi:10.1016/s0041-1345(99)00131-1 (1999).

75 Anthony, S. J. *et al.* Child and parental perspectives of multidimensional quality of life outcomes after kidney transplantation. *Pediatr Transplant* **14**, 249-256, doi:10.1111/j.1399-3046.2009.01214.x (2010).

76 Bucuvalas, J. C. *et al.* Health-related quality of life in pediatric liver transplant recipients: A single-center study. *Liver Transpl* **9**, 62-71, doi:10.1053/jlts.2003.50012 (2003).

77 Ng, V. N., D.; Dhawan, A.; Yazigi, N.; Ee, L.; Stormon, M.; PeLTQL study group. Development and Validation of the Pediatric Liver Transplantation Quality of Life: A Disease-Specific Quality of Life Measure for Pediatric Liver Transplant Recipients. *The Journal of pediatrics* **165**, 547-555 (2014).

78 Uzark, K. C. *et al.* The psychosocial impact of pediatric heart transplantation. *J Heart Lung Transplant* **11**, 1160-1167 (1992).

79 Wray, J., Radley-Smith, R. & Yacoub, M. Effect of cardiac or heart-lung transplantation on the quality of life of the paediatric patient. *Qual Life Res* **1**, 41-46, doi:10.1007/BF00435434 (1992).

80 Lawrence, K. S. & Fricker, F. J. Pediatric heart transplantation: quality of life. *J Heart Transplant* **6**, 329-333 (1987).

81 DeMaso, D. R., Twente, A. W., Spratt, E. G. & O'Brien, P. Impact of psychologic functioning, medical severity, and family functioning in pediatric heart transplantation. *J Heart Lung Transplant* **14**, 1102-1108 (1995).

82 DeMaso, D. R., Douglas Kelley, S., Bastardi, H., O'Brien, P. & Blume, E. D. The longitudinal impact of psychological functioning, medical severity, and family functioning in pediatric heart transplantation. *J Heart Lung Transplant* **23**, 473-480, doi:10.1016/S1053-2498(03)00215-8 (2004).

83 Pollock-BarZiv, S. M., Anthony, S. J., Niedra, R., Dipchand, A. I. & West, L. J. Quality of life and function following cardiac transplantation in adolescents. *Transplant Proc* **35**, 2468-2470, doi:10.1016/j.transproceed.2003.08.028 (2003).

84 Wray, J. & Radley-Smith, R. Longitudinal assessment of psychological functioning in children after heart or heart-lung transplantation. *J Heart Lung Transplant* **25**, 345-352, doi:10.1016/j.healun.2005.09.018 (2006).

85 Marcus, S. B. *et al.* Fatigue and health-related quality of life in pediatric inflammatory bowel disease. *Clin Gastroenterol Hepatol* **7**, 554-561, doi:10.1016/j.cgh.2009.01.022 (2009).

86 Graef, D. M. *et al.* Sleepiness, Fatigue, Behavioral Functioning, and Quality of Life in Survivors of Childhood Hematopoietic Stem Cell Transplant. *J Pediatr Psychol* **41**, 600-609, doi:10.1093/jpepsy/jsw011 (2016).

87 Huang, I. A., M; Gandhi, P; Tuli, S; Krull, K; Lai, J; Shenkman, E. The relationships between fatigue, quality of life, and family impact among children with special health care needs. *Journal of pediatric psychology* **38**, 722-731 (2013).

88 Petersen, I. *et al.* Fatigue in pediatric liver transplant recipients and its impact on their quality of life. *Pediatr Transplant* **23**, e13331, doi:10.1111/petr.13331 (2019).

89 Fergusson, D. H., J; Ridder, E. Show me the child at seven II: childhood intelligence and later outcomes in adolescence and young adulthood. *Journal of Child Psychology and Psychiatry* **46**, 850-858 (2005).

90 Gold, J. I., Mahrer, N. E., Yee, J. & Palermo, T. M. Pain, fatigue, and health-related quality of life in children and adolescents with chronic pain. *Clin J Pain* **25**, 407-412, doi:10.1097/AJP.0b013e318192bfb1 (2009).

91 Varni, J. W., Burwinkle, T. M., Katz, E. R., Meeske, K. & Dickinson, P. The PedsQL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. *Cancer* **94**, 2090-2106, doi:10.1002/cncr.10428 (2002).

92 Nap-van der Vlist, M. M. *et al.* Fatigue in childhood chronic disease. *Arch Dis Child* **104**, 1090-1095, doi:10.1136/archdischild-2019-316782 (2019).

93 Palermo, T. M., de la Vega, R., Murray, C., Law, E. & Zhou, C. A digital health psychological intervention (WebMAP Mobile) for children and adolescents with chronic pain: results of a hybrid effectiveness-implementation stepped-wedge cluster randomized trial. *Pain* **161**, 2763-2774, doi:10.1097/j.pain.0000000000001994 (2020).

94 Looman, W. S., Hullsiek, R. L., Pryor, L., Mathiason, M. A. & Finkelstein, S. M. Health-Related Quality of Life Outcomes of a Telehealth Care Coordination Intervention for Children With Medical Complexity: A Randomized Controlled Trial. *J Pediatr Health Care* **32**, 63-75, doi:10.1016/j.pedhc.2017.07.007 (2018).

95 Bradford, N. L. A., N. R.; Young, J. & Smith, A. C. Paediatric palliative care by video consultation at home: a cost minimisation analysis. *BMC health services research* **14**, 1-9 (2014).

96 Cady, R., Finkelstein, S. & Kelly, A. A telehealth nursing intervention reduces hospitalizations in children with complex health conditions. *J Telemed Telecare* **15**, 317-320, doi:10.1258/jtt.2009.090105 (2009).

