International Thesis/ Tesis Doctoral Internacional

Role of Exercise, Physical Activity, and Fitness on psychological health in young pediatric cancer survivors

El papel del ejercicio, la actividad física y la condición física en la salud mental en niños y adolescentes supervivientes de cáncer

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Table of contents

1

Research project and funding

The present International Doctoral Thesis was performed under the umbrella of the iBoneFIT and REBOTA-EX projects and within the Promoting Fitness & Health through Physical Activity (PROFITH) research group of the University of Granada. The research project in which this International Doctoral Thesis was developed initially received funding from the La Caixa Foundation (iBoneFIT project). Later, additional funding was provided by the Ministry of Science and Innovation (REBOTA-EX project) to support a specific part of the project and to continue the project's assessments. These research projects were funded by the following organizations:

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2

List of abbreviations

Assessing Levels of Physical Activity	(ALPHA)
Children Depression Inventory	(CDI)
International Fitness Scale	(IFIS)
Life Orientation Test-Revised	(LOT-R)
Light physical activity	(LPA)
Metabolic value	(MET)
Moderate-to-vigorous physical activity	(MVPA)
Physical Self-Inventory	(PSI)
Physical Self-Perception Profile	(PSPP)
Preferred Reporting Items for Systematic Reviews and Meta-Analyses	(PRISMA)
Positive and Negative Affect Scale for Children	(PANAS-C)
Rosenberg Self-Esteem Scale	(RSE)
Self-esteem questionnaire	(SEQ-42)
Standard deviations	(SD)
State–Trait Anxiety Inventory for Children	(STAIC-R)
Subjective Happiness Scale	(SHS)

List of abbreviations

3

Abstract

Resumen

ABSTRACT

The studies of the present International Doctoral Thesis are classified into three sections according to their design: Systematic review and meta-analysis (**Section 1 – Study I**), cross-sectional studies (**Section 2 – Study II** and **Study III**), and randomized control trial study (**Section 3 – Study IV**).

Background: Childhood cancer is a rare disease whose treatments have consequences for the individuals affected. These consequences include obesity, impaired growth, secondary malignancies, and cardiovascular disease. Additionally, among the most common consequences of cancer and its treatments are psychological effects, such as displaying more symptoms of depression and anxiety compared to their siblings and the general population. Prior research has shown that engaging in physical activity and being physically fit may be linked to enhanced psychological well-being and reduced psychological distress in both healthy populations and during and after cancer treatments. However, there is a lack of studies examining the Role of Exercise, Physical Activity, and Fitness on psychological health in young pediatric cancer survivors.

Objectives: Hence, this International Doctoral Thesis aims to review the literature on the effects of physical activity on psychological health during and after cancer treatments (**Study I**), to examine the association between physical activity and fitness and psychological health in young pediatric cancer survivors **(Studies II and III**) and to investigate the effects of a 36-week online plyometric exercise-based program on psychological health in young pediatric cancer survivors (**Study IV**).

Methods: To accomplish these objectives, four studies were conducted: one systematic review and meta-analysis (**Study I**), two cross-sectional studies

(**Study II and III**), and one randomized control trial (**Study IV**). In **Study I,** the sample comprised 3604 individuals during and after cancer treatment (all ages, 66.7% female), with self-esteem measured by various questionnaires (i.e., RSE, PSI, PSPP, KINDL questionnaire, and SEQ-42). The random effect model (DerSimonian and Laird method) was used for the statistical analysis. For the cross-sectional studies (**Studies II and III**), baseline data from 116 participants (12.1±3.3 years; 42.2% female) of the iBoneFIT project were used, while for the randomized control trial (**Study IV**) both baseline and post-intervention data from this project were analyzed. All three studies measured psychological well-being using questionnaires (i.e., positive affect [PANAS-C], happiness [SHS], optimism [LOT-R], and self-esteem [RSE]) and psychological distress (i.e., anxiety [STAIC-R], depression [CDI], and negative affect [PANAS-C]). **Study II** employed ActiGraph GT3X accelerometers to measure the 24-hour movement behavior, with data analyzed using R studio software. Compositional data analysis was used for the statistical analysis. **Study III** utilized the International Fitness Scale (IFIS) to assess perceived physical fitness levels, with multiple linear regressions used for statistical analysis. In **Study IV**, a constrained baseline longitudinal analysis was performed using a linear mixed model for the statistical analysis.

Main findings: Regarding the results of this International Doctoral Thesis are: physical activity, specifically aerobic physical activity, and mind-body exercise may improve self-esteem during and after cancer treatment. Additionally, cancer status and the length of the intervention appear to play significant roles in the impact of physical activity on self-esteem (**Study I**); promoting light and moderate-to-vigorous physical activity in pre-pubertal cancer survivors (≤-1 year from peak height velocity) appears to improve happiness, positive affect, depression, and anxiety. Similarly, engaging in moderate-to-vigorous physical activity in peri/post-pubertal cancer survivors (>-

1 year from peak high velocity) may enhance happiness, optimism, depression, and anxiety (**Study II**); increased flexibility and self-perceived overall fitness are linked to improved positive affect. Furthermore, greater self-perceived cardiorespiratory fitness, speed/agility, and flexibility are associated with lower anxiety, depression, and negative affect. In contrast, neither self-perceived nor objectively measured muscular fitness is linked to psychological distress (**Study III**); After a 36-week online plyometric exercise-based program, although the results were not statistically significant on indicators of psychological well-being, the intervention group experienced more positive changes than the control group on psychological well-being, self-esteem, optimism, and positive affect scores, while on happiness it was the control group that experienced more positive changes. In psychological distress, the intervention group achieved greater reductions in psychological distress, depression, and anxiety scores, and although not statistically significant, similar reductions were observed for negative affect (**Study IV**).

Conclusions: Overall, the main finding of this International Doctoral Thesis is that it highlights the importance of promoting exercise, physical activity, and fitness as an approach to improving psychological well-being and decreasing psychological distress in young pediatric cancer survivors. Further research on specific physical activity interventions aimed at improving the psychological health of young pediatric cancer survivors is needed to draw further conclusions.

RESUMEN

Los estudios de la presente Tesis Doctoral Internacional se clasifican en tres secciones según su diseño: Revisión sistemática y metaanálisis (**Sección 1 - Estudio I**), estudios transversales (**Sección 2 - Estudio II y Estudio III**), y ensayo controlado aleatorizado (**Sección 3 - Estudio IV**).

Antecedentes: El cáncer infantil es una enfermedad rara cuyos tratamientos tienen consecuencias para los individuos afectados. Estas consecuencias incluyen obesidad, retraso del crecimiento, neoplasias malignas secundarias y enfermedades cardiovasculares. Además, entre las consecuencias más comunes del cáncer y sus tratamientos se encuentran los efectos psicológicos, como mostrar más síntomas de depresión y ansiedad en comparación con sus hermanos y la población general. Investigaciones anteriores han demostrado que realizar actividad física y estar en buena forma física pueden estar relacionado con un mayor bienestar psicológico y una reducción del malestar psicológico tanto en población joven sin patologías como durante y después de los tratamientos del cáncer. Sin embargo, faltan estudios que examinen el papel del ejercicio físico, la actividad y la forma físicas en la salud psicológica de los jóvenes supervivientes de cáncer pediátrico.

Objetivos: Por lo tanto, esta Tesis Doctoral Internacional tiene como objetivo revisar la literatura sobre los efectos de la actividad física en la salud psicológica durante y después de los tratamientos contra el cáncer (**Estudio I**), examinar la asociación entre la actividad física y el estado físico y la salud psicológica en jóvenes supervivientes de cáncer pediátrico (**Estudios II y III**) e investigar los efectos de una intervención de ejercicio físico online de 36 semanas en la salud psicológica en jóvenes supervivientes de cáncer pediátricos (**Estudio IV**).

Métodos: Para lograr estos objetivos se realizaron cuatro estudios: una revisión sistemática y metaanálisis (**Estudio I**), dos estudios transversales (**Estudio II y III**) y un ensayo controlado aleatorizado (**Estudio IV**). **En el Estudio I**, la muestra estaba compuesta por 3604 individuos durante y después del tratamiento del cáncer (todas las edades, 66,7% mujeres) y la autoestima se midió mediante diferentes cuestionarios (RSE, PSI, PSPP, cuestionario KINDL y SEQ-42). Para el análisis estadístico se utilizó el modelo de efectos aleatorios (método de DerSimonian y Laird). Para los estudios transversales (**Estudios II y III**), se utilizaron los datos de la evaluación inicial de los 116 participantes (12,1±3,3 años; 42,2% chicas) del proyecto iBoneFIT, mientras que para el ensayo controlado aleatorizado (**Estudio IV**) se utilizaron tanto los datos de la evaluación inicial como los de la evaluación posterior a la intervención de este proyecto. Los tres estudios midieron el bienestar psicológico mediante cuestionarios (afecto positivo [PANAS-C], felicidad [SHS], optimismo [LOT-R] y autoestima [RSE]) y malestar psicológico (es decir, ansiedad [STAIC-R], depresión [CDI] y afecto negativo [PANAS-C]). En el **Estudio II** se utilizaron acelerómetros ActiGraph GT3X para medir los patrones de movimiento durante 24 horas y el software R studio para el análisis de estos datos. Para el análisis estadístico se utilizó un análisis de datos composicionales. El **Estudio III** utilizó la Escala Internacional de Condición Física (IFIS) para la percepción de los niveles de condición física y regresión lineal múltiple para el análisis estadístico. En el **Estudio IV** se utilizó un análisis longitudinal con restricción en la evaluación inicial mediante un modelo lineal mixto para el análisis estadístico.

Principales resultados: Los resultados de la presente Tesis Doctoral Internacional son: la actividad física, específicamente la actividad física aeróbica, y el ejercicio mente-cuerpo pueden mejorar la autoestima durante y después del tratamiento del cáncer. Además, el estado del cáncer y la duración de la intervención parecen desempeñar roles importantes en el impacto de la actividad

física sobre la autoestima (**Estudio I**); un aumento de la flexibilidad y de la condición física general autopercibida parecen estar relacionados con una mejora del afecto positivo. Además, una mayor aptitud cardiorrespiratoria, velocidad/agilidad y flexibilidad autopercibidas parece asociarse con una menor ansiedad, depresión y afecto negativo. Por el contrario, ni la condición física muscular autopercibida ni la medida objetivamente están relacionadas con el malestar psicológico (**Estudio II**); la promoción de la actividad física ligera y moderada-vigorosa en supervivientes de cáncer prepúberes (≤-1 año desde el pico de velocidad de crecimiento) parece mejorar la felicidad, el afecto positivo, la depresión y la ansiedad. Del mismo modo, realizar actividad física moderada-vigorosa en supervivientes de cáncer peri/post-púberes (>-1 año desde el pico de velocidad de crecimiento) puede mejorar la felicidad, el optimismo, la depresión y la ansiedad (**Estudio III**). Tras una intervención de ejercicio físico online de 36 semanas, aunque los resultados no fueron estadísticamente significativos en los indicadores de bienestar psicológico, el grupo de intervención experimentó cambios más positivos que el grupo de control en la puntuación de bienestar psicológico, autoestima, optimismo y afecto positivo, mientras que en felicidad fue el grupo de control el que experimentó más cambios positivos. En cuanto al malestar psicológico, el grupo de intervención logró mayores reducciones en la puntuación de malestar psicológico, depresión y ansiedad, y aunque no fueron estadísticamente significativas, se observaron reducciones similares para el afecto negativo (**Estudio IV**).

Conclusiones: En conjunto, el principal hallazgo de esta Tesis Doctoral Internacional es que destaca la importancia de promover el ejercicio físico, la actividad física y la condición física como una estrategia para mejorar el bienestar psicológico y disminuir el malestar psicológico en jóvenes supervivientes de cáncer pediátrico. Se necesitan más investigaciones sobre intervenciones

específicas de actividad física dirigidas a mejorar la salud psicológica de los jóvenes supervivientes de cáncer pediátrico para poder extraer más conclusiones.

4

Key concepts

CANCER

Component	Definition	Indicators
Cancer	Uncontrolled growth and metastasis of specific cells within the body[1]	**Incidence:** rate of new cancer cases in a specific population and period of time in a particular [2] **Prevalence**: total number of cancer cases in a population at a specific moment. The difference with the incidence is that prevalence includes both new and existing cancer cases at a specific moment.[2]
Cancer survivor	Due to the inconsistency of the term "survivor," we refer to individuals who have completed their cancer treatments (any type of cancer treatment).	

