



The VIE study: feasibility of a physical activity intervention in a multidisciplinary program in children with cancer

Maxime Caru^{1,2,3} · Gabrielle Duhamel^{1,3} · Valérie Marci^{3,4} · Serge Sultan^{3,5} · Caroline Meloche³ · Isabelle Bouchard³ · Simon Drouin³ · Laurence Bertout³ · Caroline Laverdiere^{3,6} · Daniel Sinnett^{3,6} · Daniel Curnier^{1,3}

Received: 7 May 2019 / Accepted: 16 September 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Background Cancer is one of the leading causes of death in the world. The physiological and psychological benefits of physical activity have been shown in children with cancer. However, almost one in two cancer patients do not follow the physical activity guidelines. The aim of this study will be to assess the feasibility of a physical activity program intervention in pediatric oncology and to assess the barriers and facilitators to the success or failure of this physical activity program.

Methods The VIE (valorization, implication, and education) intervention is a multidisciplinary program including physical activity, nutritional, and psychological interventions in pediatric oncology. This study involves one intervention group that will be followed over 2 years (evaluations and physical activity interventions) and one control group that will participate in only one evaluation. Children from the intervention group have been diagnosed and will be undergoing treatment at the Charles-Bruneau oncology center from the Sainte-Justine University Health Center (Montreal, Canada). The feasibility of this program will be measured through a comparison between sessions performed and sessions scheduled, while the security will be measured according to the number of reported incidents.

Discussion This study will examine the effects of exercise in pediatric oncology from diagnosis to the expected end of treatment (i.e., 2 years of follow-up). Currently, there are only a few longitudinal studies on physical activity and pediatric cancer. Physiological and psychological tests will allow a better knowledge of the evolution of the physical fitness and mental health of the patients during the period of care. It is necessary to document and provide complementary knowledge in the pediatric oncology field in order to engage the discourse with pediatric oncology health professionals to help patients during and after treatment. This is an important study in the exercise and oncology field to help patients and their family during and after cancer treatments.

Keywords Childhood cancer · Physical activity · Intervention · Feasibility · Exercise · VIE study

Background

Cancer is a major public health problem and one of the leading causes of death in the world with nearly 8.2 million deaths

each year [1]. Worldwide, the prevalence of cancer in children represents between 0.5 and 4.6% of the total number of cancer cases [2]. Over the past 20 years, there has been a 13% increase in new cases of childhood cancer [3]. In Canada, the

✉ Daniel Curnier
daniel.curnier@umontreal.ca

Maxime Caru
maxime.caru@umontreal.ca

¹ Laboratory of Pathophysiology of EXercise (LPEX), School of Kinesiology and Physical Activity Sciences, Faculty of Medicine, University of Montreal, Montreal, Canada

² Laboratoire EA 4430 – Clinique Psychanalyse Developement (CliPsyD), Department of psychology, University of Paris Nanterre, Nanterre, France

³ Research Center, Sainte-Justine University Health Center, Montreal, Canada

⁴ Department of Nutrition, Université de Montréal, Montreal, Canada

⁵ Department of Psychology, Université de Montréal, Montreal, Canada

⁶ Department of Pediatrics, University of Montreal, Montreal, Canada

prevalence of cancers in children is high and accounts for more than 1% of cases, or more than 1000 children are diagnosed with cancer each year [4]. In this sense, medicine has made considerable progress over the past 30 years, notably through the advancement of scientific research and the improvement of medical techniques and treatments.

Childhood cancer, which was a nearly incurable disease 50 years ago, has in recent years reached a survival rate of more than 80% [5]. However, the evolution of the treatment and the increased survival rates are to the detriment of late adverse effects resulting in several comorbidities (e.g., cardiovascular diseases, metabolic diseases, musculoskeletal disorders, mental health problems) appearing several years after the end of the treatments [6–9]. The literature shows the physiological and psychological benefits of physical activity in patients with cancer. Indeed, a reduction of the overall mortality risk, which has been associated with physical activity, has been demonstrated in cancer [10]. When practiced at a moderate and constant intensity, physical activity can lead to general improvements to the metabolism [11]. Likewise, it is an excellent way to alleviate the adverse effects of treatments, improving children's functional capacity and optimizing their rehabilitation [12–14]. These benefits may be maintained after the diagnosis of cancer. In addition, regular physical activity allows to improve the quality of life of patients by a reduction of anxiety and depressive symptoms [15]. However, almost one of two cancer patients do not follow the physical activity guidelines [16, 17], although it has been demonstrated to be safe and beneficial to their health [13, 14]. The recent systematic review by Grimshaw et al. (2016) showed that physical activity intervention is feasible during the intense treatment phase in children and adolescents with cancer. Moreover, they emphasize the need to understand the most effective ways to implement physical activity programs in this population of interest [18]. Thus, it seems to be very important to provide physical activity program interventions to children with cancer, especially to document and describe the implementation process from diagnosis to the expected end of treatment. Providing a non-drug therapy based on physical activity and educating children with cancer about the benefits of regular physical activity during the disease is a challenge that must be considered by health professionals.

Multidisciplinary approaches must be favored in order to offer the best care to cancer patients. These aspects need to be addressed during the cancer treatments and exercise physiologists, as well as nutritionists and psychologists, have an important role to play in order to minimize or prevent these adverse effects. In this sense, the VIE (valorization, implication, and education) study provides physical activity, nutritional, and psychological interventions in pediatric oncology. The main aim of the VIE study is to promote the long-term well-being of patients by accompanying them and educating them on the benefits of adopting a good lifestyle during and

after the disease. Since support (i.e., physical activity, nutrition, and psychology) is important in the care of the patient, we made the choice to present in this article, only the portion related to the physical activity program intervention. We hypothesize that the physical activity program intervention will be feasible and safe for children with cancer and that it will help them to maintain their physical function from diagnosis to the expected end of treatment. Thus, the ultimate aim of this research is to study the feasibility of a physical activity program in a multidisciplinary program for children with cancer and also to assess the barriers and facilitators to the success or failure of this physical activity program.