97 Bird, M. L., L.; Ouellete, C.; Hopkins, K.; McGillion, M. H. & Cartern, N. Use of synchronous digital health technologies for the care of children with special health care needs and their families: scoping review. *JMIR pediatrics and parenting* **2** (2019).

98 Calcaterra, V. *et al.* "CoVidentary": An online exercise training program to reduce sedentary behaviours in children with type 1 diabetes during the COVID-19 pandemic. *J Clin Transl Endocrinol* **25**, 100261, doi:10.1016/j.jcte.2021.100261 (2021).

99 Murphy, E. C. C., L.; Neal, W.; Baylis, C.; Donley, D.; Yeater, R. Effects of an exercise intervention using Dance Dance Revolution on endothelial function and other risk factors in overweight children. *International Journal of Pediatric Obesity.* **4**, 205-214 (2009).

100 Ravi, D. K., Kumar, N. & Singhi, P. Effectiveness of virtual reality rehabilitation for children and adolescents with cerebral palsy: an updated evidence-based systematic review. *Physiotherapy* **103**, 245-258, doi:10.1016/j.physio.2016.08.004 (2017).

101 Rathgeber, S. L. *et al.* A text messaging intervention and quality of life in adolescents with solid organ transplants. *Pediatr Transplant*, e14219, doi:10.1111/petr.14219 (2022).

102 Lester, R. T. R., P.; Mills, E. J.; Kariri, A.; Karanja, S.; Chung, M. H.; Plummer, F. A. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. . *The Lancet* **376**, 1838-1845 (2010).

103 Gordon, E. J. *et al.* Prevalence and determinants of physical activity and fluid intake in kidney transplant recipients. *Clin Transplant* **24**, E69-81, doi:10.1111/j.1399-0012.2009.01154.x (2010).

104 Takahashi, A., Hu, S. L. & Bostom, A. Physical Activity in Kidney Transplant Recipients: A Review. *Am J Kidney Dis* **72**, 433-443, doi:10.1053/j.ajkd.2017.12.005 (2018).

105 Harris, P. A. *et al.* Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* **42**, 377-381, doi:10.1016/j.jbi.2008.08.010 (2009).

106 Duff, D. K., De Souza, A. M., Human, D. G., Potts, J. E. & Harris, K. C. A novel treadmill protocol for exercise testing in children: the British Columbia Children's Hospital protocol. *BMJ Open Sport Exerc Med* **3**, e000197, doi:10.1136/bmjsem-2016-000197 (2017).

107 Bruce, R. A., Blackmon, J. R., Jones, J. W. & Strait, G. Exercising Testing in Adult Normal Subjects and Cardiac Patients. *Pediatrics* **32**, SUPPL 742-756 (1963).

108 Brown, T. Structural Validity of the Bruininks-Oseretsky Test of Motor Proficiency–Second Edition (BOT-2) Subscales and Composite Scales. *Journal of Occupational Therapy, Schools, & Early Intervention* **12**, 323-353 (2019).

109 Brown, T. Structural validity of the Bruininks-Oseretsky test of motor proficiency - Second edition brief form (BOT-2-BF). *Res Dev Disabil* **85**, 92-103, doi:10.1016/j.ridd.2018.11.010 (2019).

110 Wuang, Y. P. & Su, C. Y. Reliability and responsiveness of the Bruininks-Oseretsky Test of Motor Proficiency-Second Edition in children with intellectual disability. *Res Dev Disabil* **30**, 847-855, doi:10.1016/j.ridd.2008.12.002 (2009).

111 Bruininks, R. H. B., B. D. Bruininks-Oseretsky test of motor proficiency. *AGS Publishing.* (2005).

112 Voss, C., Dean, P. H., Gardner, R. F., Duncombe, S. L. & Harris, K. C. Validity and reliability of the Physical Activity Questionnaire for Children (PAQ-C) and Adolescents (PAQ-A) in individuals with congenital heart disease. *PLoS One* **12**, e0175806, doi:10.1371/journal.pone.0175806 (2017).

113 Kowalski, K. C. C., P. R.; Donen, R. M. The physical activity questionnaire for older children (PAQ-C) and adolescents (PAQ-A) manual. *College of Kinesiology, University of Saskatchewan.* **87**, 1-38 (2004).

114 Varni, J. W. S., M.; Kurtin, P. S. PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. . *Medical care*, 800-812 (2001).

115 Panepinto, J. A. T., S.; Bendo, C. B.; McCavit, T. L.; Dinu, D.; Sherman-Bien, S.; Varni, J. W. PedsQL™ Multidimensional Fatigue Scale in sickle cell disease: feasibility, reliability, and validity. *Pediatric blood & cancer.* **61**, 171-177 (2014).

116 Bacha, R. G., S. A.; Manzoor, I.; Ahmad, I.; Shah, S. F. H. The Mechanism of Prune Belly Syndrome Development: A Sonographic Sequential Assessment. *Journal of Diagnostic Medical Sonography.* **36**, 594-603 (2020).

117 Hammond, H. K. & Froelicher, V. F. Normal and abnormal heart rate responses to exercise. *Prog Cardiovasc Dis* **27**, 271-296, doi:10.1016/0033-0620(85)90010-6 (1985).

118 Wightman, A., Bradford, M. C., Hsu, E., Bartlett, H. L. & Smith, J. M. Prevalence and Long-Term Outcomes of Solid Organ Transplant in Children with Intellectual Disability. *J Pediatr* **235**, 10-17 e14, doi:10.1016/j.jpeds.2021.03.056 (2021).

119 Golubovic, S., Maksimovic, J., Golubovic, B. & Glumbic, N. Effects of exercise on physical fitness in children with intellectual disability. *Res Dev Disabil* **33**, 608-614, doi:10.1016/j.ridd.2011.11.003 (2012).