PSYCHOLOGICAL HEALTH

Psychological health	Set of conditions related to the emotional, psychological, and social well-being of individuals[3]	**Psychological well-being**: associated with positive thoughts and feelings[4] **Psychological distress:** related to negative thoughts and feelings[5]
Psychological well-being	Associated with positive thoughts and feelings[4]	**Self-esteem**: refers to how we assess our-self whether positively or negatively[6] **Optimism**: refers to how favorably people view their future[7] **Happiness**: refers to positive psychological functioning[8] **Positive affect**: perception of emotion in a good or positive way[9]

Psychological distress	Related to negative thoughts and feelings[5]	**Depression**: means a low or apathetic mood over time[10] **Anxiety**: refers to the brain's state of alertness to worry or fear[11] **Negative affect**: tendency to experience negative feelings[9]
Self-concept	Description of ourselves[12]	

PHYSICAL ACTIVITY

Physical activity	Any bodily movement generated by skeletal muscles that results in energy consumption[13]	**Aerobic physical activity**: engages large muscle groups in dynamic activities, which significantly elevate heart rate and energy consumption[14] **Resistance training**: created to enhance muscular strength, endurance, and power by varying the resistance, number of repetitions per set, number of sets performed, and the rest intervals between sets[14] **Combined physical activity**: combination of aerobic physical activity and resistance training **Mind-body exercise**: combinations of breathing exercises, meditation, and structures movements[15]
Movement behaviours	Combination of the activities throughout the day includes: moderate-to-vigorous physical activity, light physical activity, sedentary behaviour, and sleep time[16]	**Moderate-to-vigorous physical activity**: any physical activity that significantly elevates heart rate and breathing. Its MET is between 3 and 6 for moderate physical activity and ≥6 for vigorous physical activity[17] **Light physical activity**: movements that slightly elevate the heart rate but not

		significantly, and are classified with a metabolic value (MET) between 1.5 and 3[17] **Sedentary behaviour**: low-energy expenditure physical activities, such as sitting or reclining posture, with a MET of less than 1.5[18] **Sleep time**: number of hours a person sleeps during a 24 hours period[19]
Physical fitness	Capacity to perform physical activity and encompasses a comprehensive range of physiological and psychological attributes[20]. It may measure Objectively-or Self-perceive	**Overall physical fitness**: for the present Thesis, is the sum of cardiorespiratory fitness, muscular strength, flexibility, and speed/agility **Cardiorespiratory fitness**: capacity of the cardiovascular and respiratory systems to provide oxygen to large muscle groups for extended periods. This included activities such as running, cycling, and swimming[21] **Muscular strength**: the ability of a muscle or muscle group to exert force against resistance. It is typically measured by the ability to lift a maximum weight once, as in weightlifting[21] **Flexibility**: ability to stretch muscles and joints through their full range of motion. It is usually measured by tests such as the sit and reach test[21] **Speed/agility**: ability to move quickly and change direction with efficiency and control. It is a crucial component in many sports and physical activities and is measured by tests such as the shuttle run[22]

Peak height velocity	It represents the period of maximum growth in stature, which was predicted using a validated algorithm that takes into account age and height in children[23].	In one of our studies (**Study II**), participants were classified as pre-pubertal (≤-1 year from peak height velocity) and peri/post-pubertal (>-1 year from peak height velocity)[24]

5

General introduction

Cancer

Cancer is characterized by uncontrolled growth and metastasis of specific cells within the body[1]. Childhood cancer is less common than adult cancer[25], with 206,362 new cases reported worldwide in 2020 being the most common cancers are leukemia, brain tumors, and non-Hodgkin lymphoma[25]. The survival rate for childhood cancer is over 85%[2], and it is expected that there will be 279.000 new cases worldwide by 2040[26], compared to around 28 million cases in the general population globally[27]. The data in Spain are expected to be similar, with 286,664 new cases diagnosed in 2024[28] and increasing to 341,000 cases in 2040[27]. Concerning the causes of childhood cancer, the understanding remains somewhat limited[29]. It appears that approximately 8-10% of childhood cancers are attributed to genetic mutation passed down from parents. In adults, these genetic mutations are often associated with the cumulative effects of aging and prolonged exposure to carcinogens[29]. However, in childhood cancer, finding the causes is challenging due to the rarity of the disease and the difficulty in determining early-life exposures [29].

In relation to consequences of cancer and its treatments include cardiovascular diseases, impaired growth and fertility, obesity, diabetes, and secondary malignancies[30–32]. However, despite the lack of studies examining the psychosocial consequences of cancer diagnosis and treatment at different ages, it appears that it may vary depending on the developmental stage at the time of diagnosis and treatment[33]. At early ages, child cancer survivors are more dependent on their parents, which may affect their cancer experiences with cancer, including their understanding of cancer and its consequences, as well as decisions regarding their health. Additionally, due to their development stage and the fundamental cognitive milestones, cognitive difficulties may be more pronounced at this age, and this population must adapt to their new life earlier than adolescent and adult cancer survivors [33,34]. Therefore, despite it is less likely

that adolescent and adult cancer survivors are as dependent on their parents as child cancer survivors, a cancer diagnosis and treatment may alter their autonomy, identity development, and the development of higher-order cognitive skills[33]. Previous studies have shown that individuals who were older at the time of diagnosis, survivors of leukemia or central nervous system cancers, women, and those whose parents experienced distress were at a higher risk of suffering from psychological distress [35,36].

Interrelation between psychological health, physical activity, and fitness

Psychological sequelae are among the most common consequences of cancer. Psychological health is defined as a set of conditions related to the emotional, psychological, and social well-being of individuals[37]. It may be understood through key dimensions that provide a clearer understanding of the psychological status of children and adolescents[3]. These dimensions include psychological well-being and psychological distress[3]. Psychological well-being is characterized by positive psychological states and feelings[4], and includes indicators such as self-esteem, optimism, happiness, and positive affect[3]. Self-esteem refers to an individual's self-evaluation, which can be either positive or negative[6]. Optimism involves the tendency to anticipate a favorable and hopeful future[7]. Happiness refers to a state of positive psychological functioning and overall well-being[8]. Positive affect concerns the experience and perception of emotions in a positive or pleasant manner[9]. In contrast, psychological distress is associated with negative emotions and attitudes[5], including indicators such as depression, anxiety, and negative affect[3]. Depression refers to a prolonged state of low mood or apathy[10], while anxiety is a heightened state of alertness associated with worry or fear[11]. Negative affect involves a tendency to experience negative emotions and feelings[9].

Several studies focusing on childhood and adulthood cancer survivors indicate a higher prevalence of depression and anxiety persisting many years after completing therapy[38], including symptoms of post-traumatic stress[39]. That is particularly significant among women, unemployed, and individuals with low income levels[40]. These psychological consequences may influence maladaptive lifestyle habits such as sedentary behaviours, alcohol consumption, and social functioning (school, employment), as well as the fear of recurrence[32,41]. Young pediatric cancer survivors are at a higher risk of experiencing symptoms such as depression and anxiety, antisocial behaviour, and impaired social competence compared to their siblings[39]. Specifically, young pediatric cancer survivors tend to experience a higher prevalence of anxiety (ranging from 1%-27%) and depression symptoms (ranging from 2%-40%) compared to both their siblings and the general population[42]. These challenges contribute to diminished psychological well-being and lower quality of life[39,43].

Physical activity offers many health benefits for the healthy population, including reduced premature mortality, improved physical fitness, enhanced cognitive function, and the reduction of symptoms of depression and anxiety in diverse populations[44–46]. It refers to any bodily movement generated by skeletal muscles that results in energy consumption[13] while exercise is a subcategory of physical activity, which is planned, structured, and repetitive[24]. Specifically in the oncology population, previous research has shown that physical activity may be safe both during and after cancer treatments[47]. However, other studies indicate a lack of evidence on potential harms, making it difficult to conduct evidence-based risk-benefit assessments for prescribing physical activity during cancer treatment[48,49]. During and after cancer treatment, different types of physical activity are associated with reductions in anxiety, depression, and fatigue[50,51]. Additionally, physical activity benefits for cancer survivors include improved cardiopulmonary fitness, muscle strength, body composition, quality of life, and

reduced psychological distress [52,53]. While most studies focus on anxiety, depression, fatigue, and quality of life[50–53], research on the relationship between physical activity intervention and self-esteem during and after cancer treatment remains limited. This limitation applies not only to the case of self-esteem but there are also a limited number of studies examining the effects of physical activity interventions on any other parameter of psychological health in young pediatric cancer survivors. This fact, together with the lack of consistency in the findings, highlights the importance of synthesizing all available evidence to better understand the literature (**Study I**), the connection between physical activity and fitness with psychological health (**Studies II and III**), and the effects of performing an online exercise program on psychological health in young pediatric cancer survivors (**Study IV**).

Physical activity is a modifiable lifestyle factor that effectively reduces adipose tissue and corrects metabolic problems, thereby lowering the risk of some cancers[54]. Despite evidence from a previous study showing the safety and feasibility of physical activity among childhood cancer population[55], these individuals have lower levels of physical activity compared to their healthy peers[32]. Additionally, just like physical activity provides health benefits, sedentary behaviour may impact negatively the psychological health of adolescents[56]. Considering that various movement behaviours occur throughout the day (including moderate-to-vigorous physical activity (MVPA), light physical activity (LPA), sedentary behaviour, and sleep time), each type correlated with the duration of the others. Thus, some studies have explored how reallocating one type of movement behaviour from the others influences various health parameters. Previous research has specifically shown that reducing 10 minutes of sedentary behaviour and increasing 10 minutes of LPA are associated with lower levels of anxiety and depression in apparently healthy young populations[57]. So, it is important to understand how reallocating time to each

movement behaviour affects indicators of psychological health. However, to our knowledge, no study has examined the association between movement behaviour and psychological health in young pediatric cancer survivors (**Study II**).

Physical fitness refers to the capacity to perform physical activity and encompasses a comprehensive range of physiological and psychological attributes[20]. Its association with better psychological health may be attributed to the fact that physically fit individuals tend to look and feel better, thereby linking physical fitness with improved physical and psychological health. Additionally, enhanced fitness can increase the levels of certain hormones, such as serotonin, which contribute to mood elevation[20]. Previous research has shown that higher fitness levels reduce psychological distress[58,59] and improve psychological well-being indicators[20,60] in both healthy young populations and adults with lung cancer. Thus, given the potential association between physical fitness and psychological health, and considering that young pediatric cancer survivors have compromised psychological health due to cancer and its treatment, more studies are needed to examine the contribution of fitness to psychological health in this population to better understand these association (**Study III**)

Structure and gaps addressed in this Thesis

This international Doctoral Thesis comprises three sections according to the design of the studies: Section 1 (**Study I**) includes a systematic review and meta-analysis, Section 2 (**Study II and III**) cross-sectional studies, and Section 3 (**Study IV**) a multicentre randomized control trial.

Table 1 provides an overview of the identified gaps in the literature.

	GAP	Contribution
Section 1	Most systematic reviews and meta-analyses on the effect of physical activity interventions on psychological health in young pediatric cancer survivors focus on psychological distress (i.e., anxiety and depression). However, there is a lack of systematic review and meta-analysis on self-esteem in this population. In addition, there are very few studies examining the effect of physical activity on self-esteem in young pediatric cancer survivors.	Systematic review and meta-analysis on the effect of physical activity interventions on self-esteem, not only in young pediatric survivors but also during and after cancer treatment at all ages (**Study I**)

Section 2	Most studies have focused on the association between objectively measured physical fitness and psychological health. However, little research has been conducted on the association between self-perceived physical fitness and psychological health. Nonetheless, there are increasingly more studies that use compositional data analysis to estimate the association between the reallocation of 24-hour movement behaviours (MVPA, LPA, sedentary behaviour, and sleep time) and other health parameters in various populations. However, there is a lack of this type of analysis in young pediatric cancer survivors to understand how reallocating one type of movement behaviour from the others influences psychological health.	Cross-sectional study on associations between 24-hour movement behaviours (i.e., MVPA, LPA, sedentary behaviour, and sleep time) with psychological well-being indicators (i.e., happiness, optimism, positive affect, and self-esteem) and psychological distress (i.e., depression, anxiety and negative affect) using compositional data analysis in young pediatric cancer survivors (**Study II**) Cross-sectional studies on the association of self-perceived (i.e., overall fitness, cardiorespiratory fitness, muscular fitness, speed/agility, and flexibility) and objectively measured fitness components (i.e., upper and lower body) with psychological well-being indicators (i.e., positive affect, happiness, optimism, and self-esteem) and psychological distress (i.e., anxiety, depression, and negative affect) in young pediatric cancer survivors (**Study III**)
Section 3	The effect of physical activity interventions on psychological health in children and adolescents during and after cancer treatment is not clear due to the different psychological health indicators used by the studies.	Multicentre randomized control trial focuses on examining the effects of a 36-week online physical activity intervention on psychological well-being indicators (i.e., happiness, optimism, positive affect, and self-esteem) and psychological distress (i.e., depression, anxiety and negative affect) in young pediatric cancer survivors (**Study IV**).

Table 1. Overview of the identified gaps and contribution of this Thesis.

6

Aims and hypothesis

Hypothesis

Physical activity is associated with beneficial effects on psychological health (i.e., psychological well-being and distress) in young pediatric cancer survivors.