Methods

Design and ethical considerations

The VIE (valorization, implication, and education) intervention is a multidisciplinary program including physical activity, nutritional, and psychological interventions in pediatric oncology. Physical activity, nutritional, and psychological interventions have a complementary role in this multidisciplinary study in pediatric oncology. While our protocol explores the feasibility of a physical activity program during cancer treatments in children, nutritional researchers will describe the implementation process of a nutrition education program for families of children with cancer and researchers in psychology will offer a psychological intervention for parents of children with cancer to strengthen the perceived control and problem-solving skills of each parent while focusing on dyadic coping to prevent distress early in the trajectory. We have chosen to provide a protocol article for the physical activity program only in order to focus and to encourage the replication of our study and especially its follow-up. This study involves one intervention group that will be followed over 2 years (evaluations and physical activity interventions) and one control group that will participate in only one evaluation. All study procedures were approved by the Ethics Review Committee of the Sainte-Justine University Health Center (Montréal, Canada) and will be conducted in accordance with the Declaration of Helsinki. Written informed consent will be obtained from every patient or parent/legal guardian.

Recruitment and patients

Intervention group The intervention group will target children with cancer (i.e., acute lymphoblastic leukemia, acute myeloid leukemia, lymphoma, medulloblastoma, neuroblastoma, Wilms tumors, sarcoma, rare tumors) diagnosed and treated at the Charles-Bruneau oncology center of the Sainte-Justine University Health Center (Montreal, Canada). Eligible participants must be under the age of 18 years at diagnosis, be

treated with chemotherapy and/or radiation therapy, not have received a hematopoietic stem cell transplant, have a life expectancy of at least 12 months, and be able to consent (by parents or legal guardians) to the study in an informed manner. The agreement of the attending physician (i.e., oncologist) will be required for the participation of patients eligible for this study. The oncologist will have the right to withdraw patients from the study if they deem that the health of their patient no longer allows them to participate (e.g., if a patient must receive palliative care). In the event that oncologists have to make this decision, justifications will be collected as part of this study in order to document this aspect.

Control group The control group will be recruited from the cohort of patients diagnosed at the Charles-Bruneau oncology center of the Sainte-Justine University Health Center (Montréal, Canada) in 2013, 2014, and 2015. They will need to have completed their treatments and be followed as an outpatient with the same inclusion and exclusion criteria as the intervention group.

Procedure and timeline

Eligible patients will join the study between the second and the fourth week after their diagnosis of cancer. It is the oncologist who will decide when the patients can participate in the first evaluation of physical fitness, depending on their physical condition. The informed consent of the patient for the study will be obtained by the research coordinator at the time of their diagnosis. A 2-year follow-up will be provided to patients in the intervention group, as well as meetings every 2 months to allow the implementation of an adapted physical activity program—coupled with therapeutic education sessions—which will help patients optimize their rehabilitation process. The control group will participate in only one complete evaluation and will not participate in any others intervention. The timeline of the longitudinal protocol is presented in Fig. 1. This follow-up will allow to assess the barriers and facilitators to the success or failure of this physical activity program and also to assess sessions performed in addition to the follow-up. Primary follow-ups will be dedicated to patient follow-up, whereas the secondary follow-up will be dedicated to patient's physical fitness and their physical evaluation. The feasibility of the physical activity program will be measured by a comparison between sessions performed and sessions scheduled, by acceptability (how many patients of the eligible patients agree to participate) and attrition (how many patients complete the study). The security will be measured according to the number of reported incidents. Barriers and facilitators, in the success or failure of the physical activity program, will be reported in the patient's notebook from Reacts platform for each session scheduled—this includes sessions that have been completed or not realized. Managing missing data may be a

challenge due to the participant's compliance in their capacity to report their barriers and facilitators. However, the protocol is set up to avoid missing data and if participants did not report barriers and facilitators, this will be documented to inform the reader about the implementation process. After 1 year, all data on barriers or facilitators will be computed to propose remediation.

The physical activity program will be performed by professionals in physical activity which are kinesiologists. The kinesiologist will make the physical tests, the physical activity program, and the patients' follow-up. Everybody on the research team will receive training in exercise and oncology, as well as training specific to the study to standardize the administration of our protocol in order to maintain the quality and validity of the data. Each kinesiologist will also receive training of the hospital environment to enable them to work safely and to support patients in care. They will be under the supervision of exercise physiologist with a specialty in exercise oncology, as well as the principal investigator of the physical activity program intervention.

Primary follow-up The patient will meet the professional in physical activity (i.e., kinesiologist) every 2 months following the initial meeting. At the beginning of each meeting, a period of time will be given to the follow-up of the patient and information on what has been done at home to determine new goals with the patient will allow to adjust their training program. The physical fitness level and motivation of the patient will be discussed at each meeting with the parents or legal guardians. The integration of the family in the process will be very important for the success of the study, in particular regarding the use of the platform of telemedicine (Reacts). This platform will be proposed to the patients to allow them to have access to a web-training notebook. The patients will be able to record their daily activities, which will allow the kinesiologist to regularly and accurately monitor the level of physical activity of the patient. This information will be verified by the use of a self-reported questionnaire of the patient's physical activity level in order to avoid information bias. A questionnaire evaluating the patient's physical activity enjoyment and a questionnaire measuring the patient's quality of life will be distributed.

Secondary follow-up The patient will meet with the kinesiologist at the initial meeting, at 2 months, at 6 months, and every 6 months to assess the patient's physical fitness. Between the initial meeting and the second month, no patient in the intervention group will receive a training program. Because this could be stressful for young patients and for their parents, we decided not to conduct in the intervention group the physical activity program prior to secondary follow-up at 2 months. This study must not be a constraint for the patients and their family, but rather a source of support during their treatment.