120 Hartman, E., Smith, J., Westendorp, M. & Visscher, C. Development of physical fitness in children with intellectual disabilities. *J Intellect Disabil Res* **59**, 439-449, doi:10.1111/jir.12142 (2015).

121 Vuijk, P. J., Hartman, E., Scherder, E. & Visscher, C. Motor performance of children with mild intellectual disability and borderline intellectual functioning. *J Intellect Disabil Res* **54**, 955-965, doi:10.1111/j.1365-2788.2010.01318.x (2010).

122 Hartman, E. H., S.; Schreder, E.; Visscher, C. On the relationship between motor performance and executive functioning in children with intellectual disabilities. *Journal of Intellectual Disability Research* **54**, 468-477 (2010).

123 Frey, G. C. C., B. Relationship between BMI, physical fitness, and motor skills in youth with mild intellectual disabilities. *International journal of obesity.* **30**, 861-867 (2006).

124 Westendorp, M., Houwen, S., Hartman, E. & Visscher, C. Are gross motor skills and sports participation related in children with intellectual disabilities? *Res Dev Disabil* **32**, 1147-1153, doi:10.1016/j.ridd.2011.01.009 (2011).

125 Lotan, M., Isakov, E., Kessel, S. & Merrick, J. Physical fitness and functional ability of children with intellectual disability: effects of a short-term daily treadmill intervention. *ScientificWorldJournal* **4**, 449-457, doi:10.1100/tsw.2004.97 (2004).

126 Halle, J. W., Gabler-Halle, D. & Chung, Y. B. Effects of a peer-mediated aerobic conditioning program on fitness levels of youth with mental retardation: two systematic replications. *Ment Retard* **37**, 435-448, doi:10.1352/0047-6765(1999)037<0435:EOAPAC>2.0.CO;2 (1999).

127 MacKelvie, K. J., Petit, M. A., Khan, K. M., Beck, T. J. & McKay, H. A. Bone mass and structure are enhanced following a 2-year randomized controlled trial of exercise in prepubertal boys. *Bone* **34**, 755-764, doi:10.1016/j.bone.2003.12.017 (2004).

128 Van Langendonck, L., Claessens, A. L., Vlietinck, R., Derom, C. & Beunen, G. Influence of weight-bearing exercises on bone acquisition in prepubertal monozygotic female

twins: a randomized controlled prospective study. *Calcif Tissue Int* **72**, 666-674, doi:10.1007/s00223-002-2030-5 (2003).

129 MacKelvie, K. J. K., K. M.; Petit, M. A.; Janssen, P. A.; McKay, H. A. . A school-based exercise intervention elicits substantial bone health benefits: a 2-year randomised controlled trial in girls. *Pediatrics* **112**, 447-452 (2003).

130 McKay, H. A. M., L.; Petit, M.; MacKelvie-O'Brien, K.; Janssen, P.; Beck, T.; Khan, K. M. "Bounce at the Bell": a novel program of short bouts of exercise improves proximal femur bone mass in early pubertal children. *British Journal of Sports Medicine* **39**, 521-526 (2005).

131 Heinonen, A. *et al.* High-impact exercise and bones of growing girls: a 9-month controlled trial. *Osteoporos Int* **11**, 1010-1017, doi:10.1007/s001980070021 (2000).

132 Iuliano-Burns, S., Saxon, L., Naughton, G., Gibbons, K. & Bass, S. L. Regional specificity of exercise and calcium during skeletal growth in girls: a randomized controlled trial. *J Bone Miner Res* **18**, 156-162, doi:10.1359/jbmr.2003.18.1.156 (2003).

133 Hind, K. & Burrows, M. Weight-bearing exercise and bone mineral accrual in children and adolescents: a review of controlled trials. *Bone* **40**, 14-27, doi:10.1016/j.bone.2006.07.006 (2007).

134 Peek, K., Carey, M., Mackenzie, L. & Sanson-Fisher, R. Patient adherence to an exercise program for chronic low back pain measured by patient-report, physiotherapist-perception and observational data. *Physiother Theory Pract* **35**, 1304-1313, doi:10.1080/09593985.2018.1474402 (2019).

135 Teo, J. L. Z., Z.; Bird, S. R. Identifying the factors affecting ‘patient engagement’ in exercise rehabilitation. *BMC Sports Science, Medicine and Rehabilitation* **14**, 1-11 (2022).

136 Dos Santos, H., Bredehoft, M. D., Gonzalez, F. M. & Montgomery, S. Exercise Video Games and Exercise Self-Efficacy in Children. *Glob Pediatr Health* **3**, 2333794X16644139, doi:10.1177/2333794X16644139 (2016).

137 O'Connor, T. M., Jago, R. & Baranowski, T. Engaging parents to increase youth physical activity a systematic review. *Am J Prev Med* **37**, 141-149, doi:10.1016/j.amepre.2009.04.020 (2009).

138 Young, K. M., Northern, J. J., Lister, K. M., Drummond, J. A. & O'Brien, W. H. A meta-analysis of family-behavioral weight-loss treatments for children. *Clin Psychol Rev* **27**, 240-249, doi:10.1016/j.cpr.2006.08.003 (2007).

139 Murray, M. C. *et al.* Health care providers' perspectives on a weekly text-messaging intervention to engage HIV-positive persons in care (WelTel BC1). *AIDS Behav* **19**, 1875-1887, doi:10.1007/s10461-015-1151-6 (2015).

140 van der Kop, M. L. M., J.; Smillie, K.; Coleman, J.; Hajek, J.; Natasha Van Borek, M. A.; Marra, F. Use of the WelTel mobile health intervention at a tuberculosis clinic in British Columbia: a pilot study. *Journal of Mobile Technology in Medicine* **2**, 7-14 (2013).