Aims

The overall aim of this International Doctoral Thesis was to study the role of physical activity, physical fitness, and movement behaviours on psychological health in young pediatric cancer survivors. This objective is addressed through four specific studies divided in three sections.

Specific aims:

Section 1. Systematic review and meta-analysis: Physical activity interventions on self-esteem during and after cancer treatment.

· Specific aim I: to conduct a systematic review and meta-analysis of the literature on the effects of physical activity interventions (both general and by its type) on self-esteem during and after cancer treatment (**Study I**)

Section 2. Cross-sectional studies: Physical activity and fitness in young pediatric cancer survivors.

· Specific aim II: to examine the associations between 24-hour movement behaviours with psychological well-being indicators and psychological distress using compositional data analysis in young pediatric cancer survivors (**Study II**).

· Specific aim III: to examine the associations of self-perceived and objectively-measured fitness components with psychological well-being and psychological distress indicators in young pediatric cancer survivors (**Study III**).

Section 3. Randomized control trial: Effects of an exercise program on psychological health in young pediatric cancer survivors.

· Specific aim IV: to examine the effects of a 36-week online plyometric exercise-based program on psychological well-being and distress indicators in young pediatric cancer survivors (**Study IV**).

7

General methods

The present International Doctoral Thesis, which comprises four studies, is conducted under the umbrella of the iBoneFIT and REBOTA-EX project. A comprehensive study design and methods description is available in a previously published work[61]. The intervention implemented within the iBoneFIT project is explained below. This International Doctoral Thesis focused on psychological health, which is a secondary outcome of the iBoneFIT project.

Study characteristics

The iBoneFIT project was a multicentre, parallel-group randomized control trial (1:1) designed to examine the effect of a 36-week online plyometric exercise-based program on bone health in 116 young pediatric cancer survivors (Clinical Trial registration no. ISRCTN61195625) from the Virgen de las Nieves (Granada) and Reina Sofía (Córdoba) University Hospitals (Spain). This project received approval from the Ethics Committee on Human Research of the Junta de Andalucía (Reference: 4500, December 2019) and followed the principles described in the Declaration of Helsinki (2013 revision). It also followed the guidelines of the Consolidated Standards of Reporting Trials (CONSORT). The inclusion criteria required that participants were not receiving cancer therapies at the time of enrollment, had previously received radiation and/or chemotherapy, and had been diagnosed at least a year earlier while exclusion criteria included individuals who were concurrently participating in another study that could pose additional risks, cause discomfort or interfere with the results of both studies; those with a prior diagnosis of anorexia nervosa/bulimia, known pregnancy and/or known alcohol and drug abuse; requiring chronic oral glucocorticoid therapy; those with injuries that could affect daily life activities and can be aggravated by exercise, and; with a lower limb prosthesis that prevents bone assessment.

Due to COVID-19 restrictions, the data was collected in two phases: 1) from October 2020 to February 2021, and 2) from December 2021 to March 2022.).

Eligible participants from the two hospitals were contacted via telephone calls and informed about the inclusion criteria and the intervention and, if they met the criteria and provided consented, they were enrolled in the study. The randomization was conducted by an external partner independent of the participant recruitment and enrolment process. Participants were randomized by age and sex into an intervention group (exercise intervention plus diet counseling focused on calcium and vitamin D) or a control group (diet counseling focused on calcium and vitamin D). The control group was asked about performing the intervention after finishing the study[61]. The allocation of participants to their respective groups was blinded to the evaluators of outcomes until all assessments were completed. However, it was not feasible to blind participants due to the inherent characteristics of the exercise intervention. The measurements were performed at baseline (T0) and after 36 weeks of a plyometric exercise-based program at the Sport and Health University Research Institute (iMUDS, University of Granada) (**Figure 1**).

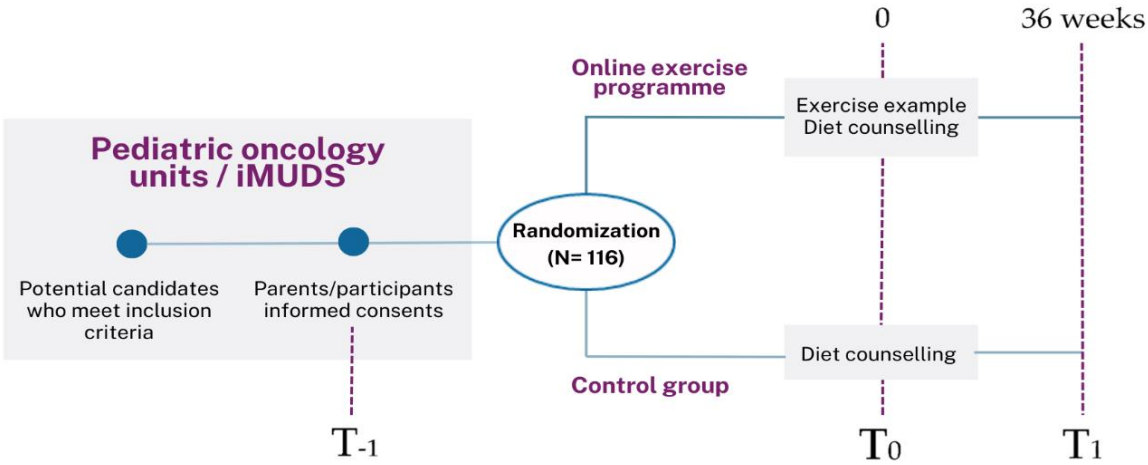


Figure 1. Modified from Figure 1 *The effect of an online exercise program on bone health in pediatric cancer survivors (iBoneFIT): study protocol of a multi-centre randomized controlled trial* by Gil-Cosano et al. *BMC Public Health* (2020) 20:1520. Desing of the iBoneFIT study.

T_{-1}, meeting parents and participants; T_0, baseline assessment; T_1, post-intervention assessment; iMUDS, Sport and Health University Research Institute

Sample size

The sample size of the iBoneFIT project was calculated considering the femoral neck areal bone mineral density, thus playing an important role in the osteoporosis diagnosis. The project, which included children and adolescents aged 6-18 years, has calculated the sample size to account for subgroup analysis by age groups (6-11 years and 12-18 years). A minimum of 116 participants was needed (58 in each group), with an estimated effect size of 0.25 for changes in femoral neck areal bone mineral density, an α level of 0.05, and 80% power. This estimate adds 20% to account for occasional losses and refusals and 10% for multivariable analyses[61]. G*Power (v.3.1.9.2) was used to calculate the repeated measures (within-between interactions) for two groups (between factors) and two-time points (before, post, within factors) using analysis of variance. For the aim of assessing bone outcomes, a correlation between measurements of 0.7 was assumed[62].

Intervention

Participants in the control group continued their usual routines, while those in the intervention group engaged in a 36-week online plyometric exercise-based program. The exercise sessions were developed and recorded on video and uploaded to YouTube by a personal trainer. Participants or their parents were added to a WhatsApp group where training videos were shared via a webpage link (https://t.ly/iNqS6) and updated twice a month. Researchers who monitored participants through WhatsApp groups contacted them once a week. During these interactions, they updated training videos, provided additional information, or proposed challenges based on five behaviour change techniques. These techniques (i.e. action planning and goal setting, providing instructions

and demonstrations of how to perform the behaviour, self-monitoring of behaviour, providing feedback on performance and information about health consequences) were incorporated into the platform along with gamification elements to maintain and boost the motivation of the participants during the exercise intervention including infographics, challenges, etc., The home-based exercise program consisted of three phases, with progressive plyometric jump sessions held three to four days per week, each lasting approximately 15 minutes. The exercise sessions were designed to involve a warm-up, followed by a squat/jump workout, and ending with a cool-down. Although specific days for training sessions were recommended, participants had the flexibility to complete the sessions on any day at any time that suited their schedules, as the sessions were recorded. Over 136 sessions, participants completed 7296 squats/jumps (2000 squats + 5296 jumps). Both groups received information on dietary counseling regarding calcium and vitamin D. After the study, the control group was offered the same online plyometric exercise-based program. The Consensus Exercise Reporting Template (CERT) was used to explain the rationale behind the iBoneFIT exercise program[63]. **Table 2** provides a detailed explanation of the training volume and its progression.

Phase	Warm up[a]	Exercise[b]	Level	Repetitions	Sets a day (Rest[c])	Sessions a Week	Squats/Jumps a Week
1	RAMP	Body mass-based Squat	1 (1–4 week)	15	3	4	180
			2 (5–8 week)	20	4	4	320
Total phase 1 (8 weeks)							2000
2	RAMP	Squat jump	1 (9–12 week)	10	3	3	90
			2 (13–16 week)	15	3	4	180
			3 (17–20 week)	20	4	4	320
Total phase 2 (12 weeks)							2360
3	RAMP	Countermovement jump	1 (21–24 week)	10	3	3	90
			2 (25–28 week)	12	3	4	144
			3 (29–32 week)	15	3	4	180
			4 (33–36 week)	20	4	4	320
Total phase 3 (16 weeks)							2936
Total intervention (36 weeks)							7296

Table 2 detailed explanation of the training volume and its progression.

RAMP raise, activate, mobilise and potentiate. [a]Warm up focused on dynamic exercises with progressive intensity enhancing optimal core body temperature, motor unit excitability, kinesthetic awareness and ranges of motion. [b]Each exercise suggested to be performed at the pace of the personal trainer managing the session. If not, a self-paced performance was recommended. [c]Phase 1 rest = 45 s; Phases 2 and 3 rest = 1 min

Participants adherence

Adherence was monitored using a diary, in which participants or their parents recorded their entries after training sessions and sent a photo to the WhatsApp group once a month. During each phase of the intervention, a minimum compliance rate of 50% was required. However, by the end of the intervention, the overall compliance rate needed to reach 70%. If a participant had not completed 70% adherence to the intervention by the end of this but was projected to reach this threshold within an additional two weeks, the exercise program was extended accordingly.

Key variables

Figure 2 shows the key variables used in this International Doctoral Thesis, along with the instruments employed and the studies in which they were implemented.

Figure 2. Key variables of the iBoneFIT project used in this International Doctoral Thesis

*Due to COVID-19 restriction, masks were mandatory, and because the available evidence at that time showed impaired performance when using FFP2/N95 face masks, and to ensure the safety of our participants, cardiorespiratory fitness and speed/agility were excluded.

Methodology of the four studies included in this Thesis

Table 3 provides the methodology of the studies included in this International Doctoral Thesis

Section 1

Studies	Design; Target population	Search strategy	Variables studied (instruments)	Statistical analysis
Study I	Systematic review and meta-analysis (systematic review=32 studies; meta-analysis=15 studies) 3604 Individuals during and after cancer treatment (all ages, 66.7% female)	("physical conditioning" OR "motor activity" OR "physical activity" OR "activity" OR "physical education" OR exercis* OR move* OR moving OR active OR inactive OR sedentary OR sport* OR train*) AND ("psychological wellbeing" OR "psychological well-being" OR "self-esteem" OR "self-concept" OR "self-worth") AND (cancer OR onco* OR myelo* OR leukaemia OR leukemia OR neoplasm* OR lympho* OR carcinoma OR tumor OR tumour OR sarcoma)	Predictor: physical activity interventions (aerobic physical activity, resistance training, combined physical activity and mind-body exercise) Outcome: self-esteem (measured by RSE, PSI, PSPP, KINDL questionnaire, and SEQ-42)	Random effect model (DerSimonian and Laird method)

Section 2

Study	Design; Target population	Project	Variables studied (instruments)	Statistical analysis
Study II	Cross-sectional 110-116 young pediatric cancer survivors, depending on the outcome (12.1±3.3 years; 42.2% female)	iBoneFIT project	Predictors: 24-hour movement behaviours (accelerometry ActiGraph GT3X) Outcome: psychological well-being indicators (i.e., positive affect [PANAS-C], happiness [SHS], optimism [LOT-R], and self-esteem [RSE]) and psychological distress (i.e., anxiety [STAIC-R], depression [CDI], and negative affect [PANAS-C])	Compositional data analysis
Study III	Cross-sectional 110-116 young pediatric cancer survivors, depending	iBoneFIT project	Predictors: physical fitness: self-perceived fitness (IFIS questionnaire) and objective fitness (i.e., upper and lower body [handgrip strength and standing long jump]) Outcome: psychological well-being indicators (i.e., positive affect [PANAS-	Multiple linear regressions adjusted by key covariates (i.e., sex, years from peak height velocity, years

	on the outcome (12.1 ± 3.3 years, 56.9% boys*)		C], happiness [SHS], optimism [LOT-R], and self-esteem [RSE]) and psychological distress (i.e., anxiety [STAIC-R], depression [CDI], and negative affect [PANAS-C])	between diagnosis and testing, body mass index, and type of neoplasm)
		Section 3		
Study	Design; Target population	Project	Variables studied (instruments)	Statistical analysis
Study IV	Multicentre randomized control trial 116 young pediatric cancer survivors throughout intention-to-treat analysis (12.1±3.3 years; 42.2% female) 90 young pediatric cancer survivors through per-protocol analysis (12.2±3.4 years; 42% female)	iBoneFIT project	Intervention program: 36-week plyometric exercise-based program, 3-4 sessions/week, 10-16 minutes/session. Based on the weight-bearing impact of high intensity. Outcome: psychological well-being indicators (i.e., positive affect [PANAS-C], happiness [SHS], optimism [LOT-R], and self-esteem [RSE]) and psychological distress (i.e., anxiety [STAIC-R], depression [CDI], and negative affect [PANAS-C])	Constrained baseline longitudinal analysis via a linear mixed model

* This data changed between Study III and Studies II and IV due to an error detected in the Sex variable in Study III

Table 3. Overview of the methodology of the four studies included in this Thesis

8

Results and discussion

Section 1	Systematic review and meta-analysis: Physical activity interventions on self-esteem during and after cancer treatment.	**Study I**	The effects of physical activity interventions on self-esteem during and after cancer treatment: a Systematic Review and Meta-Analysis	Under review
Section 2	Cross-sectional studies: Physical activity and fitness in young pediatric cancer survivors.	**Study II**	24-hour movement behaviours and psychological health in young pediatric cancer survivors. A compositional data analysis from the iBoneFIT project.	Under review
		Study III	Is higher physical fitness associated with better psychological health in young pediatric cancer survivors? A cross-sectional study from the iBoneFIT project.	Article published in Scandinavian Journal of Medicine and Science in Sports. 2023
Section 3	Randomized Control Trial: Effects of an exercise program on psychological health in young pediatric cancer survivors	**Study IV**	The effects of an online plyometric exercise-based program on psychological health in young pediatric cancer survivors: the iBoneFIT multicentre randomized control trial.	Drafting manuscript

Results and Discussion

Section 1

Systematic review and meta-analysis: Physical activity interventions on self-esteem during and after cancer treatment.