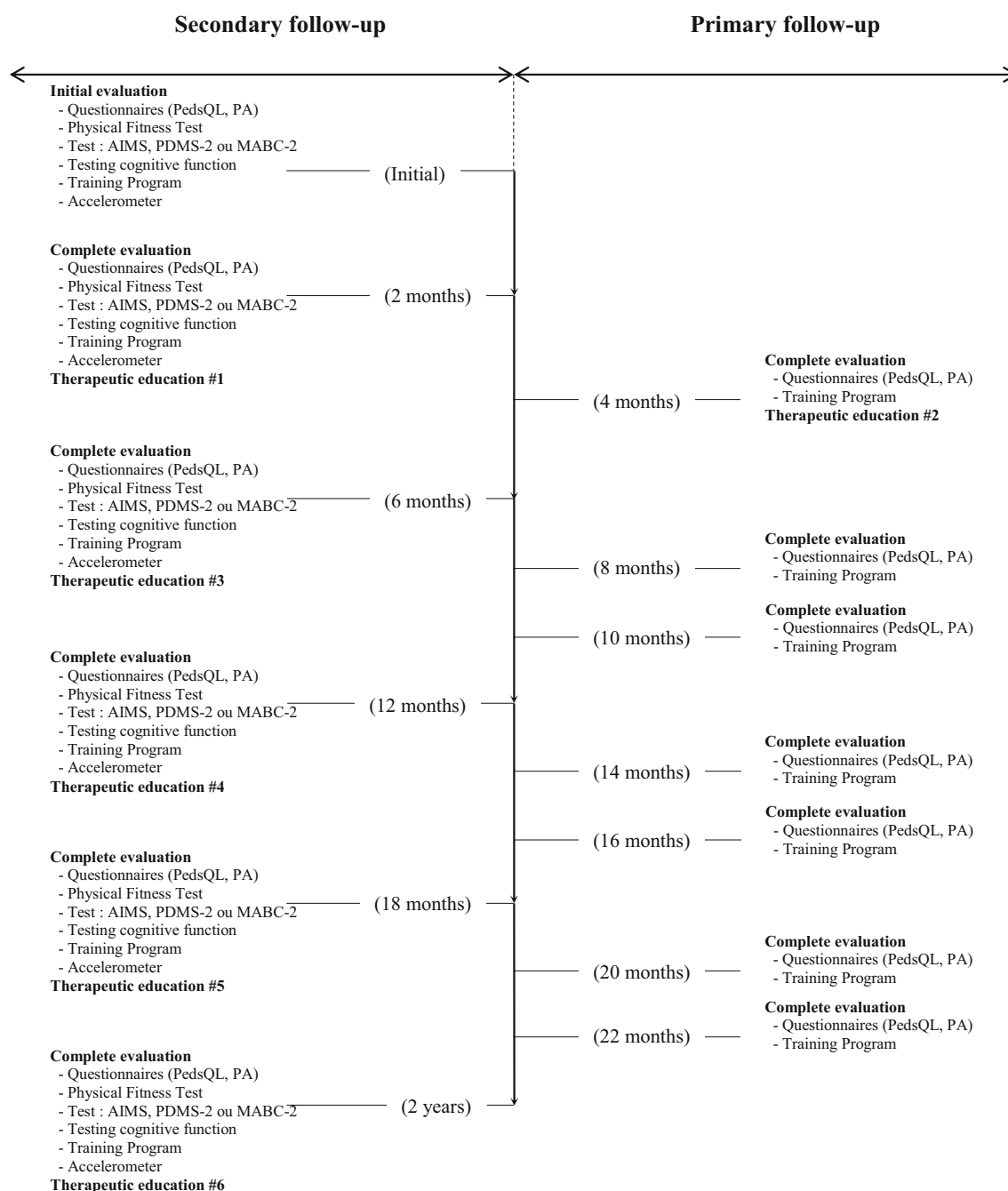


Fig. 1 The timeline of the longitudinal protocol. PedsQL, pediatric quality of life; PA, physical activity; AIMS, Alberta Infant Motor Scale; PDMS-2, Peabody Developmental Motor Scales, 2nd edition; MABC-2, Movement Assessment Battery for Children, 2nd edition

At the beginning of each meeting, a period of time will be given to the follow-up of the patient and information on what has been done at home to determine new goals with the patient will allow to adjust their training program. Subsequently, depending on age, the physical fitness of the patient will be measured by the kinesiologist and their motor skills by the physiotherapist. Physical activity will be assessed by a self-reported questionnaire, as well as by a 1-week accelerometer. As with the primary follow-up, the patient's quality of life and

their enjoyment of physical activity will be measured. The entire battery of tests should not last more than an hour and a half. This is an important aspect to reduce the lack of compliance and concentration in children, especially when it is necessary to fill out questionnaires. It is important to note that the physical evaluation part is more enjoyable for children. Also, regarding nutrition and psychological surveys, they are not conducted on the same day as the physical evaluations and questionnaires in order to decrease the lack of

concentration in children. A test of cognitive function will also be proposed. Finally, at the end of each meeting, a therapeutic education session will be offered to the patient.