141 Poureslami, I. P. *et al.* A pilot randomized controlled trial on the impact of text messaging check-ins and a web-based asthma action plan versus a written action plan on asthma exacerbations. *J Asthma*, 1-13, doi:10.1080/02770903.2018.1500583 (2018).

142 Bowen, D. J. K., M.; Spring, B.; Cofta-Woerpel, L.; Linnan, L.; Weiner, D; Fernandez, M. How we design feasibility studies. *American journal of preventative medicine.* **36**, 452-457 (2009).

143 Faigenbaum, A. D. Psychosocial benefits of prepubescent strength training. *Strength and Conditioning* **17**, 28-28 (1995).

144 Tucker, L. A. Effect of weight training on body attitudes: Who benefits most? *The Journal of Sports Medicine and Physical Fitness* **27**, 70-78 (1987).

145 Tucker, L. A. Effect of weight training on self-concept: A profile of those influenced most. *Research Quarterly for Exercise and Sport* **54**, 389-397 (1983).

146 Wu, X. Y. H., L. H.; Zhang, J. H.; Luo, S.; Hu, J. W.; Sun, K. . The influence of physical activity, sedentary behavior on health-related quality of life among the general population of children and adolescents: A systematic review. *PloS one* **12** (2017).

147 Gu, X. C., M.; Solmon, M. A. Physical activity, physical fitness, and health-related quality of life in school-aged children. . *Journal of Teaching in Physical Education* **35** (2016).

148 Oberoi, S. *et al.* Physical activity reduces fatigue in patients with cancer and hematopoietic stem cell transplant recipients: A systematic review and meta-analysis of randomized trials. *Crit Rev Oncol Hematol* **122**, 52-59, doi:10.1016/j.critrevonc.2017.12.011 (2018).

149 Gomes, T. N., Dos Santos, F. K., Katzmarzyk, P. T. & Maia, J. Active and strong: physical activity, muscular strength, and metabolic risk in children. *Am J Hum Biol* **29**, doi:10.1002/ajhb.22904 (2017).

150 Tan, V. P. *et al.* Influence of physical activity on bone strength in children and adolescents: a systematic review and narrative synthesis. *J Bone Miner Res* **29**, 2161-2181, doi:10.1002/jbmr.2254 (2014).

151 Hamiwka, L. A., Cantell, M., Crawford, S. & Clark, C. G. Physical activity and health related quality of life in children following kidney transplantation. *Pediatr Transplant* **13**, 861-867, doi:10.1111/j.1399-3046.2009.01195.x (2009).

152 Patterson, C., So, S., Schneiderman, J. E., Stephens, D. & Stephens, S. Physical activity and its correlates in children and adolescents post-liver transplant. *Pediatr Transplant* **20**, 227-234, doi:10.1111/petr.12662 (2016).

153 Sallis, J. F., Prochaska, J. J. & Taylor, W. C. A review of correlates of physical activity of children and adolescents. *Med Sci Sports Exerc* **32**, 963-975, doi:10.1097/00005768-200005000-00014 (2000).

154 Magaret, N. D. C., T. A.; Warden, C. R.; Magnusson, A.R.; Hedges, J. R. Patient satisfaction in the emergency department—a survey of pediatric patients and their parents. *Academic Emergency Medicine* **9**, 1379-1388 (2002).

155 Bervoets, L. *et al.* Reliability and Validity of the Dutch Physical Activity Questionnaires for Children (PAQ-C) and Adolescents (PAQ-A). *Arch Public Health* **72**, 47, doi:10.1186/2049-3258-72-47 (2014).

156 Wang, J. J. B., T.; Lau, W. P.; Chen, T. A.; Pitkethly, A. J. Validation of the Physical Activity Questionnaire for Older Children (PAQ-C) among Chinese Children. *Biomedical and Environmental Sciences* **29**, 177-186 (2016).

157 Molnar, D. & Livingstone, B. Physical activity in relation to overweight and obesity in children and adolescents. *Eur J Pediatr* **159 Suppl 1**, S45-55, doi:10.1007/pl00014365 (2000).

158 Rothon, C. *et al.* Physical activity and depressive symptoms in adolescents: a prospective study. *BMC Med* **8**, 32, doi:10.1186/1741-7015-8-32 (2010).

159 Steptoe, A. & Butler, N. Sports participation and emotional wellbeing in adolescents. *Lancet* **347**, 1789-1792, doi:10.1016/s0140-6736(96)91616-5 (1996).

160 Ussher, M. H. O., C. G.; Cook, D. G.; Whincup, P. H. The relationship between physical activity, sedentary behaviour and psychological wellbeing among adolescents. *Social psychiatry and psychiatric epidemiology.* **42**, 851-856 (2007).

161 Kremer, P. E., C.; Leslie, E.; Toumbourou, L. W.; Patton, G. C.; Williams, J. Physical activity, leisure-time screen use and depression among children and young adolescents. *Journal of science and medicine in sport.* **17**, 183-187 (2014).

162 Ochman, M. *et al.* Nordic Walking in Pulmonary Rehabilitation of Patients Referred for Lung Transplantation. *Transplant Proc* **50**, 2059-2063, doi:10.1016/j.transproceed.2018.02.106 (2018).

163 Didsbury, M. *et al.* Exercise training in solid organ transplant recipients: a systematic review and meta-analysis. *Transplantation* **95**, 679-687, doi:10.1097/TP.0b013e31827a3d3e (2013).

164 Williams, F. R. *et al.* Home-Based Exercise in Patients Awaiting Liver Transplantation: A Feasibility Study. *Liver Transpl* **25**, 995-1006, doi:10.1002/lt.25442 (2019).

165 Lazor, T., Grasemann, H., Solomon, M. & Anthony, S. J. Quality of life outcomes following pediatric lung transplantation. *Pediatr Pulmonol* **52**, 1495-1501, doi:10.1002/ppul.23788 (2017).