Study I

The effects of physical activity interventions on self-esteem during and after cancer treatment: a Systematic Review and Meta-Analysis

Study 1

ABSTRACT

Objective: to investigate the effect of physical activity (PA) (both general and its type) on self-esteem during and after cancer treatment.

Methods: A systematic search was conducted across PubMed, Web of Science, Scopus, SPORTDiscuss, and PsycINFO from their inception to February 2024. The systematic review included 32 studies, with 15 studies (13 RCT and 2 quasi-experimental) and 3604 participants (66.7% female) included in the meta-analysis involving controlled trials using a control group and at least one PA intervention group. The study was registered in PROSPERO (CRD42022309771). Risk of bias for RCTs was assessed using the Cochrane Collaboration's tool for assessing risk of bias (RoB2), and quasi-experimental studies with the Joanna Briggs Institute critical appraisal tool.

Results: PA significantly improved self-esteem during and after cancer treatment (pooled SMD=0.32, p<0.01). Specifically, aerobic PA (pooled SMD=0.33, p=0.04) and mind-body exercise (pooled SMD=0.70, p=0.03) had positive effects on self-esteem. Overall, PA interventions improved self-esteem during cancer treatment (pooled SMD=0.50, p=0.01) and in PA interventions lasting more than 12 weeks (pooled SMD=0.44, p=0.02).

Conclusion: PA (specifically, aerobic and mind-body exercises) may have a positive effect on self-esteem during and after cancer treatment, with cancer status and the duration of the intervention being key factors.

INTRODUCTION

Cancer is slightly more common in men than women (40,9% vs. 39.1%) and remains one of the leading global causes of mortality [1]. The five-year relative survival rate is approximately 68%[1] but surviving cancer and undergoing cancer-related treatment increases the risk of side effects, such as impaired growth in pediatric population, cardiovascular disease, and secondary malignancy [2–4].

Individuals during and after cancer treatment may experience psychological issues that contribute to maladaptive lifestyle habits, such as sedentarism and alcoholism [5], as well as impaired social functioning (e.g., difficulties in school or employment), anxiety, depression, and fear of recurrence [4,6,7]. These psychological sequels, affecting emotional well-being, can lead to changes in self-esteem levels [6]. A study of young adults after cancer treatment [8] found that low self-esteem, defined as a score of ≤ 25 score on The Rosenberg Self-Esteem scale, was present in 10% of the participants.

Self-esteem is one component of self-perception, alongside self-concept. While self-concept refers to how we describe ourselves, self-esteem relates to how we assess that self-concept, either positively or negatively [9,10]. High self-esteem is associated with better physical and psychological health, academic performance, and quality of interpersonal relationships [9,11]. In contrast, low self-esteem is linked to dissatisfaction, self-loathing, self-contempt, and self-rejection [9]. Factors that can influence self-esteem include negative body image and personal experiences. Self-esteem develops gradually over time, shaped by social interactions and life experiences[12]. It tends to be high during childhood, declines until adolescence [13,14], rises from mid-adolescence to mid-adulthood, peaks between the ages of 50 and 60, and eventually declines in older age [15].

The benefits of physical activity (PA) in healthy population are well established [16]. After cancer treatment, PA may not only improve fitness and

quality of life but may also reduce depression, psychosocial distress, and recurrence of cancer [17]. Previous research has shown that physical exercise may be safe during and after cancer treatments[18]. However, a more recent study highlights that there is insufficient research on the potential harms of PA to make fully evidence-based risk-benefit assessments for its prescription during cancer treatment [19,20]. Previous studies have shown that different types of PA can reduce depression, anxiety, and fatigue during and after cancer treatment [21,22]. Additionally, while some research found associations between PA interventions and improved self-esteem during and after cancer treatment[23–25], this area has been less extensively explored. A comprehensive compilation of available studies through a systematic review and meta-analysis is needed. Thus, to the best of our knowledge, this is the first systematic review and meta-analysis aimed at examining the effects of PA interventions (both general and by type) on self-esteem during and after cancer treatment.

METHODS

Protocol and Registration

This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis PRISMA guidelines and PRISMA-S [26,27] (**Supplementary table S1 and Supplementary table S2**). The systematic review and meta-analysis were registered in the International Prospective Register of Systematic Reviews in 2022, with an update made in 2024 (registration number: CRD42022309771). The update was performed through email alerts and by reapplying the search strategy over the past two years to identify any newly published articles.

Data Sources

A systematic search was conducted using MEDLINE (via PubMed), Web of Science (Clarivate), Scopus (Elsevier), SPORTDiscuss (EBSCOhost) and Psycinfo (Ovid) from database inception to February 2024. The search strategy used for each database and the search terms used are available in Supplementary Material (**Table S3**) which was carried out in parallel with a previous study and was adapted to the subject matter of this study.

Eligibility Criteria

Two reviewers (A.R-S and A.R-T) independently screened and identified studies that potentially met the inclusion criteria. Any disagreements were resolved through consensus, or if necessary, with the involvement of a third researcher (E.U-G). The inclusion criteria were defined as follows: a) Population: individuals during and after cancer treatment; b) Age: all age groups; c) Cancer types: all types of cancers; d) Study design: observational and experimental studies; e) Outcome: self-esteem measured using any validated questionnaire; f) Intervention: any form of PA; g) Control: groups without a PA intervention (including flexibility-focused activities); h) Language: studies written in English or Spanish. Exclusion criteria included non-eligible publication types, such as conference proceedings, theses, editorials, letters to the editor, systematic reviews, and meta-analyses.

Study selection

The study selection process was carried out in several steps. First, records were identified through database searches and duplicates were removed using Endnote X7 0.1. Secondly, titles and abstracts were screened to determine their potential eligibility. Articles that appeared eligible were then read in full to decide on their final inclusion or exclusion in the systematic review and meta-analysis. All steps were completed and reviewed by two investigators (A.R-S and

A.R-T). Disagreements were resolved through discussion, adhering to the established inclusion and exclusion criteria. When the inclusion status of a study was unclear, a third reviewer (E.U-G) was involved to reach through discussion. **Figure 1** presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study selection process. Finally, reference lists of the included articles were examined for other relevant studies. Authors of articles with missing data were contacted, and 2 of the 7 studies that had not reported the required information responded and provided the necessary data. Additionally, efforts were made to obtain the full text of certain articles by contacting the respective authors (27 in total); however, the majority (21 authors) did not respond to our requests. A citation index and email alerts were established to track potential new studies published during the course of this study.

Classification as 'during' or 'after' cancer treatment

Studies involving patients receiving any form of cancer treatment, whether as initial cancer therapy or for metastasis or cancer recurrence, were classified as 'during' treatment. Studies that included patients not currently undergoing any cancer treatment or receiving androgen suppression therapy or hormone therapy without any other cancer treatment, were defined as 'after' treatment. Studies including both types of patients were categorized as 'both'.

Risk-of Bias Assessment

The Cochrane Collaboration's tool for assessing risk of bias (RoB2) was used for randomized controlled trials (RCTs) [28]. This tool evaluated five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Overall, a study is considered to have a "low risk of bias" if all domains are rated as "low risk", "some concerns" if at least one domain is rated as "some concern",

and “high risk of bias” if at least one domain is rated as “high risk”, or if multiple domains are rated as “some concerns”.

The Joanna Briggs Institute critical appraisal tool was used to evaluated the quality of quasi-experimental Studies [29]. This tool assesses nine domains: the cause and effect of variables, similar comparison groups and treatment/care, control group, multiple measurements of outcomes, follow-up, similar measurements of outcomes in the different groups, outcome measurements in a reliable way, and statistical analysis. Each domain is rated with one of four responses: “yes” (criterion met), “no” (criterion not met), “unclear”, or “not applicable” (N/A). A study was classified as “high quality” if it achieved a quality score of at least 0.75 (i.e., 75%), and as “low quality” if the score was below 0.75. Additionally, a score for each criterion was calculated by dividing the number of positive ratings by the total number of studies evaluated, providing an overview of how well the current literature performs on each criterion. Two researchers (A.R-S and A.R-T) independently assessed the risk of bias to determine the quality of the included studies, with any discrepancies resolved by a third reviewer (E.U-G).

Data Extraction

Articles retrieved from the databases were exported and managed using an EndNote library (Endnote version X7.0.1). Data extracted from the original reports, based on the inclusion and exclusion criteria, included: a) first author and year of publication; b) country of data collection; c) study design; d) sample characteristics; e) method used for measuring self-esteem at baseline and follow-up; f) type of control group intervention; and g) type of PA intervention. Data extraction was independently verified by two researchers (A.R-S and A.R-T), and any discrepancies were resolved through consensus with a third researcher (E.U-G).

Statistical considerations

The DerSimonian and Laird method was used to compute Standardized Mean Difference (SMD) and 95% confidence intervals (95% CIs), as the summary measure. For data synthesis and meta-analysis, random-effects models were employed. When studies provided mean self-esteem values at baseline and endpoint or reported mean value changes, SMD was calculated. SMD of 0.2 to 0.5 were considered small, 0.5 to 0.8 were considered medium, and values greater than 0.8 were considered large [30,31]. The heterogeneity of results across studies was assessed using the I^2 statistic [32]. In addition, exploratory subgroup analyses were performed to examine how the intervention affects self-esteem depending on the type of PA (aerobic PA, resistance training, combined PA, and mind-body exercise), cancer status (during and after cancer treatments), and lasting of the intervention (12 weeks or less and more than 12 weeks). Furthermore, exploratory subgroup analyses were conducted to explore differences across groups of age (children and adolescents under 18 years of age and adults with 18 years of age or older), study design (randomized controlled trial and quasi-experimental study), and self-esteem questionnaires (Rosenberg self-esteem scale and other than Rosenberg self-esteem scale questionnaires). Funnel plots were examined to assess the risk of potential publication bias, with Egger's regression asymmetry test used to detect asymmetry. Further, the 'trim and fill' procedure [33] was also applied to identify and correct for funnel plot asymmetry potentially due to publication bias. A leave-one-out cross-validation analysis was performed to evaluate the impact of excluding individual studies on the combined pooled SMD by sequentially omitting one study at a time. The summary measure used in this study was the SMD.

Statistical analyses were performed using Comprehensive Meta-Analysis software version 2.2 (Biostat Inc., Englewood, NJ, USA), with statistical significance set at $p<0.05$.

Classification of physical activity interventions

Due to the diversity of PA interventions, they were classified into four categories: aerobic PA, resistance training, combined PA, and mind-body exercise. Aerobic PA interventions include belly dance, treadmill, elliptical, and walking. Resistance training encompasses exercises like leg extensions, leg curls, leg presses, calf raises, chest presses, seated rowing, triceps extensions, biceps curls, and modified curl-ups. Combined PA includes a variety of sports and recreational activities, as well as programs combining aerobic and resistance training. Mind-body exercise refers to practices such as yoga and Pilates.