Intervention

Exercise intervention The exercise intervention will take place at the home of the patient and will be monitored regularly through the Reacts platform. Each patient will receive a training program with long-term goals following the Canadian guidelines in physical activity. The training program will be offered to the patients starting at the second meeting (at 2 months) and will be readjusted every 2 months during the primary follow-up. In the case where major changes are to be made (e.g., complete modifications to the training program), a prior, complete, evaluation will be necessary in a meeting during the secondary follow-up. The main structure of the training program will be based on the FITT concepts [19] with a cardiovascular period of about 30 min, followed by an exercise session and adapted functional activities (e.g., balance, resistance, flexibility training, muscular fitness) of about 15 min, for a total of 45 min. Physical activity intensity will be monitored through the patient's heart rate and their rate of perceived exertion. The patient will start the training program at a rate of 3 times per week. The training program will be chosen according to different parameters having an influence on the patient's motor capacity. For young children, the training program will focus primarily on the child's enjoyment and mobility, rather than a classic physical activity model that incorporates the FITT concepts. A session can be noted as a completed session if the child only completes the cardiovascular or resistance part. There is no specific minimum bout duration for moderate to vigorous physical activities according to the recent Canadian guidelines in physical activity for children and adolescents [20]. However, in the previous version of the Canadian guidelines in physical activity, a minimum bout duration of 5 min was specified [21, 22]. This bout duration is our reference since the recent physical activity guidelines for Americans reported that every single minute of physical activity contributes to better health [23]. In this study, the patient's long-term goal will be to achieve a minimum of 60 min of recommended cardiovascular activity (i.e., moderate to vigorous physical activities) per day and to maintain or improve their ability to perform the various tasks of daily living. Cardiovascular stress from moderate to intense physical activity will improve the cardiorespiratory fitness of the patient and will reduce the general fatigue felt and noted during the treatments [15, 24, 25]. The training program will be adapted, according to the treatment received by the patient and their tolerance, by modifying the different criteria composing the session (i.e., frequency, intensity, time, type). The program will also be adapted according to the recommendations of the occupational therapists and physiotherapists who

take care of the acute intervention with the patient. They will be able to modify or shift the management of the patient if it is necessary in order to subsequently propose a safe chronic intervention by the kinesiologist.

Therapeutic education intervention Six therapeutic education sessions on exercise and adaptation responses will be offered to the patients and their families to provide them with various knowledge and skills related to physical activity [26, 27]. These will include the implementation and monitoring of a training program. The selection of themes and the development of therapeutic education workshops will be validated during consultations with families and health professionals in the hematology-oncology department to meet the specific needs of the patients and their families. Therapeutic education is an important way to educate patients about the benefits of physical activity. These workshops will focus on the following themes: (1) Knowledge of the beneficial effects of exercise on cancer; (2) sport hygiene and recommendations for good practice; (3) sport, physical activity, and sedentary behavior; (4) physical activity management; (5) physical fitness; and (5) sport autonomy.

Measurements

All measurements will be dependent on the age of the patients, as well as on their motor abilities to use the most appropriate clinical test.

Alberta infant motor scale The AIMS is a reliable and valid clinical tool which has been demonstrated to have excellent psychometric properties for measuring motor development in infants (ages 0–18 months) [28, 29]. This test evaluates the movement of the children in four positions: prone, supine, sitting, and standing.

Peabody developmental motor scales—2nd ed. The PDMS-2 is a reliable and valid clinical tool which will allow to evaluate the fine and overall motor skills of young children (ages 15 months–3 years old) in order to estimate their motor competence [30, 31]. The PDMS-2 is composed of two main items which are overall motor skills (reflexes, balance, locomotion, manipulation of objects) and fine motor skills (grips and clamps, visual-motor integration).

Movement assessment battery for children—2nd ed. The MABC-2 is a reliable and valid clinical tool which measures overall motor capacity in children (ages 3–16) on three axes: manual dexterity, ability to aim and catch, and static and dynamic balance [32].

Assessment of the physical fitness From 5 years of age, and if the patient's physical fitness is sufficient, they will carry out different tests to measure their physical fitness.

- **Maximum voluntary isometric contraction.** Maximum voluntary isometric contraction of the forearm muscles will be measured with a hydraulic hand Jamar dynamometer (Saehan Corporation, Masan, South Korea). Moreover, the grip test provides a valid and reliable measure that is easy for the young patient to use and understand [33].
- **Balance test.** The one leg stance test is a simple and effective method to screen for balance disorders in patients [34]. The one leg stance test consists of calculating the time the patient is able to remain balanced on their leg of choice, for a maximum of 45 s. The same procedure is repeated for the other leg. If the patient reaches 45 s, the test is repeated with the eyes closed according to the same procedure.
- **Incremental shuttle walk test.** The incremental shuttle walk test will be used in this study [35]. It consists of 12 levels of 1 min each with a minimum running speed of 1.9 km/h (level 1), up to a maximum of 8.5 km/h (level 12). When the test is done, the patient must continue to walk 2 shuttles for a recovery period. Blood pressure will be measured at the beginning and at the end of the test, heart rate and perceived exertion will be measured during the test using the OMNI scale [36].
- **Sit and reach test.** The sit and reach test (SRT) measures the forward bending of the trunk with a flexometer [37]. This test, involving the movement of the body as a whole, is an indirect measure of the muscular extensibility of the hamstrings [38]. The protocol was detailed by the American College of Sports Medicine [37].
- **Ankle dorsiflexion test.** The ankle dorsiflexion will be measured using a standard goniometer. This measure will evaluate the joint mobility of the ankle [39].
- **Vertical jump test.** The vertical jump test will be performed on the Leonardo Mechanograph Ground Reaction Force Plate (GRFP; Novotec Medical GmbH, Germany) for mechanography to estimate the functional strength of the lower limbs [40]. The GRFP for mechanography is a valid tool to measuring the force, vertical velocity, and power of vertical movements [41]. The patients will perform multiple two-legged hopping (M2LH) and the single two-legged jump (S2LJ) [42].

Testing cognitive function The continuous performance test, 3rd edition (CPT-3) is a cognitive test that measures the attention and executive functions of a child [43]. The CPT-3 will be administered by the intermediate of a computer to the patient in the meetings during the secondary follow-up.