166 Madan-Swain, A. K., E. R.; LaGory, J. School and social reintegration after a serious illness or injury. *Handbook of pediatric psychology in school settings.*, 657-676 (2003).

167 Annunziato, R. A., Jerson, B., Seidel, J. & Glenwick, D. S. The psychosocial challenges of solid organ transplant recipients during childhood. *Pediatr Transplant* **16**, 803-811, doi:10.1111/j.1399-3046.2012.01749.x (2012).

168 Varni, J. W. *et al.* Effects of perceived stress on pediatric chronic pain. *J Behav Med* **19**, 515-528, doi:10.1007/BF01904901 (1996).

169 Grimaldi Capitello, T. F., C.; Placidi, S.; Vallone, R.; Drago, F.; Gentile, S. What factors influence parents' perception of the quality of life of children and adolescents with neurocardiogenic syncope? *Health and Quality of Life Outcomes* **14**, 1-9 (2016).

170 Varni, J. W., Limbers, C. A., Bryant, W. P. & Wilson, D. P. The PedsQL Multidimensional Fatigue Scale in type 1 diabetes: feasibility, reliability, and validity. *Pediatr Diabetes* **10**, 321-328, doi:10.1111/j.1399-5448.2008.00482.x (2009).

171 Varni, J. W., Burwinkle, T. M. & Szer, I. S. The PedsQL Multidimensional Fatigue Scale in pediatric rheumatology: reliability and validity. *J Rheumatol* **31**, 2494-2500 (2004).

172 Armbrust, W. *et al.* Fatigue in patients with juvenile idiopathic arthritis: A systematic review of the literature. *Semin Arthritis Rheum* **45**, 587-595, doi:10.1016/j.semarthrit.2015.10.008 (2016).

173 Walter, L. M., Nixon, G. M., Davey, M. J., Downie, P. A. & Horne, R. S. Sleep and fatigue in pediatric oncology: A review of the literature. *Sleep Med Rev* **24**, 71-82, doi:10.1016/j.smrv.2015.01.001 (2015).

174 Nijhof, N. v. d. P., E. M.; Wulffraat, N. M.; Nijhof, S. L. Prevalence of severe fatigue among adolescents with pediatric rheumatic diseases. *Arthritis Care & Research.* **68**, 108-114 (2016).

175 Nap-van der Vlist, M. M. D., G. W.; Grootenhuis, M. A.; van der Ent, K.; van den Heuvel-Eibrink, M. M.; Swart, J. F.; Nijhof, S. L. Fatigue among children with a chronic disease: a cross-sectional study. *BMJ paediatrics opn* **5** (2021).

176 Menting, J. T., C; Bleijenberg, G.; Donders, R; Droogleever Fortuyn, H. A.; Fransen, J.; Knoop, H. Is fatigue a disease-specific or generic symptom in chronic medical conditions? *Health Psychology* **37** (2018).

177 Taylor, R. M., Franck, L. S., Dhawan, A. & Gibson, F. The stories of young people living with a liver transplant. *Qual Health Res* **20**, 1076-1090, doi:10.1177/1049732310368405 (2010).

178 Street, D. L. Controlling extraneous variables in experimental research: A research note. *Accounting Education* **4**, 188 (1995).

Appendix

A.1: Individual Raw BOT-2 Scores Pre and Post Intervention (n=10)

	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1001	15	22	38	37	40	60	12	20	46.00	47.00
1004	10	15	33	50	43	60	12	16	61.00	57.00
1005	12	23	33	45	25	60	17	25	42.00	42.50
1008	8	21	23	16	35	38	14	21	42	30.00
1009	6	11	8	5	19	48	8	15	20.00	32.25
1010	12	21	15	17	40	46	14	23	37.40	33.20
1014	8	6	22	10	22	33	8	8	24.60	15.10
1016	0	4	3	14	10	10	5	5	29.00	27.00
1017	13	14	20	17	21	29	17	19	54.00	68.50
1018*	12	-	36	-	42	-	15	-	60.50	-
1019	5	19	34	45	43	60	12	26	39.40	45.50

*one participant did not complete the post-assessment BOT-2 test

A.2: Breakdown of Weekly Exercises

	Monday	Wednesday	Thursday
Week 1: 3 circuits, 20 seconds on and 20 seconds off (repeat twice)	**Circuit 1:** Punch step outs, Knee push-ups, Sit-ups, Ankle-taps **Circuit 2:** Side to sides, Knee to elbow (standing), Frog jumps, Shoulder press (no weights) **Circuit 3:** Jumping jacks, Plank, Superman, Scissors	**Circuit 1:** Jumping jacks, Planks, Sitting twists, Scissors **Circuit 2:** Punch steo-outs, Side to side, Tricep dips, Toe taps **Circuit 3:** Speed skaters, Chair pose, Bird dog, Ankle taps	**Circuit 1:** Ski jumps, Knee push-ups, Toe taps, Sitting twists **Circuit 2:** Speed skaters, Sitting chair, Bird dog, Bicycles **Circuit 3:** High knees, Knee to elbow (standing), Shoulder taps in plank position, Ankle taps
Week 2: 3 circuits, 25 seconds on and 20 seconds off (repeat twice)	**Circuit 1:** Ski jumps, Knee push-ups, Sit-ups, Ankle taps **Circuit 2:** Forward lunges, Side to side shuffles, Plank, Scissors **Circuit 3:** High knees, Bird dog, Shoulder taps, Sitting twists	**Circuit 1:** Forward lunges, High knees, Sit-ups, Flutter kicks **Circuit 2:** Frog jumps, Knee push-ups, Supermans, Sitting twist **Circuit 3:** Diamond hops, Knee to elbow (standing), Crab walks, Ankle taps	**Circuit 1:** Diamond hop, Plank circles, Mountain climber, Raised leg circles **Circuit 2:** Side leg lift (right), Side leg lift (left), Tricep dips, Flutter kicks **Circuit 3:** Speed skaters, Frog jump, Shoulder press (no weights), Elbow to knee (supine)
Week 3: 3 circuits, 25 seconds on and 15 seconds off (repeat twice)	**Circuit 1:** Frog jumps, Knee to elbow (standing), Mountain climbers, Raised leg circles **Circuit 2:** Jumping jacks, Forward lunges, Knee push-ups, Ankle taps	**Circuit 1:** Speed skaters, Forward lunges, Planks, Superman **Circuit 2:** High knees, Elbow to knee (standing), Bird dog, Flutter kicks	**Circuit 1:** Diamond hops, Squats, Knee push-ups, Sit-ups **Circuit 2:** Side leg lifts (right), Side leg lifts (left), Mountain climbers, Toe taps