RESULTS

Study selection and adverse effects

A total of 7151 studies were identified from the literature search, of which 2399 were excluded before screening due to duplication. After screening by title and abstract, 369 full-text articles were reviewed for eligibility. Finally, 32 studies were included in the systematic review, of which 13 RCT's and 2 Quasi-Experimental Studies were included in the meta-analysis (**Figure 1**).

In this systematic review and meta-analysis, 13 studies reported "no significant adverse effects" while 20 studies did not provide information on whether any adverse effects were observed.

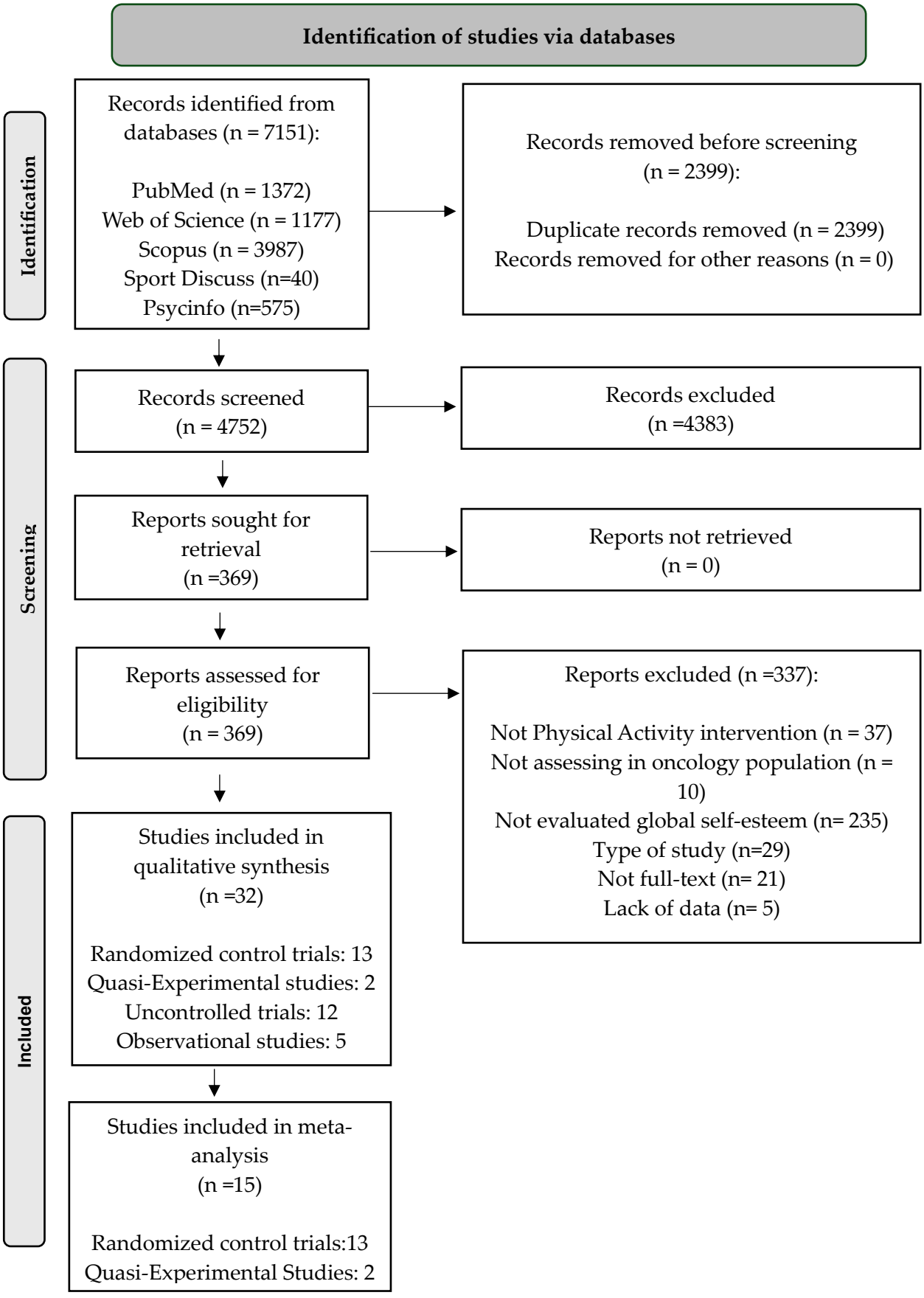

Identification of studies via databases
Identification
Records identified from databases (n = 7151):
PubMed (n = 1372)
Web of Science (n = 1177)
Scopus (n = 3987)
Sport Discuss (n=40)
Psycinfo (n=575)
Records removed before screening (n = 2399):
Duplicate records removed (n = 2399)
Records removed for other reasons (n = 0)
Screening
Records screened (n = 4752)
Records excluded (n =4383)
Reports sought for retrieval (n =369)
Reports not retrieved (n = 0)
Reports assessed for eligibility (n = 369)
Reports excluded (n =337):
Not Physical Activity intervention (n = 37)
Not assessing in oncology population (n = 10)
Not evaluated global self-esteem (n= 235)
Type of study (n=29)
Not full-text (n= 21)
Lack of data (n= 5)
Included
Studies included in qualitative synthesis (n =32)
Randomized control trials: 13
Quasi-Experimental studies: 2
Uncontrolled trials: 12
Observational studies: 5
Studies included in meta-analysis (n =15)
Randomized control trials:13
Quasi-Experimental Studies: 2

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of study selection.

Risk-of Bias Assessment

The quality of the RCTs included in the meta-analysis (n=13, **Table S4**) showed that six studies (46.2%) had a low risk of bias, while seven studies (53.8%) had some concerns. In terms of specific domains, all studies were rated as low risk for the randomization process, missing outcome data, and measurement of the outcome (100%). For deviations from intended interventions, eight studies (61.5%) were rated as low risk, and five studies (38.5%) were rated as having some concerns. Regarding the selection of reported results, ten studies (76.9%) were rated as low risk, and three studies (23.1%) had some concerns. Of these 13 articles, 62% were analyzed using intention-to-treat principle, while 38% were analyzed using per-protocol principle.

The risk of bias in the quasi-experimental studies (n=2, **Table S4**) indicated that both studies had high-quality scores. In terms of specific domains, 100% of the studies met the methodological quality criteria for the cause and effect of variables, similar treatment/care groups, presence of a control group, multiple measurements of outcomes, consistency of outcomes measurements across groups, reliability of outcome measurements, and statistical analysis. For the domain of similar comparison groups, one study did not meet the methodological quality criterion (50%), while the other was rated as unclear (50%). In the follow-up domain, one study was rated as unclear (50%), and the other met the methodological quality criterion (50%). Both of these articles (100%) were analyzed using per-protocol principle.

Study characteristics

Table 1 presents the characteristics of the studies included in the systematic review and meta-analysis. A total of 3604 participants (66.7% female)

during or after cancer treatment were involved in the select studies of this systematic review. These studies were conducted in 12 different countries, with participants having the following cancer types: Ewing sarcoma (n=1), Testicular cancer (n=1), Breast cancer (n=17), Rectal cancer (n=1), and various malignancy disease types (n=13). The age of the participants ranges from 8 years and older, with the sample sizes varying between 16 to 618 (median=107 participants). Regarding self-esteem measurements, 24 studies (72.7%) used the Rosenberg Self-Esteem Scale, three used the Physical Self-Inventory (PSI) (9.1%), three (9.1%) the Physical self-perception Profile, two (6.1%) the KINDL questionnaire, and one (3%) the Self-esteem questionnaire (SEQ-42). Despite the variety of questionnaires, all studies in this meta-analysis provided self-esteem scores.

Table 2 shows the characteristics of the interventions from studies included in the meta-analysis. Control groups received various interventions: usual care (73.3%) [24,25,34–41], three educational sessions (13.3%) [42,43], recreational activity (6.7%) [23], dietary guidelines and information about healthy habits (6.7%) [44], and not have a control group (6.7%) [45]. PA interventions were categorized as follows: combined (i.e., aerobic + resistance PA) (38%) [23,34,38,40,41,44,45], aerobic (33%) [25,35–37,39,43,45], mind-body (19%) [24,25,42,43], and resistance (10%) [35,45]. Most interventions involved supervised exercises (69%), with the remainder either unsupervised (25%) or a combination of both (6%). The duration of the interventions ranged from 1 to 24 weeks (median=13.4) with the weekly exercise duration of the intervention ranging from 45 to 330 minutes. Characteristics of intervention studies not included in the meta-analysis are detailed in **Table S5**.

Study characteristics		Population characteristics at baseline				Outcome		
Authors and year	**Country**	**Age**	**Sample size [n (% male)]**	**Cancer-type**	**Time period**	**Method**	**Baseline (mean ± SD)**	**Follow-up (mean ± SD)**
Randomized Controlled Trials [n=14]								
Adams et al. 2018 [37]	Canada	43.7 ± 10.8	63 (100% male) Walking: 35 CG: 28	Testicular cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Walking: 32.5 ± 5.5 CG: 36.0 ± 4.8	Walking: 34.5 ± 4.1 CG: 35.0 ± 5.0
Boing et al. 2023 [43]	Brazil	18 years or older	52 (100% female) Pilates: 18 Belly: 18 CG:16	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Pilates: 30.2 ± 1.1 Belly dance: 32 ± 1.4 CG: 30.1 ± 1.7	Pilates: 32.6 ± 1.2 Belly dance: 33 ± 0.9 CG: 32 ± 1.1
Cadmus et al. 2009 [1] [34]	USA	35-75	50 (100% female) Sports/recreational activities: 25 CG: 25	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Sports/recreational activities: 34.8 ± 4.2 CG: 35.2 ± 3.8	Sports/recreational activities: 34.3 ± 4.9 CG: 34.5 ± 3.6
Cadmus et al. 2009 [2] [34]	USA	40–75	74 (100% female) Sports/recreational activities: 37 CG: 37	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Sports/recreational activities: 34.2 ± 5.5 CG: 33.2 ± 5.7	Sports/recreational activities: 34.5 ± 5.2 CG: 33.4 ± 5.9
Courneya et al. 2007 [35]	Canada	25-78 (Mean 49 years)	242 (100% female) Resistance training: 82 Aerobic physical activity: 78 CG: 82	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Resistance training: 34.1 ± 4.2 Aerobic physical activity: 34.0 ± 5.1 CG: 34.1 ± 4.6	Resistance training: 34.7 ± 4.2 Aerobic physical activity: 34.5 ± 5.1 CG: 33.2 ± 5.5
Fretta et al. 2021 [42]	Brazil	55.3 ± 11	34 (100% female) Pilates: 18 CG: 16	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Pilates: 30.4 ± 5.1 CG: 30.5 ± 6.6	Pilates: 35.1 ± 3.8 CG: 33.1 ± 4.3
Gokal et al. 2016 [36]	UK	18-75	50 (100% female) Walking: 25 CG: 25	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Walking: 21.7 ± 4.4 CG: 20.4 ± 4.9	Walking: 23.8 ± 4.6 CG: 19.5 ± 4.2
Kovačič et al. 2011 [24]	Slovenia	≥40	32 (100% female) Yoga: 16 CG: 16	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Yoga: 21.3 ± 1.3 CG: 21.2 ± 1.4	Yoga: 23.7 ± 1.1 CG: 21.2 ± 1.7
Leite et al. 2021 [25]	Brazil	55 ± 10	52 (100% female) Belly dance: 18	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Belly dance: 32.1 ± 1.3	Belly dance: 33.3 ± 1.0 Mat Pilates:32.7 ± 1.0