Self-reported physical activity questionnaire The energy expenditure will be determined qualitatively by the measurement of the practice of physical activity from a questionnaire

adapted to the age of the patient in order to know their habits in regard to physical activity. This questionnaire will be an adaptation of the Minnesota Leisure Time Physical Activity Questionnaire [44, 45] and the Tecumseh Self-Administered Occupational Physical Activity Questionnaire [46]. It will highlight the patient's energy expenditure as well as their sedentary activities, sleeping habits, and active transportation. It has been shown that self-reported physical activity measured from the Minnesota Leisure Time Physical Activity Questionnaire and the Tecumseh Self-Administered Occupational Physical Activity Questionnaire is strongly associated with accelerometer data [47–49].

Accelerometer Patients will be required to wear an ActiGraph GT3X + Accelerometer (ActiGraph LLC, Pensacola, Florida) at home for a period of 7 consecutive days. Their movements will allow us to calculate the energy expenditure of the patients and the intensity of their exercises [50, 51].

Psychological measurements

Pediatric Quality of Life Inventory Generic Core Scales The PedsQL Inventory Generic Core Scales will allow to measure the health-related quality of life (HRQOL) of children and adolescents aged 2 to 18 [52]. The PedsQL Inventory Generic Core Scales is composed of 23 items divided in four scales: (1) physical functioning, (2) emotional functioning, (3) social functioning, and (4) school functioning. According to age, the PedsQL allows a child to self-report (ages 5 to 7, 8 to 12, and 13 to 18 years) and allows the parent to proxy-report (ages 2 to 4 (toddler), 5 to 7 (young child), 8 to 12 (child), and 13 to 18 (adolescent)) to assess parents' perceptions of their child's HRQOL. A 5-point Likert scale or a 3-point Likert scale, depending on the age, is used to answer the starting question, which is "how much of a problem each item has been during the past 1 month?"

Pediatric Quality of Life Cancer Module The PedsQL 3.0 Cancer Module is specific to patients in pediatric oncology and allows to measure the HRQOL of these patients [52]. It is composed of 27 multidimensional items, which encompass 8 scales: (1) pain and hurt, (2) nausea, (3) procedural anxiety, (4) treatment anxiety, (5) worry, (6) cognitive problems, (7) perceived physical appearance, and (8) communication. Each response is evaluated with an Likert scale identical to the PedsQL 4.0 Generic Core Scales. A higher scale score indicates a better HRQOL (fewer problems or symptoms).

Pediatric Quality of Life Brain Tumor Module The PedsQL™ Brain tumor Module allows to measure HRQOL specifically in patients with brain tumors. It includes six scales [53]: (1) cognitive problems, (2) pain and hurt, (3) movement and balance, (4) procedural anxiety, (5) nausea, and (6) worry. The

child self-report (5 to 7, 8 to 12, and 13 to 18 years) and the parent proxy-report (to 4, 5 to 7, 8 to 12, and 13 to 18 years) differs by age group. Each scale is composed of items that are rated on a Likert scale identical to the PedsQL 4.0 Generic Core Scales. A higher scale score indicates a better HRQOL.

Assessment of the physical activity enjoyment The Physical Activity Enjoyment Scale (PACES) [54] allows to assess the enjoyment of the physical activity with an 18-item scale using a 7-point bipolar Likert scale (from 1 (I enjoy it) to 7 (I hate it)). The patient is asked to rate “how do you feel at the moment about the physical activity you have been doing”. Higher scores indicate higher enjoyment.

Analyses

Sample size calculations

Intervention group The VIE study wants to include all patients from the Charles-Bruneau oncology center of the Sainte-Justine University Health Center (Montréal, Canada) who are eligible. This is to be done over a 2-year period in order to propose a feasibility study which is representative of the pediatric oncology. About 140 children per year are diagnosed of cancer at the Charles-Bruneau oncology center of the Sainte-Justine University Health Center (Montréal, Canada). According to the distribution of the different types of cancer recorded at the Sainte-Justine University Health Center (Montréal, Canada), about 110 patients would be eligible to participate in this study per year; based on the inclusion and exclusion criteria. All eligible patients with cancer over 2 years will be recruited in this study from the Charles-Bruneau oncology center of the Sainte-Justine University Health Center (Montréal, Canada).

Control group About 420 children were diagnosed of a cancer at the Charles-Bruneau oncology center from the Sainte-Justine University Health Center (Montréal, Canada) between 2013 and 2015. According to the eligibility criteria, about 330 control participants would be included in this study. Assuming a 5-year relative survival rate of 80% and taking into consideration the patients' refusal to take part in the study, about 184 control participants will be recruited.

Statistical analyses

To analyze data, a secure database will be created at the Sainte-Justine University Health Center (Montréal, Canada). The data will be “cleaned” to ensure that there are no outliers and to correct any errors that may have occurred during the data entry. Checks will also be made to explore missing data. For the dropouts and missing values, a maximum likelihood

estimation based on the expectation-maximization (EM) algorithm with the observed data will be used in an iterative process [55]. In the first step, descriptive statistics will be used to report the clinical and treatment characteristics of the cancer patients in the studied cohort. The baseline characteristics of the two groups, such as sex, age, weight, height, body mass index, and the treatment for cancer, will be analyzed by an unpaired *t* test or paired *t* tests. Quantitative variables will be represented by their mean and median and their dispersion will be evaluated by the standard deviation (SD). Qualitative variables will be represented by their frequency. In the second step, a Wilcoxon-Mann-Whitney test will be used to examine the distribution of data in each group (intervention and control). Finally, an analysis of variance (ANOVA), for the multiple comparisons of the means, will be performed to observe the effect of the intervention on the variables studied. When the data are significant, an analysis of multiple comparisons will be performed for the important variables using a Bonferroni correction. To complete statistical analyses, a linear mixed model that accounts for age, sex, and diagnosis will be used to take into consideration that different cancer populations respond differently to physical activity and also because both cardiorespiratory fitness and muscle strength which are associated with age and sex. All statistical analyses will be performed with IBM SPSS statistics, version 25.0 (IBM Corp., Armonk, NY, USA). The significance level will be set to 5%.