	Circuit 3: Diamond hop, Squats, Crab walk, Sit-ups	**Circuit 3:** Side leg lifts (right), Side leg lifts (left), Elbow to knee crunches, Plank shoulder taps	**Circuit 3:** Jumping jacks, Forward lunges, Crab walks, Sitting twists
Week 4: 3 circuits, 25 seconds on and 20 seconds off (repeat twice)	**Circuit 1:** Twisting dabs, Y-lunges, Planks, Sit-ups **Circuit 2:** Jumping jacks, Star toe taps, Crab walk, Raised leg circles **Circuit 3:** Side leg lifts (right), Side leg lifts (left), Knee push-ups, Bird dog	**Circuit 1:** Frog jumps, Forward lunges, Superman, Banana **Circuit 2:** Ski jumps, Squats, Mountain climbers, Ankle taps **Circuit 3:** Speed skaters, Star toe taps, Tricep dip, Toe taps	**Circuit 1:** Jumping jacks, Side lunges, Crab walk, Bicycle **Circuit 2:** Side leg lift (right), Side leg lift (left), Knee push-up, Supermans **Circuit 3:** Bird dog, Sitting twists, Side crunch (right), Side crunch (left)
Week 5: 3 circuits, 30 seconds on 15 seconds off (repeat three times)	**Circuit 1:** Plank, Push-ups, Superman **Circuit 2:** Standing forward lunge (right), Standing forward lunge (left), Squats **Circuit 3:** Single leg hops (right), Single leg hops (left), Star toe taps	**Circuit 1:** Bird dog, Knee push-ups, Sit-ups **Circuit 2:** Frog jumps, Squat hold, Side to side shuffle **Circuit 3:** Toe taps, Planks, Ankle taps	**Circuit 1:** Jumping jacks, Chair pose, High knees **Circuit 2:** Knee push-ups, Side plank (right), Side plank (left) **Circuit 3:** Diamond hops, Knee plank clock, Deadbug
Week 6: 3 circuits, 30 seconds on 15 seconds off (repeat three times)	**Circuit 1:** Standing forward lunge (right), Standing forward lunge (left), Plank **Circuit 2:** Side plank (right), Side plank (left), Sit-ups **Circuit 3:** Diamond hops, Deadbug, Knee plank walks	**Circuit 1:** Burpees, Plank walks, Sitting twist **Circuit 2:** Jumping jacks, Chair pose, Side to side shuffles **Circuit 3:** Bird dog, Knee push-ups, Superman	**Circuit 1:** Speed skaters, Squat hold, Knee plank **Circuit 2:** Standing forward lunge (right), Standing forward lunge (left), Deadbug **Circuit 3:** Star jumps, Plank arm reaches, Toe taps
Week 7: 3 circuits, 30 seconds on 15 seconds off (repeat three times)	**Circuit 1:** Bird dog, Knee push-ups, Sit-ups	**Circuit 1:** Star jumps, Squat hold, Plank holds	**Circuit 1:** Standing forward lunge (right), Standing forward

	Circuit 2: Jumping jacks, Chair pose, Side shuffles **Circuit 3:** Diamond hops, Knee plank walk, Deadbug	**Circuit 2:** Speed skaters, Knee push-ups, Supermans **Circuit 3:** Diamond hop, Plank arm reaches, Sitting twists	lunge (left), Plank walks **Circuit 2:** High knees, Bird dogs, Ankle tap crunches **Circuit 3:** Frog jumps, Plank arm reaches, Toe taps
Week 8: 3 circuits, 30 seconds on 20 seconds off (repeat three times)	**Circuit 1:** Jumping jacks, Knee push-ups, Sit-ups **Circuit 2:** Frog jumps, Planks, Toe taps **Circuit 3:** Speed skaters, Chair pose, Sitting twists	**Circuit 1:** Diamond hops, Plank arm reaches, Toe taps **Circuit 2:** Star jumps, Superman, Mountain climbers **Circuit 3:** Speed skaters, Plank walks, Deadbug	**Circuit 1:** Burpees, Tricep dips, Elbow to knee crunch **Circuit 2:** Y-lunges, Knee push-ups, Ankle tap crunch **Circuit 3:** High knees, Inchworm, Scissors

A.3: Physical Activity Questionnaire (Child)

Physical Activity Questionnaire (Elementary School)

Name:_________________________ Age:___________

Sex: M_______ F_______ Grade:__________

Teacher:_______________________

We are trying to find out about your level of physical activity from ***the last 7 days*** (in the last week). This includes sports or dance that make you sweat or make your legs feel tired, or games that make you breathe hard, like tag, skipping, running, climbing, and others.

Remember:

1. There are no right and wrong answers — this is not a test.
2. Please answer all the questions as honestly and accurately as you can — this is very important.