			Mat Pilates: 18 CG: 16				Mat Pilates: 30.4 ± 1.2 CG: 31.9 ± 1.4	CG: 32.2 ± 1.1
Musanti 2012 [45]	USA	50.5 ± 7.5	55 (100% female) Aerobic physical activity: 12 Resistance training: 17 Combined physical activity: 13 CG*: 13	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Aerobic physical activity: 23 ± 6.6 Resistance training: 25.3 ± 3.2 Combined physical activity: 24.4 ± 4.8 CG*: 25.7 ± 4.0	Aerobic physical activity: 21.7 ± 4.4 Resistance training: 26.4 ± 2.6 Combined physical activity: 23.6 ± 1.2 CG*: 26.3 ± 3.9
Rastogi et al. 2020 [44]	USA	54.4 ± 11.2	48 (96% female) Combined physical activity: 26 CG: 22	Breast and colorectal cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Combined physical activity: 22.6 ± 3.4 CG: 20.2 ± 3.7	Combined physical activity: 23 ± 4.2 CG: 20.2 ± 4.7
Saultier et al. 2021 [23]	France	10.4 ± 0.5	70 (42.5% female) Combined physical activity: 37 CG :33	Various cancer types	During cancer treatment	Self-esteem with the "Physical Self-Inventory—Very Short Form" (PSI-VSF)	Combined physical activity: 4.4 ± 0.2 CG: 4.6 ± 0.1	Combined physical activity: 5.0 ± 0.1 CG: 4.8 ± 0.1
Van Dijk-Lokkart et al. 2016 [38]	Netherlands	8-18	68 (46.7% female) Combined physical activity:30 CG: 38	Various cancer types	During cancer treatment	Global Self-worth with the Dutch versions of the Self Perception Profile for children and adolescents	Combined physical activity: 61.4 ± 29.6 CG: 61.3 ± 28.6	Combined physical activity: 73 ± 25.6 CG: 64.7 ± 33.1
Wurz et al. 2019 [40]	Canada	32.3 ± 7.8	16 (85.7% female) Combined physical activity: 7 GC: 9	Various malignancy disease types	After cancer treatment	The Rosenberg Self-Esteem Scale	Combined physical activity: 29.1 ± 2.2 CG: 28.1 ± 5.5	Combined physical activity: 29.5 29.5± 2.3 CG: 28.56 ± 5.8
Quasi-Experimental studies [n=2]								
Carminatti et al. 2019 [39]	Brazil	54.5 ± 8.3	19 (100% female) Belly: 11 CG: 8	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Belly: 29 ± 1 CG: 32 ± 1	Belly: 32 ± 2 CG: 32 ± 1
Rosenberg et al. 2014 [41]	USA	30.6	199 (82.9% female) Outdoor adventure 1: 87 Outdoor adventure 2: 41 CG: 71	Various malignancy disease types	After cancer treatment	Self-esteem with the Psychological Screening Inventory-2	Outdoor adventure 1: 52.2 ±10.3 Outdoor adventure 2: 52.3 ± 9.8 CG: 53.8 ± 11.2	Outdoor adventure 1: 50.4 ± 8.9 Outdoor adventure 2: 51.9 ± 10.2 CG: 55 ± 10.2

Uncontrolled trials [n=12]								
Barrio et al. 2012 [54]	Spain	49.1 ± 9.4	31 (100% female)	Breast cancer	Women affected by breast cancer	The Rosenberg Self-Esteem Scale	Self-esteem 1: 1.8 ± 0.6 Self-esteem 2: 1.9 ± 0.8	Self-esteem 1: 1.5 ± 0.6 Self-esteem 2: 1.5 ± 0.6
Caru et al. 2020 [55]	Canada	12.1 ± 3.6	16 (50% female) N Total: 16 N Male:8 N Female: 8	Various cancer types	During cancer treatment	Self-esteem with the Physical Self-Perception Profile (PSPP)	Total: 5.3 ± 0.5 Male: 5.1 ± 0.4 Female: 5.4 ± 0.5	Total: 5.7 ± 0.5 Male: 5.8 ± 0.5 Female: 5.6 ± 0.5
Caru et al. 2021 [56]	Canada	12.1 ± 3.6	16 (50% female) Boys: 8 Girls: 8	Various malignancy disease types	During cancer treatment	Self-esteem with the Physical Self-Perception Profile (PSPP)	Total: 5.8 ± 0.5 Boys: 5.6 ± 0.5 Girls: 5.9 ± 0.4	Total: 5.3 ± 0.5 Boys: 5.1 ± 0.4 Girls: 5.4 ± 0.5
Courneya et al. 2014 [57]	Canada	> 18 years old	301 (100% female) Standard aerobic exercise: 96 High standard dose: 101 Combined physical activity: 104	Breast cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Standard aerobic exercise: 33.5 ± 4.3 High standard dose: 34.3 ± 5.2 Combined physical activity: 34.0 ± 5.2	Standard aerobic exercise: 34.8 ± 2.8 High standard dose: 34.5 ± 2.8 Combined physical activity: 33.9 ± 2.8
Ho, Rainbow et al. 2005 [58]	Hong Kong	50.2 ± 7.1	Dance: 22	Various cancer types	During cancer treatment	The Rosenberg Self-Esteem Scale	Dance: 16.7 ± 3.3	Dance: 18.2 ± 3.6
Morielli et al. 2016 [59]	Canada	57.5	18 (33.3 % female) Total: 18	Rectal cancer	During cancer treatment	The Rosenberg Self-Esteem Scale	Total During NACRT[6]: 4.9 ± 1	Total Post-NACRT/pre-surgery: 4.8 ± 1
Muller et al. 2016 [60]	Germany	10.7 ± 4.3	150 (49% female) Total: 150 N Leukemia/ lymphoma = 86 N Brain tumor = 38 N Sarcoma = 26	Various cancer types	After cancer treatment	Self-esteem with the KINDL questionnaire	Total: 67 ± 17.7	Total: 69 ± 17.1
Osypiuk et al. 2020 [61]	USA	54 ± 10.2	21 (100% female) Qigong: 21	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Qigong :21.7 ± 6.1	Qigong: 23.7 ± 5.5
Rey-Barth et al. 2022 [62]	France	52 (Range 46-55)	14 (100% female) Aerobic physical activity: 14	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Aerobic physical activity: 30.4 ± 6.6	Aerobic physical activity: 32.6 ± 5.5

Speed-Andrews et al. 2010 [63]	Canada	54.8 ± 5.3	17 (100% female) Yoga: 17 52	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Yoga: 31.5 ± 5.7	Yoga: 33.8 ± 5.6
Török et al. 2006 [64]	Hungary	15.6 ± 1.5	(57.7% female) Therapeutic recreation camping: 44	Various malignancy disease types	During cancer treatment	The Rosenberg Self-Esteem Scale	Therapeutic recreation camping: 27.2 ± 3.6	Therapeutic recreation camping: 28.3 ± 4.1
Vallet et al. 2015 [65]	France	14.3 ± 2.9	11 (36.4% female) Combined physical activity: 11	Various cancer types	During cancer treatment	Self-esteem with the physical self-inventory (PSI-6)	Combined physical activity: 6.2 ± 2.1	Combined physical activity: 7.7 ± 1.8
Observational studies [n=5]								
Awick et al. 2017 [66]	USA	56.2 ± 9.3	370 (100% female) Total: 370	Breast cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	Total: 40.5 ± 6	Total: 40.5 ± 5.6
Belanger et al. 2013 [67]	Canada	38.2 ± 5.6	588 (43.7% female) No sport participation: 397 Sport participation: 191	Young adult cancer	After cancer treatment	The Rosenberg Self-Esteem Scale	No sport participation: 31.7 ± 5.8 Sport participation: 34.4 ± 4.8	N/A
Deisenroth et al. 2016 [68]	Germany	11.4 ± 4.1	40 (57.5% female) Total: 40	Various cancer types	During cancer treatment	Self-esteem with the KINDL questionnaire	Total: 52.4 ± 20.9	N/A
Patsou et al. 2018 [69]	Greece	51.7 ± 7.3	171 (100% male) Low fitness: 89 CG: 82	Breast cancer	After cancer treatment	Self-esteem with the Greek version of the Self-Esteem Scale	IG: 41.61 ± 3.30 CG: 32.67 ± 6.07	N/A
Ranft et al. 2017 [70]	Germany	30 (Range 9-69)	909 (44.4% female) Survivors: 613 CG: 296	Ewing Sarcoma	After cancer treatment	The Rosenberg Self-Esteem Scale	Survivors: 23.2 CG: 24	N/A

CG: Control Group; Outdoor adventure 1: people for whom it was their first outdoor adventure program; Outdoor adventure 2: people for whom it was their second outdoor adventure program; Self-esteem 1: I have the feeling that I have some good qualities; Self-esteem 2: I have the feeling that I am a person of worth, at least as much as most people; During NACRT[6]: neoadjuvant chemoradiotherapy. *We considered flexibility as the control group. SD: Standard deviation

Age is shown as mean ± standard deviation, or range. N/A: not applicable.

Table 2. Characteristic of studies' interventions included in the meta-analysis

Reference	Control group	Intervention type	Categorization	Duration (weeks)	Volume (minutes per week)	Supervision
Randomized Controlled Trials [n=13]						
Adams et al. 2018 [37]	Received usual care	Uphill treadmill walking or running, and to maintain all other exercise they were performing at baseline	Aerobic physical activity	12 weeks	180 minutes	Yes
Boing et al. 2023 [43]	Received an invitation to three educational sessions	IG 1: Pilates IG 2: Belly dance	IG 1: Mind-body exercise IG 2: Aerobic physical activity	16 weeks	180 minutes	Yes
Cadmus et al. 2009 [1] [34]	Received usual care	Variety of sports/recreational activities	Combined physical activity	24 weeks	150 minutes	Yes
Cadmus et al. 2009 [2] [34]	Received usual care	Variety of sports/recreational activities	Combined physical activity	24 weeks	150 minutes	Yes
Courneya et al. 2007 [35]	Received usual care	IG 1: Aerobic physical activity IG 2: Resistance training	IG 1: Aerobic physical activity IG 2: Resistance training	17 weeks	>135 minutes	Yes
Fretta et al. 2021 [42]	Three educational sessions	Pilates method intervention	Mind-body exercise	16 weeks	180 minutes	Yes
Gokal et al. 2016 [36]	Received usual care	Moderate intensity walking	Aerobic physical activity	12 weeks	About 150 minutes	No
Kovačič et al. 2011 [24]	Received usual care	Relaxation training sessions according to the Yoga in Daily Life system.	Mind-body exercise	3 weeks	105 minutes	No
Leite et al. 2021 [25]	Received usual care	IG 1: Belly dance IG 2: Mat Pilates	IG 1: Aerobic physical activity IG 2: Mind-body exercise	16 weeks	180 minutes	Yes
Musanti 2012 [45]	No CG (Participant divided in Aerobic, Resistance, Combined and flexibility*)	IG 1: Aerobic physical activity IG 2: Resistance training IG 3: Aerobic + Resistance training	IG 1: Aerobic physical activity IG 2: Resistance training IG 3: Combined physical activity	12 weeks	45-90 minutes	No
Rastogi et al. 2020 [44]	Received Dietary Guidelines, standardized e-mails at 1, 2, 4, and 8 weeks with information on healthy eating and stress management	Multi-component intervention	Combined physical activity	12 weeks	170 ± 131min	No

Saultier et al. 2021 [23]	Received recreational activities the first 6 month and later do the physical activity program of 6 month	Strength and muscle building, balance and proprioception training and 15 multi-activity sessions (dance, basketball, badminton, yoga, skiing, swimming, paddling, etc.).	Combined physical activity	24 weeks	120-330 minutes	Yes
Van Dijk-Lokkart et al. 2016 [38]	Received usual care	Cardiorespiratory and muscle strength training	Combined physical activity	12 weeks	90 minutes	Yes
Wurz et al. 2019 [40]	Received usual care	Aerobic and strength training sessions	Combined physical activity	12 weeks	100-180 minutes	Mixed
Quasi-Experimental studies [n=2]						
Carminatti et al. 2019 [39]	Received usual care	Belly dance	Aerobic physical activity	12 weeks	120 minutes	Yes
Rosenberg et al. 2014 [41]	Received usual care	IG 1: Outdoor adventure program 1 IG 2: Outdoor adventure program 2	Combined physical activity	1 week	-	Yes

Additional information of the intervention studies not included in the meta-analysis can be found in the supplementary material **Table S5.**

IG: Intervention group; CG: Control group

Meta-analysis

A total of 15 studies examining the effect of PA intervention with a control group on self-esteem during (36.4%), after (54.5%), and both during and after cancer treatment (9.1%) were included in this meta-analysis. The pooled SMD of all PA interventions on self-esteem was 0.32 (95% CI: 0.10 to 0.55, p<0.01, I^2=76%) for changes in self-esteem across all types of exercise (**Figure 2**). There was no statistically significant publication bias according to Egger's test (P=0.097) or based on a visual inspection of the funnel plot for self-esteem outcome (**Supplementary figure S1**). However, after incorporating imputed studies (N=3) using the "trim and fill" procedure, the SMD estimate was 0.418 (95% CI: 0.186 to 0.650). Thus, correction for potential publication bias did not alter the significance of the results.