Discussion

This study will examine the feasibility of a physical activity program in a multidisciplinary program for children with cancer from diagnosis to the expected end of treatment (i.e., 2 years of follow-up). This study will also assess the barriers and facilitators to the success or failure of this physical activity program. Currently, there are only a few longitudinal studies or pilot studies dealing with physical activity and pediatric cancer [56–58]. Physiological and psychological tests will allow a better knowledge of the evolution of the physical fitness and the mental health of the patients during the period of care. Moreover, if our findings confirm our main hypothesis, this would highlight the importance of integrating a physical activity program that is workable, reliable, and safe, into the pediatric cancer population. Empirical evidence suggests that in the past, oncologists recommended complete rest of the patient by avoiding any physical exercise, which resulted in a reduction of their functional state and their quality of life [59]. Although attitudes toward the benefits of physical activity have evolved over the past few years, the implementation of a physical activity program in pediatric oncology in Canada is still very innovative. A clearer vision of the benefits of physical activity in this population would be a first step in this

direction. This would provide solid evidence of its efficacy and engage the discourse of pediatric oncology health professionals in order to make physical activity be clinically recognized as patient care.

Methodological strengths

The main strength of this research protocol concerns its design. Indeed, it is interesting in a very heterogeneous population of children from across Canada who are diagnosed and treated at the Charles-Bruneau oncology center from the Sainte-Justine University Health Center (Montréal, Canada). These inclusion criteria will allow intervening with children of different ages and with different types of cancers because the Sainte-Justine University Health Center (Montréal, Canada) takes care of all cancers, even the most specific ones. Moreover, the literature observes a lack of data concerning the physical fitness level of patients at the time of the diagnosis and its evolution over time [60]. Many studies have been performed with adult subjects, but it is not the case with children. Also, many studies have used a randomized controlled trial model without having carried out a preliminary feasibility study which can limit the scope of their physical activity program. According to Sir Bradford Hill (1965) and Hill's criteria for causation, the feasibility study is a mandatory step to establish evidence of a causal relationship between a presumed cause (i.e., physical activity program) and an observed effect [61]. This method was widely used in public health research and it is a robust epidemiological methodology [61]. It is necessary to document and provide complementary knowledge in the pediatric oncology field. Our study will allow this by measuring the evolution of the physiological and psychological parameters of children with cancer over 2 years, with a follow-up every 2 months. Finally, with one of two cancer patients who do not follow the physical activity guidelines [16, 17], it seems essential to educate this population about the benefits of a good practice of physical activity from an early age. Strengthening this aspect, through the integration of therapeutic education sessions, will strengthen the structure of our study.

Methodological weaknesses

The main weakness of this research protocol concerns the recruitment of patients, which rejects certain children with cancer. Indeed, those who have a vital prognosis inferior to 12 months are excluded. However, there is a lack in the literature regarding these children with cancer, but the implementation of a physical activity program for the first time in the hospital environment requires caution for this population. Future research should have a design that does not exclude

patients based on certain characteristics. Indeed, they should include patients who have or have not received chemotherapy or radiation therapy and patients who have or do not have a life expectancy of more than 12 months. All benefits from physical activity need to be documented in all childhood cancer populations. Another methodological weakness is that information bias is always a possibility when using self-reported questionnaires to measure patients' daily physical activities. However, measuring daily physical activities may be a challenging task, especially in home-based programs. The use of the Minnesota Leisure Time Physical Activity Questionnaire and the Tecumseh Self-Administered Occupational Physical Activity Questionnaire will reduce this methodological weakness, since these questionnaires are strongly associated with accelerometer data [47–49]. Finally, our very heterogeneous patients with cancer need to be mentioned since it will be important to work with children of different ages, different types of cancers, therapy protocols, physical conditions (e.g., amputation...). Our ability to adapt will be an asset in this feasibility study. For example, in the case of a change in the patients' physical conditions or a change in their treatment, we will continue to offer the same approach to the patient, and we will be able to adapt the sessions according to their state of health. It is a challenge which deserves to be documented in the exercise oncology field to identify the barriers and facilitators of a physical activity program in pediatric oncology.

Acknowledgments We would like to thank all the families and the clinical team of the oncology unit at the Sainte-Justine University Health Center. We appreciate the assistance of Ariane Levesque (McGill University) for her review of the article in the English language.

Funding information This research was funded by The Fondation Charles-Bruneau, IGA, Fondation du plaisir de mieux manger, the Fonds de Recherche du Québec en Santé, and the Canadian Institutes of Health Research.

Compliance with ethical standards

All study procedures were approved by the Ethics Review Committee of the Sainte-Justine University Health Center (Montréal, Canada) and will be conducted in accordance with the Declaration of Helsinki. Written informed consent will be obtained from every patient or parent/legal guardian.

Competing interests The authors declare that they have no competing interests.

References

1. Organisation Mondiale de la Santé (2015) Cancer, Aide-mémoire N°297: Organisation Mondiale de la Santé [Available from: <http://www.who.int/mediacentre/factsheets/fs297/fr/>]
2. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. (2014) GLOBOCAN 2012 v1. 0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11. 2013. International