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1. Physical activity in your spare time: Have you done any of the following activities in the past 7 days (last week)? If yes, how many times? (Mark only one circle per row.)

	No	1-2	3-4	5-6	7 times or more
Skipping	❍	❍	❍	❍	❍
Rowing/canoeing	❍	❍	❍	❍	❍
In-line skating	❍	❍	❍	❍	❍
Tag	❍	❍	❍	❍	❍
Walking for exercise	❍	❍	❍	❍	❍
Bicycling	❍	❍	❍	❍	❍
Jogging or running	❍	❍	❍	❍	❍
Aerobics	❍	❍	❍	❍	❍
Swimming	❍	❍	❍	❍	❍
Baseball, softball	❍	❍	❍	❍	❍
Dance	❍	❍	❍	❍	❍
Football	❍	❍	❍	❍	❍
Badminton	❍	❍	❍	❍	❍
Skateboarding	❍	❍	❍	❍	❍
Soccer	❍	❍	❍	❍	❍
Street hockey	❍	❍	❍	❍	❍
Volleyball	❍	❍	❍	❍	❍
Floor hockey	❍	❍	❍	❍	❍
Basketball	❍	❍	❍	❍	❍
Ice skating	❍	❍	❍	❍	❍
Cross-country skiing	❍	❍	❍	❍	❍
Ice hockey/ringette	❍	❍	❍	❍	❍
Other:					
_________________________	❍	❍	❍	❍	❍
_________________________	❍	❍	❍	❍	❍

2. In the last 7 days, during your physical education (PE) classes, how often were you very active (playing hard, running, jumping, throwing)? (Check one only.)

- I don't do PE .... ❍
- Hardly ever .... ❍
- Sometimes .... ❍
- Quite often .... ❍
- Always .... ❍

3. In the last 7 days, what did you do most of the time *at recess*? (Check one only.)

- Sat down (talking, reading, doing schoolwork)...... ❍
- Stood around or walked around .... ❍
- Ran or played a little bit .... ❍
- Ran around and played quite a bit .... ❍
- Ran and played hard most of the time .... ❍

4. In the last 7 days, what did you normally do *at lunch* (besides eating lunch)? (Check one only.)

- Sat down (talking, reading, doing schoolwork)...... ❍
- Stood around or walked around .... ❍
- Ran or played a little bit .... ❍
- Ran around and played quite a bit .... ❍
- Ran and played hard most of the time .... ❍

5. In the last 7 days, on how many days *right after school*, did you do sports, dance, or play games in which you were very active? (Check one only.)

- None .... ❍
- 1 time last week .... ❍
- 2 or 3 times last week .... ❍
- 4 times last week .... ❍
- 5 times last week .... ❍

6. In the last 7 days, on how many *evenings* did you do sports, dance, or play games in which you were very active? (Check one only.)

- None .... ❍
- 1 time last week .... ❍
- 2 or 3 times last week .... ❍
- 4 or 5 last week .... ❍
- 6 or 7 times last week .... ❍

7. *On the last weekend*, how many times did you do sports, dance, or play games in which you were very active? (Check one only.)

None .... ❍
1 time .... ❍
2 — 3 times .... ❍
4 — 5 times .... ❍
6 or more times .... ❍

8. Which *one* of the following describes you best for the last 7 days? Read *all five* statements before deciding on the *one* answer that describes you.

A. All or most of my free time was spent doing things that involve little physical effort .... ❍

B. I sometimes (1 — 2 times last week) did physical things in my free time (e.g. played sports, went running, swimming, bike riding, did aerobics) .... ❍

C. I often (3 — 4 times last week) did physical things in my free time .... ❍

D. I quite often (5 — 6 times last week) did physical things in my free time .... ❍

E. I very often (7 or more times last week) did physical things in my free time .... ❍

9. Mark how often you did physical activity (like playing sports, games, doing dance, or any other physical activity) for each day last week.

	None	Little bit	Medium	Often	Very often
Monday	❍	❍	❍	❍	❍
Tuesday	❍	❍	❍	❍	❍
Wednesday	❍	❍	❍	❍	❍
Thursday	❍	❍	❍	❍	❍
Friday	❍	❍	❍	❍	❍
Saturday	❍	❍	❍	❍	❍
Sunday	❍	❍	❍	❍	❍

10. Were you sick last week, or did anything prevent you from doing your normal physical activities? (Check one.)

Yes .... ❍
No .... ❍

If Yes, what prevented you? ___________________________________

A.4: Physical Activity Questionnaire (Adolescent)

Physical Activity Questionnaire (High School)

Name:_________________________ Age:___________

Sex: M_______ F_______ Grade:__________

Teacher:_______________________

We are trying to find out about your level of physical activity from ***the last 7 days*** (in the last week). This includes sports or dance that make you sweat or make your legs feel tired, or games that make you breathe hard, like tag, skipping, running, climbing, and others.

Remember:

3. There are no right and wrong answers — this is not a test.
4. Please answer all the questions as honestly and accurately as you can — this is very important.

---

1. Physical activity in your spare time: Have you done any of the following activities in the past 7 days (last week)? If yes, how many times? (Mark only one circle per row.)