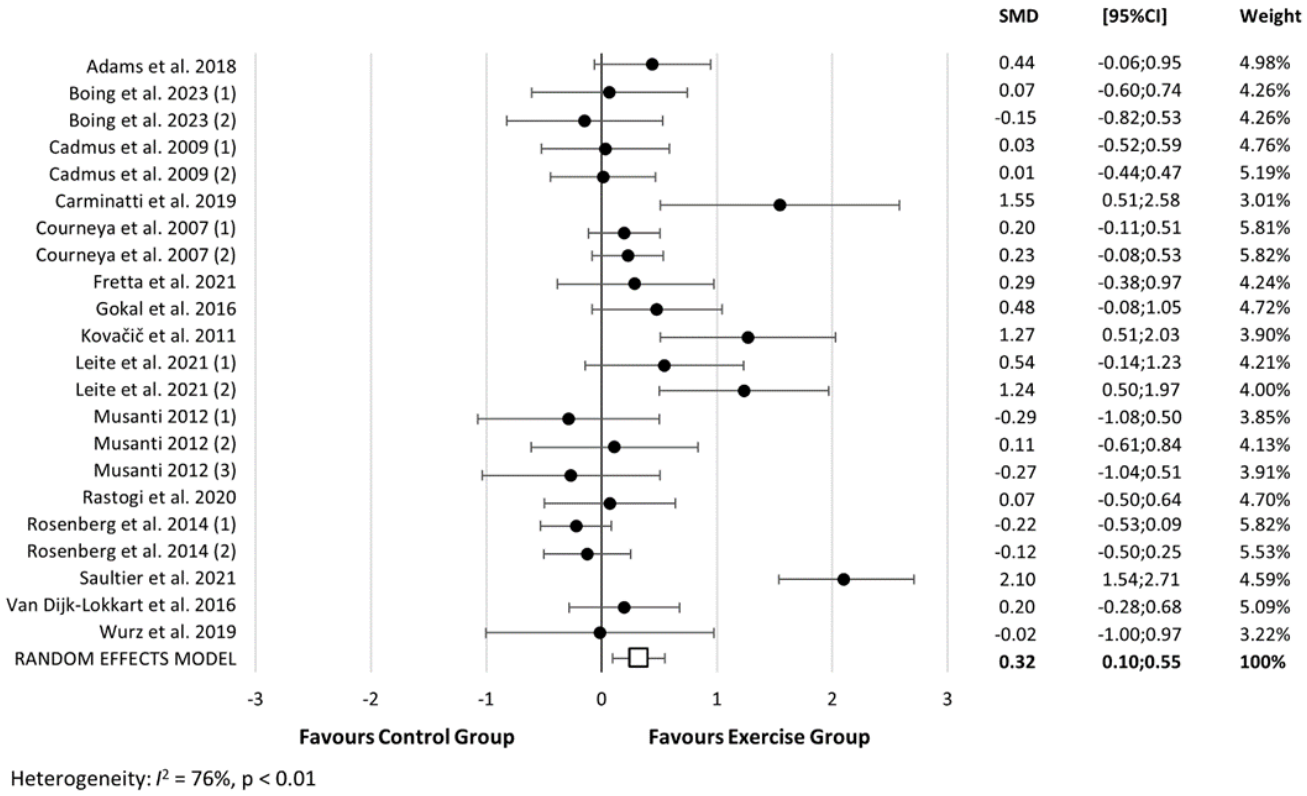


Figure 2. Forest plot of overall physical activity interventions on self-esteem during and after cancer treatment.

SMD: Standardized mean difference; CI: confidence intervals.

Boing et al. 2023 (1): represents the mind-body exercise; Boing et al. 2023 (2): aerobic physical activity; Cadmus et al. 2009 (1): combined physical activity during cancer treatment; Cadmus et al. 2009 (2): combined physical activity after cancer treatment; Courneya et al. 2007 (1): aerobic physical activity; Courneya et al. 2007 (2): resistance training; Leite et al. 2021 (1): aerobic physical activity; Leite et al. 2021 (2): mind-body exercise; Musanti 2012 (1): aerobic physical activity; Musanti 2012 (2): resistance training; Musanti 2012 (3): combined physical activity; Rosenberg et al. 2014 (1): outdoor adventure 1 (people for whom it was their first outdoor adventure program); Rosenberg et al. 2014 (2): outdoor adventure 2: people for whom it was their second outdoor adventure program.

Exploratory subgroup analyses were conducted to assess changes in self-esteem based on the type of PA intervention (**Figure 3**). For aerobic PA interventions, the SMD was 0.33 (95% CI: -0.02 to 0.65, p=0.04, I^2=52%). Mind-body exercise interventions showed a larger SMD of 0.70 (95% CI: 0.09 to 1.31, p=0.03, I^2=69%). The 'trim and fill' procedure for this analysis indicated no changes in estimates, and no correction for potential publication bias was needed (data not shown). Similarly, the leave-one-out analysis did not alter the results (data not shown). For combined PA interventions, the SMD was 0.20 (95% CI: -0.23 to 0.63, p=0.37, I^2=85%). Given the limited number of studies examining resistance training interventions on self-esteem (n=2), the SMD appeared to align with that of combined PA interventions (SMD=0.21, 95% CI: -0.07 to 0.49, p=0.14, I^2=0%). The leave-one-out analysis for these exploratory subgroup analyses did not alter the results (data not shown).

Regarding the effects of overall PA interventions on self-esteem considering cancer status (during vs. after cancer treatment) and the length of the intervention (12 weeks or less vs more than 12 weeks), for patients during cancer treatment, the SMD was 0.50 (95% CI: 0.11 to 0.89, p=0.01, I^2=87%), whereas for those after cancer treatment, the SMD was 0.09 (95% CI: -0.10 to 0.29, p=0.35, I^2=40%) (**Supplementary figure S2**). Additionally, interventions lasting 12 weeks or less had an SMD of 0.21 (95% CI: -0.06 to 0.48, p=0.13, I^2=64%), while those lasting more than 12 weeks showed a higher SMD of 0.44 (95% CI: 0.06 to 0.82,

p=0.02, I^2=82%) (**Supplementary figure S3**). The leave-one-out analysis for these exploratory analyses did not alter the results (data not shown).

When examining the exploratory subgroup analyses across groups of age, study design, and self-esteem questionnaire, the limited number of studies makes it difficult to draw any definitive conclusions. For children and adolescents, the SMD was 1.15 (95% CI: -0.74 to 3.04, p= 0.23, I^2=96%), while for adults the SMD was 0.22 (95% CI: 0.04 to 0.40, p=0.02, I^2=56%) (**Supplementary Figure S4**). For quasi-experimental studies, the SMD was 0.21 (95% CI: -0.44 to 0.86, p=0.53, I^2=83%) whereas for randomized controlled trials the SMD was 0.35 (95% CI: 0.11 to 0.59, p<0.01, I^2=72%) (**Supplementary Figure S5**). For questionnaires other than the Rosenberg Self-Esteem Scale, the SMD was 0.47 (95% CI: -0.40 to 1.34, p= 0.29, I^2=94%) while for the Rosenberg self-esteem scale, the SMD was 0.28 (95% CI: 0.10 to 0.47, p<0.01, I^2= 48%) (**Supplementary Figure S6**).

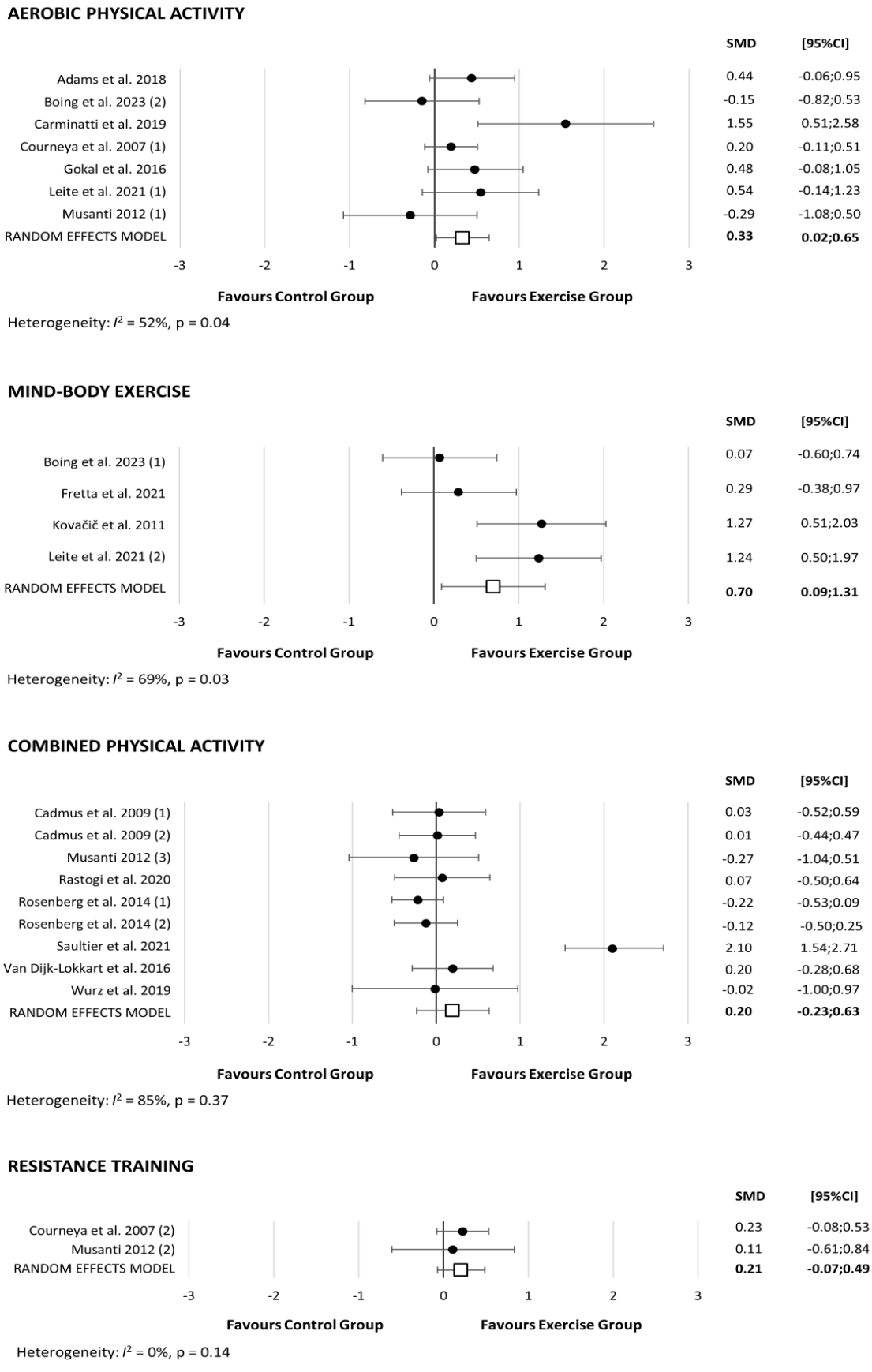


Figure 3. Forest plot of physical activity interventions divided by its type on

self-esteem during and after cancer treatment.

SMD: Standardized mean difference; CI: confidence intervals.

Boing et al. 2023 (1): represents the mind-body exercise; Boing et al. 2023 (2): aerobic physical activity; Cadmus et al. 2009 (1): combined physical activity during cancer treatment; Cadmus et al. 2009 (2): combined physical activity after cancer treatment; Courneya et al. 2007 (1): aerobic physical activity; Courneya et al. 2007 (2): resistance training; Leite et al. 2021 (1): aerobic physical activity; Leite et al. 2021 (2): mind-body exercise; Musanti 2012 (1): aerobic physical activity; Musanti 2012 (2): resistance training; Musanti 2012 (3): combined physical activity; Rosenberg et al. 2014 (1): outdoor adventure 1 (people for whom it was their first outdoor adventure program); Rosenberg et al. 2014 (2): outdoor adventure 2: people for whom it was their second outdoor adventure program.

DISCUSSION

To our knowledge, this is the first systematic review and meta-analysis to focus on the effects of PA on self-esteem during and after cancer treatment. Our findings suggest that PA interventions have a small but positive effect on self-esteem in this population. Specifically, aerobic PA showed a small positive effect on self-esteem, while mind-body exercise showed a medium positive effect. However, no significant effects were observed for combined PA or resistance training on self-esteem. Regarding the interventions conducted during cancer treatments, as well as those lasting more than 12 weeks, it had a positive effect on self-esteem, with medium and small effect, respectively. No significant effects were found in additional analyses in groups of age, study design, and self-esteem questionnaires.

Our findings indicate that aerobic PA interventions improved self-esteem during cancer treatment, but not after cancer treatment. The study by Carminatti et al. [39] notably contributed to these results, although some studies showed trends toward significance [25,36,37]. In the studies by Carminatti et al. [39], Boing et al. [43], and Leite et al. [25], belly dance interventions were used for women with breast cancer during and after cancer treatment. However, only Carminatti et al. reported significant improvements in self-esteem. One possible explanation for these

differing results is that participants in the studies by Boing et al. and Leite et al. reported higher baseline self-esteem scores compared to those in Carminatti et al., suggesting the latter group may had more room for improvement. In addition, the use of a mirror during Carminatti et al., intervention may have played a role in enhancing self-esteem, as the authors noted that mirrors may help participants refine technique and posture, fostering greater confidence and self-esteem [43]. Other studies employed treadmill, elliptical, or moderate-intensity walking interventions, such as Courneya et al. [35] and Musanti et al.[45] after breast cancer treatment, Gokal et al. [36] during breast cancer, and Adams et al. [37] after testicular cancer treatment. Of these, only Gokal et al. [36] and Adams et al. [37] reported results tending towards significance. These findings may be influenced by higher baseline self-esteem in the control group, except Gokal et al.[36]. Moreover, the authors suggest that the intensity and duration of the interventions might have been insufficient to yield significant improvements.