- Agency for Research on Cancer Web site Available online: <http://globocan.iarc.fr>. Accessed 24 Nov 2014
3. Steliarova-Foucher E, Colombet M, Ries LA, Moreno F, Dolya A, Bray F, et al (2017) International incidence of childhood cancer, 2001–10: a population-based registry study. *Lancet Oncol*
 4. Canadian Cancer Society (2016) Canadian Cancer Statistics 2016 - special topic: HPV-associated cancers. Canadian Cancer Society, Statistic Canada, Toronto
 5. Smith MA, Seibel NL, Altekruse SF, Ries LA, Melbert DL, O'Leary M et al (2010) Outcomes for children and adolescents with cancer: challenges for the twenty-first century. *J Clin Oncol* 28(15): 2625–2634
 6. Sarfati D, Koczwara B, Jackson C (2016) The impact of comorbidity on cancer and its treatment. *CA Cancer J Clin* 66(4):337–350
 7. Hudson MM, Ness KK, Gurney JG, Mulrooney DA, Chemitilly W, Krull KR et al (2013) Clinical ascertainment of health outcomes among adults treated for childhood cancer. *Jama* 309(22):2371–2381
 8. Caru M, Samoilenko M, Drouin S, Lemay V, Kern L, Romo L, et al (2019) Childhood acute lymphoblastic leukemia survivors have a substantially lower cardiorespiratory fitness level than healthy Canadians despite a clinically equivalent level of physical activity. *J Adolesc Young Adult Oncol*
 9. Lemay V, Caru M, Samoilenko M, Drouin S, Alos N, Lefebvre G et al (2019) Prevention of long-term adverse health outcomes with cardiorespiratory fitness and physical activity in childhood acute lymphoblastic leukemia survivors. *J Pediatr Hematol Oncol*
 10. Hupin D, Edouard P, Gremaux V, Garet M, Celle S, Pichot V et al (2017) Physical activity to reduce mortality risk. *Eur Heart J* 38(20): 1534–1537
 11. Pedersen BK, Hoffman-Goetz L (2000) Exercise and the immune system: regulation, integration, and adaptation. *Physiol Rev* 80(3): 1055–1081
 12. Pedersen BK, Saltin B (2006) Evidence for prescribing exercise as therapy in chronic disease. *Scand J Med Sci Sports* 16(Suppl 1):3–63
 13. Fiuza-Luces C, Padilla JR, Soares-Miranda L, Santana-Sosa E, Quiroga JV, Santos-Lozano A et al (2017) Exercise intervention in pediatric patients with solid tumors: the physical activity in pediatric cancer trial. *Med Sci Sports Exerc* 49(2):223–230
 14. Thorsteinsson T, Larsen HB, Schmiegelow K, Thing LF, Krstrup P, Pedersen MT et al (2017) Cardiorespiratory fitness and physical function in children with cancer from diagnosis throughout treatment. *BMJ Open Sport Exerc Med* 3(1):e000179
 15. Braam KI, van der Torre P, Takken T, Veening MA, van Dulmen-den Broeder E, Kaspers GJ (2016) Physical exercise training interventions for children and young adults during and after treatment for childhood cancer. *Cochrane Database Syst Rev* 3:Cd008796
 16. Florin TA, Fryer GE, Miyoshi T, Weitzman M, Mertens AC, Hudson MM et al (2007) Physical inactivity in adult survivors of childhood acute lymphoblastic leukemia: a report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev* 16(7):1356–1363
 17. Winter C, Muller C, Hoffmann C, Boos J, Rosenbaum D (2010) Physical activity and childhood cancer. *Pediatr Blood Cancer* 54(4): 501–510
 18. Grimshaw SL, Taylor NF, Shields N (2016) The feasibility of physical activity interventions during the intense treatment phase for children and adolescents with cancer: a systematic review. *Pediatr Blood Cancer* 63(9):1586–1593
 19. Iyengar NM, Jones LW (2019) Development of exercise as interception therapy for cancer: a review development of exercise as interception therapy for cancer. *JAMA Oncol*
 20. Canadian Society for Exercise Physiology (CSEP) (2018) Canadian 24-hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep
 21. Janssen I (2007) Guidelines for physical activity in children and young people. *Appl Physiol Nutr Metab* 32(Suppl 2F):S122–S135
 22. Tremblay MS, Carson V, Chaput J-P, Connor Gorber S, Dinh T, Duggan M et al (2016) Canadian 24-hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep. *Appl Physiol Nutr Metab* 41(6):S311–S327
 23. U.S. Department of Health and Human Services (2018) Physical activity guidelines for Americans, 2nd edn. U.S. Department of Health and Human Services, Washington, DC
 24. Huang TT, Ness KK (2011) Exercise interventions in children with cancer: a review. *Int J Pediatr* 2011:461512
 25. Thorsen L, Skovlund E, Stromme SB, Hornslien K, Dahl AA, Fossa SD (2005) Effectiveness of physical activity on cardiorespiratory fitness and health-related quality of life in young and middle-aged cancer patients shortly after chemotherapy. *J Clin Oncol* 23(10):2378–2388
 26. World Health Organization Working Group (1998) Therapeutic Patient Education. Continuing education programmes for health care providers in the field of prevention of chronic diseases Copenhagen
 27. Perol D, Toutenu P, Lefranc A, Regnier V, Chvetzoff G, Saltel P et al (2007) Therapeutic education in oncology: involving patient in the management of cancer. *Bull Cancer* 94(3):267–274
 28. Spittle AJ, Doyle LW, Boyd RN (2008) A systematic review of the clinimetric properties of neuromotor assessments for preterm infants during the first year of life. *Dev Med Child Neurol* 50(4): 254–266
 29. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ (1992) Construction and validation of the Alberta Infant Motor Scale (AIMS). *Can J Public Health* 83(Suppl 2):S46–S50
 30. Tavasoli A, Azimi P, Montazari A (2014) Reliability and validity of the Peabody Developmental Motor Scales-second edition for assessing motor development of low birth weight preterm infants. *Pediatr Neurol* 51(4):522–526
 31. van Hartingsveldt MJ, Cup EH, Oostendorp RA (2005) Reliability and validity of the fine motor scale of the Peabody Developmental Motor Scales-2. *Occup Ther Int* 12(1):1–13
 32. Ellinoudis T, Evaggelidou C, Kourtessis T, Konstantinidou Z, Venetsanou F, Kambas A (2011) Reliability and validity of age band 1 of the Movement Assessment Battery for Children-second edition. *Res Dev Disabil* 32(3):1046–1051
 33. Molenaar HM, Zuidam JM, Selles RW, Stam HJ, Hovius SE (2008) Age-specific reliability of two grip-strength dynamometers when used by children. *J Bone Joint Surg Am* 90(5):1053–1059
 34. Anemaet WK, Moffa-Trotter ME (1999) Functional tools for assessing balance and gait impairments. *Top Geriatr Rehabil* 15(1):66–83
 35. Lanza Fde C, Zagatto Edo P, Silva JC, Selman JP, Imperatori TB, Zanatta DJ et al (2015) Reference equation for the incremental shuttle walk test in children and adolescents. *J Pediatr* 167(5): 1057–1061
 36. Utter AC, Robertson RJ, Nieman DC, Kang J (2002) Children's OMNI Scale of Perceived Exertion: walking/running evaluation. *Med Sci Sports Exerc* 34(1):139–144
 37. American College of Sports Medicine Position Stand (1998) The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 30(6):975–991
 38. Ayala F, Sainz de Baranda P, De Ste Croix M, Santonja F (2012) Reproducibility and criterion-related validity of the sit and reach test and toe touch test for estimating hamstring flexibility in recreationally active young adults. *Phys Ther Sport* 13(4):219–226
 39. Hartman A, van den Bos C, Stijnen T, Pieters R (2008) Decrease in peripheral muscle strength and ankle dorsiflexion as long-term side effects of treatment for childhood cancer. *Pediatr Blood Cancer* 50(4):833–837