	No	1-2	3-4	5-6	7 times or more
Skipping	❍	❍	❍	❍	❍
Rowing/canoeing	❍	❍	❍	❍	❍
In-line skating	❍	❍	❍	❍	❍
Tag	❍	❍	❍	❍	❍
Walking for exercise	❍	❍	❍	❍	❍
Bicycling	❍	❍	❍	❍	❍
Jogging or running	❍	❍	❍	❍	❍
Aerobics	❍	❍	❍	❍	❍
Swimming	❍	❍	❍	❍	❍
Baseball, softball	❍	❍	❍	❍	❍
Dance	❍	❍	❍	❍	❍
Football	❍	❍	❍	❍	❍
Badminton	❍	❍	❍	❍	❍
Skateboarding	❍	❍	❍	❍	❍
Soccer	❍	❍	❍	❍	❍
Street hockey	❍	❍	❍	❍	❍
Volleyball	❍	❍	❍	❍	❍
Floor hockey	❍	❍	❍	❍	❍
Basketball	❍	❍	❍	❍	❍
Ice skating	❍	❍	❍	❍	❍
Cross-country skiing	❍	❍	❍	❍	❍
Ice hockey/ringette	❍	❍	❍	❍	❍
Other:					
_________________________	❍	❍	❍	❍	❍
_________________________	❍	❍	❍	❍	❍

2. In the last 7 days, during your physical education (PE) classes, how often were you very active (playing hard, running, jumping, throwing)? (Check one only.)

- I don't do PE .... ❍
- Hardly ever .... ❍
- Sometimes .... ❍
- Quite often .... ❍
- Always .... ❍

3. In the last 7 days, what did you normally do *at lunch* (besides eating lunch)? (Check one only.)

- Sat down (talking, reading, doing schoolwork)........ ❍
- Stood around or walked around .... ❍
- Ran or played a little bit .... ❍
- Ran around and played quite a bit .... ❍
- Ran and played hard most of the time .... ❍

4. In the last 7 days, on how many days *right after school*, did you do sports, dance, or play games in which you were very active? (Check one only.)

- None .... ❍
- 1 time last week .... ❍
- 2 or 3 times last week .... ❍
- 4 times last week .... ❍
- 5 times last week .... ❍

5. In the last 7 days, on how many *evenings* did you do sports, dance, or play games in which you were very active? (Check one only.)

- None .... ❍
- 1 time last week .... ❍
- 2 or 3 times last week .... ❍
- 4 or 5 last week .... ❍
- 6 or 7 times last week .... ❍

6. *On the last weekend*, how many times did you do sports, dance, or play games in which you were very active? (Check one only.)

- None .... ❍
- 1 time .... ❍
- 2 — 3 times .... ❍
- 4 — 5 times .... ❍
- 6 or more times .... ❍

7. Which *one* of the following describes you best for the last 7 days? Read *all five* statements before deciding on the *one* answer that describes you.

F. All or most of my free time was spent doing things that involve little physical effort ....❍

G. I sometimes (1 — 2 times last week) did physical things in my free time (e.g. played sports, went running, swimming, bike riding, did aerobics) ....❍

H. I often (3 — 4 times last week) did physical things in my free time ....❍

I. I quite often (5 — 6 times last week) did physical things in my free time ....❍

J. I very often (7 or more times last week) did physical things in my free time .....❍

8. Mark how often you did physical activity (like playing sports, games, doing dance, or any other physical activity) for each day last week.

	None	Little bit	Medium	Often	Very often
Monday	❍	❍	❍	❍	❍
Tuesday	❍	❍	❍	❍	❍
Wednesday	❍	❍	❍	❍	❍
Thursday	❍	❍	❍	❍	❍
Friday	❍	❍	❍	❍	❍
Saturday	❍	❍	❍	❍	❍
Sunday	❍	❍	❍	❍	❍

9. Were you sick last week, or did anything prevent you from doing your normal physical activities? (Check one.)

Yes ....❍
No ....❍

If Yes, what prevented you? ___________________________________

A.5: Exit Interview

BC CHILDREN'S HOSPITAL
An Agency of the Provincial Health Services Authority

Children's Heart Centre
B.C. Children's Hospital
4480 Oak Street, 1F Clinic
Vancouver, B.C.
V6H 3V4

VEXT: Post Intervention Survey

Please answer as truthfully as you can:

1. Did you find the virtual exercise program enjoyable?
    a. Yes
    b. No

    Please explain why or why not:

    ____

    ____

    ____

2. Did you find it useful to be able to text your health care team?
    a. Yes
    b. No

    Please explain why:

    ____

    ____

    ____

3. Would you recommend this program to others?
    a. Yes
    b. No

    Please explain why:

    ____

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4. Did you have any problems receiving text messages?
    a. Yes
    b. No

5. Did you have any problems sending text messages?
    a. Yes
    b. No

6. Did you have any problems accessing the Zoom link?
    a. Yes
    b. No

7. Did participating in this exercise training program:
    a. Increase your daily physical activity levels
        i. Strongly agree
        ii. Agree
        iii. Neutral
        iv. Disagree
        v. Strongly disagree

    b. Increase your wellbeing
        i. Strongly agree
        ii. Agree
        iii. Neutral
        iv. Disagree
        v. Strongly disagree

    c. Increase your confidence with exercise
        i. Strongly agree
        ii. Agree
        iii. Neutral
        iv. Disagree
        v. Strongly disagree

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8. How did you feel about the frequency of the exercise classes each week?
    a. Too frequent
    b. Just right
    c. Not frequent enough

    If you think the classes occurred too frequently, would you rather have the exercise classes:
    a. Once a week
    b. Twice a week

    If you think the classes occurred not frequently enough, would you want to have the exercise classes:
    a. Four times a week
    b. Five times a week
    c. Six times a week
    d. Seven times a week

9. How did you feel about the duration of each exercise class?
    a. Too long
    b. Just right
    c. Too short

    If you think that the classes were too long or too short, what duration would you have preferred the exercise classes to be?

    ____

    ____

    ____

10. How did you feel about the difficulty of the exercises?
    a. Too difficult
    b. Just right
    c. Too easy

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If you think that the exercises were either too difficult or too easy, please explain why that was and what you would want to change to account for that.

11. What was the greatest obstacle to participating in this virtual exercise program?

12. What was the greatest benefit that you received from this virtual exercise program?