40. Bosco C, Luhtanen P, Komi PV (1983) A simple method for measurement of mechanical power in jumping. *Eur J Appl Physiol Occup Physiol* 50(2):273–282
41. Runge M, Rittweger J, Russo CR, Schiessl H, Felsenberg D (2004) Is muscle power output a key factor in the age-related decline in physical performance? A comparison of muscle cross section, chair-rising test and jumping power. *Clin Physiol Funct Imaging* 24(6):335–340
42. Veilleux LN, Rauch F (2010) Reproducibility of jumping mechanography in healthy children and adults. *J Musculoskeletal Neuronal Interact* 10(4):256–266
43. Campbell JM, Brown RT, Cavanagh SE, Vess SF, Segall MJ (2008) Evidence-based assessment of cognitive functioning in pediatric psychology. *J Pediatr Psychol* 33(9):999–1014 discussion 5–20
44. Taylor HL, Jacobs DR Jr, Schucker B, Knudsen J, Leon AS, Debacker G (1978) A questionnaire for the assessment of leisure time physical activities. *J Chronic Dis* 31(12):741–755
45. Kriska AM, Caspersen CJ (1997) Introduction to a collection of physical activity questionnaires. *Med Sci Sports Exerc* 29(6):5–9
46. Montoye H (1971) Estimation of habitual physical activity by questionnaire and interview. *Am J Clin Nutr* 24(9):1113–1118
47. Sabia S, van Hees VT, Shipley MJ, Trenell MI, Hagger-Johnson G, Elbaz A et al (2014) Association between questionnaire- and accelerometer-assessed physical activity: the role of sociodemographic factors. *Am J Epidemiol* 179(6):781–790
48. Richardson MT, Leon AS, Jacobs DR Jr, Ainsworth BE, Serfass R (1994) Comprehensive evaluation of the Minnesota leisure time physical activity questionnaire. *J Clin Epidemiol* 47(3):271–281
49. Steele R, Mummery K (2003) Occupational physical activity across occupational categories. *J Sci Med Sport* 6(4):398–407
50. Santos-Lozano A, Santin-Medeiros F, Cardon G, Torres-Luque G, Bailon R, Bergmeir C et al (2013) Actigraph GT3X: validation and determination of physical activity intensity cut points. *Int J Sports Med* 34(11):975–982
51. Hikiyara Y, Tanaka C, Oshima Y, Ohkawara K, Ishikawa-Takata K, Tanaka S (2014) Prediction models discriminating between nonlocomotive and locomotive activities in children using a triaxial accelerometer with a gravity-removal physical activity classification algorithm. *PLoS One* 9(4):e94940
52. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P (2002) 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(7):2090–2106
53. Palmer SN, Meeske KA, Katz ER, Burwinkle TM, Varni JW (2007) The PedsQL brain tumor module: initial reliability and validity. *Pediatr Blood Cancer* 49(3):287–293
54. Kendzierski D, DeCarlo KJ (1991) Physical activity enjoyment scale: two validation studies. *J Sport Exerc Psychol* 13(1):50–64
55. Dempster AP, Laird NM, Rubin DB (1977) Maximum likelihood from incomplete data via the EM algorithm. *J R Stat Soc Ser B (methodol)* 1–38
56. Chamorro-Vina C, Valentin J, Fernandez L, Gonzalez-Vicent M, Perez-Ruiz M, Lucia A et al (2017) Influence of a moderate-intensity exercise program on early NK cell immune recovery in pediatric patients after reduced-intensity hematopoietic stem cell transplantation. *Integr Cancer Ther* 16(4):464–472
57. San Juan AF, Fleck SJ, Chamorro-Vina C, Mate-Munoz JL, Moral S, Perez M et al (2007) Effects of an intrahospital exercise program intervention for children with leukemia. *Med Sci Sports Exerc* 39(1):13–21
58. San Juan AF, Chamorro-Vina C, Moral S, Fernandez del Valle M, Madero L, Ramirez M et al (2008) Benefits of intrahospital exercise training after pediatric bone marrow transplantation. *Int J Sports Med* 29(5):439–446
59. Dimeo F (2000) Exercise for cancer patients: a new challenge in sports medicine. *Br J Sports Med* 34(3):160–161
60. Gotte M, Taraks S, Boos J (2014) Sports in pediatric oncology: the role(s) of physical activity for children with cancer. *J Pediatr Hematol Oncol* 36(2):85–90
61. Hill AB (2005) The environment and disease: association or causation? *Bull World Health Organ* 83(10):796–798

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.