For mind-body exercise interventions, our results suggest a positive effect on improving self-esteem during and after cancer treatment. Supporting this, a study on university students found a positive relationship between a Yoga Nidra intervention and self-esteem [46]. The authors of the study attribute this effect to the relaxation mechanisms of the intervention, which may increase parasympathetic system activity, reducing psychological stress and, in turn, enhancing self-esteem [46]. Additionally, most of the articles in this meta-analysis (75%) featured interventions lasting more than 12 weeks, which may further explain the positive effect of mind-body exercise on self-esteem in this population.

Finally, our analysis found no significant effect of combined PA and resistance training interventions on self-esteem during and after cancer treatment. Several factors may explain these results. First, three of the interventions were home-based, which limited social interaction. Second, only 28.6% of the interventions lasted longer than 12 weeks, which may be insufficient

time to see a significant effect. Third, many interventions allocated more time to aerobic PA than resistance training, and most studies (75%) focused on individuals after cancer treatment. Regarding resistance training, the limited number of studies and small sample sizes reduce the statistical power, making it difficult to determine whether this type of intervention has a positive impact on self-esteem

Our exploratory subgroup analyses identified two key factors: cancer status (during cancer treatment) and intervention duration (over 12 weeks), that contributed to the effects of PA on self-esteem. Firstly, a stress response is common after a cancer diagnosis and usually decreases over time [47]. However, prolonged stress can lead to chronic issues that require professional intervention [47,48]. This suggests that individuals after cancer treatment who are highly stressed and not fully recovered may need more than just PA to improve self-esteem; psychological support may be necessary. Secondly, regular PA boosts the production and release of brain-derived neurotrophic factor (BDNF) [49], a vital protein for the central nervous system that supports synaptic formation, maintenance, and neuroplasticity [50]. Increased BDNF levels are linked to enhanced cognitive function and emotional well-being [51]. A meta-analysis on exercise and depression found that the most significant improvements occurred around the 16-week mark [52]. Given the strong connection between depression and self-esteem [53], this could explain why longer PA interventions have a more pronounced positive effect on self-esteem. In relation to the additional exploratory subgroup analyses in group of age, study design, and self-esteem questionnaire, along with the analysis of resistance training interventions, it is difficult to draw a conclusion due to the limited number of studies in these conditions.

Strengths and limitations

This systematic review and meta-analysis provide a thorough qualitative and quantitative assessment of PA interventions and their effects on self-esteem during and after cancer treatment. However, several limitations should be noted. First, the limited number of studies focusing on the pediatric population prevents us from drawing robust conclusions for this specific group. Second, the findings should be interpreted with caution due to the overall limited number of studies on this topic and the lack of evidence regarding the safety of PA during cancer treatments. Third, high levels of heterogeneity among studies necessitate careful interpretation of the results. Fourth, some studies could not be included in the analysis due to inaccessible full-text articles and a lack of response from authors when contacted.

CONCLUSION

Our systematic review and meta-analysis indicate that PA (primarily aerobic and mind-body exercise) may enhance self-esteem during and after cancer treatment. Additionally, the cancer status and duration of the intervention appear to significantly influence the impact of PA on self-esteem.

CRITICAL REVIEW

Psychological factors, including altered levels of self-esteem, are among the most common causes of cancer and its treatment. While previous systematic reviews and meta-analyses have shown that different types of PA reduce depression, anxiety, and fatigue during and after cancer treatment, the impact of PA on self-esteem has been less thoroughly investigated. This systematic review and meta-analysis may help existing research on this topic, revealing that PA interventions, particularly aerobic and mind-body exercise, may enhance self-esteem both during and after cancer treatment. Additionally, factors such as the cancer status (i.e., individuals during cancer treatment) and the duration of the

intervention (more than 12 weeks) significantly influence the effectiveness of PA on self-esteem.

REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023 Jan 12;73(1):17–48.
2. Erdmann F, Frederiksen LE, Bonaventure A, Mader L, Hasle H, Robison LL, et al. Childhood cancer: Survival, treatment modalities, late effects and improvements over time. Cancer Epidemiol. 2021 Apr;71.
3. Henderson TO, Nathan PC. Childhood cancer survivors: Considerations for surgeons in the transition from pediatric to adult care. Semin Pediatr Surg. 2015;24(2):93–9.
4. Antwi GO, Jayawardene W, Lohrmann DK, Mueller EL. Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies. Support Care Cancer. 2019 Sep 16;27(9):3183–94.
5. Wang YH, Li JQ, Shi JF, Que JY, Liu JJ, Lappin JM, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. Mol Psychiatry. 2020;25(7):1487–99.
6. Tonsing KN, Ow R. Quality of Life, Self-Esteem, and Future Expectations of Adolescent and Young Adult Cancer Survivors. Health Soc Work. 2018 Feb 1;43(1):15–21.
7. Ness KK, Mertens AC, Hudson MM, Wall MM, Leisenring WM, Oeffinger KC, et al. Limitations on Physical Performance and Daily Activities among Long-Term Survivors of Childhood Cancer. Ann Intern Med. 2005 Nov 1;143(9):639.
8. Wurz A, Brunet J. Describing and exploring self-esteem, physical self-perceptions, physical activity and self-efficacy in adolescent and young adult cancer survivors. Eur J Cancer Care (Engl). 2020 Jan 24;29(1):e13179.
9. Silvestri PR, Baglioni V, Cardona F, Cavanna AE. Self-concept and self-esteem in patients with chronic tic disorders: A systematic literature review. Eur J Paediatr Neurol. 2018;22(5):749–56.
10. Levesque RJR. Sadistic Personality Disorder. In: Encyclopedia of Adolescence. Cham: Springer International Publishing; 2018. p. 3229–30.
11. Baumeister RF, Campbell JD, Krueger JI, Vohs KD. Does High Self-Esteem Cause Better Performance, Interpersonal Success, Happiness, or Healthier Lifestyles? Psychol Sci Public Interes. 2003 May 24;4(1):1–44.
12. Arsandaux J, Galéra C, Salamon R. The association of self-esteem and psychosocial outcomes in young adults: a 10-year prospective study. Child Adolesc Ment Health. 2021 May 13;26(2):106–13.

13. Tirlea L, Bonham M, Dordevic A, Bristow C, Day K, Brennan L, et al. Measuring Self-Esteem Changes in Children and Adolescents Affected by Overweight or Obesity: A Scoping Review of Instruments Currently Used in Multicomponent Weight-Management Interventions. Child Obes. 2019;15(8):485–501.

14. Evan EE, Kaufman M, Cook AB, Zeltzer LK. Sexual health and self-esteem in adolescents and young adults with cancer. Cancer. 2006;107:1672–9.

15. Orth U, Erol RY, Luciano EC. Development of self-esteem from age 4 to 94 Years: A meta-analysis of longitudinal studies. Psychol Bull. 2018;144(10):1045–80.

16. Warburton DER, Bredin SSD. Health benefits of physical activity. Curr Opin Cardiol. 2017 Sep;32(5):541–56.

17. Choudhary A, Chou J, Heller G, Sklar C. Prevalence of vitamin D insufficiency in survivors of childhood cancer. Pediatr Blood Cancer. 2013 Jul;60(7):1237–9.

18. Maddocks M. Physical activity and exercise training in cancer patients. Clin Nutr ESPEN. 2020 Dec;40:1–6.

19. Ligibel JA, Bohlke K, May AM, Clinton SK, Demark-Wahnefried W, Gilchrist SC, et al. Exercise, Diet, and Weight Management during Cancer Treatment: ASCO Guideline. J Clin Oncol. 2022;348(22).

20. Thomsen SN, Lahart IM, Thomsen LM, Fridh MK, Larsen A, Mau-Sørensen M, et al. Harms of exercise training in patients with cancer undergoing systemic treatment: a systematic review and meta-analysis of published and unpublished controlled trials. eClinicalMedicine. 2023;59:101937.

21. Fong DYT, Ho JWC, Hui BPH, Lee AM, Macfarlane DJ, Leung SSK, et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. BMJ. 2012 Jan 30;344(jan30 5):e70–e70.

22. Li J, Li C, Puts M, Wu Y chen, Lyu M meng, Yuan B, et al. Effectiveness of mindfulness-based interventions on anxiety, depression, and fatigue in people with lung cancer: A systematic review and meta-analysis. Int J Nurs Stud. 2023;140:104447.

23. Saultier P, Vallet C, Sotteau F, Hamidou Z, Gentet JC, Barlogis V, et al. A Randomized Trial of Physical Activity in Children and Adolescents with Cancer. Cancers (Basel). 2021 Jan 2;13(1):121.

24. Kovačič T, Kovačič M. Impact of Relaxation Training According to Yoga in Daily Life ® System on Self-Esteem After Breast Cancer Surgery. J Altern Complement Med. 2011 Dec;17(12):1157–64.

25. Leite B, de Bem Fretta T, Boing L, Coutinho de Azevedo Guimarães A. Can belly dance and mat Pilates be effective for range of motion, self-esteem, and depressive symptoms of breast cancer women? Complement Ther Clin Pract. 2021 Nov;45:101483.

26. Ardern CL, Büttner F, Andrade R, Weir A, Ashe MC, Holden S, et al. Implementing the 27 PRISMA 2020 Statement items for systematic reviews in the sport and exercise medicine, musculoskeletal rehabilitation and sports science fields: The PERSiST

(implementing Prisma in Exercise, Rehabilitation, Sport medicine and SporTs sc. Br J Sports Med. 2023;175–95.

27. Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev. 2021 Jan 26;10(1):39.

28. Higgins JP, Savović J, Page MJ, Sterne JAC. RoB 2 Guidance: Parallel Trial. Cochrane Collab. 2019;1–24.

29. Tufanaru C et al. Chapter 3: Systematic reviews of effectiveness. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. Joanna Briggs Inst. 2017;

30. Cohen J. A power primer. Psychol Bull. 1992;112(1):155–9.

31. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Vol. 112, Psychological Bulletin. Routledge; 2013. 155–159 p.

32. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002 Jun 15;21(11):1539–58.

33. Shi L, Lin L. The trim-and-fill method for publication bias: practical guidelines and recommendations based on a large database of meta-analyses. Medicine (Baltimore). 2019 Jun;98(23):e15987.

34. Cadmus LA, Salovey P, Yu H, Chung G, Kasl S, Irwin ML. Exercise and quality of life during and after treatment for breast cancer: results of two randomized controlled trials. Psychooncology. 2009 Apr;18(4):343–52.

35. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Effects of Aerobic and Resistance Exercise in Breast Cancer Patients Receiving Adjuvant Chemotherapy: A Multicenter Randomized Controlled Trial. J Clin Oncol. 2007 Oct 1;25(28):4396–404.

36. Gokal K, Wallis D, Ahmed S, Boiangiu I, Kancherla K, Munir F. Effects of a self-managed home-based walking intervention on psychosocial health outcomes for breast cancer patients receiving chemotherapy: a randomised controlled trial. Support Care Cancer. 2016 Mar 15;24(3):1139–66.

37. Adams SC, Delorey DS, Davenport MH, Fairey AS, North S, Courneya KS. Effects of high-intensity interval training on fatigue and quality of life in testicular cancer survivors. Br J Cancer. 2018;118(10):1313–21.

38. van Dijk-Lokkart EM, Braam KI, van Dulmen-den Broeder E, Kaspers GJL, Takken T, Grootenhuis MA, et al. Effects of a combined physical and psychosocial intervention program for childhood cancer patients on quality of life and psychosocial functioning: results of the QLIM randomized clinical trial. Psychooncology. 2016;822(October 2015):815–22.

39. Carminatti M, Boing L, Leite B, Sperandio FF, Korpalski T, Fretta T de B, et al. Effects of belly dancing on body image and self-esteem in women with breast cancer – pilot study. Rev Bras Med do Esporte. 2019;25(6):464–8.

40. Wurz A, Brunet J. Exploring the feasibility and acceptability of a mixed-methods pilot randomized controlled trial testing a 12-week physical activity intervention with adolescent and young adult cancer survivors. Pilot Feasibility Stud. 2019 Dec 20;5(1):154.

41. Rosenberg RS, Lange W, Zebrack B, Moulton S, Kosslyn SM. An Outdoor Adventure Program for Young Adults with Cancer: Positive Effects on Body Image and Psychosocial Functioning. J Psychosoc Oncol. 2014 Sep 3;32(5):622–36.

42. Fretta T de B, Boing L, Stein F, Dos Santos L, Guimarães AC de A. Improved self-esteem after mat Pilates method intervention in breast cancer women undergoing hormone therapy: randomized clinical trial pilot study. Rev Bras Cineantropometria e Desempenho Hum. 2021;23.

43. Boing L, de Bem Fretta T, Stein F, Lyra VB, Moratelli JA, da Silveira J, et al. Can mat Pilates and belly dance be effective in improving body image, self-esteem, and sexual function in patients undergoing hormonal treatment for breast cancer? A randomized clinical trial. Arch Womens Ment Health. 2023;141–51.

44. Rastogi S, Tevaarwerk AJ, Sesto M, Van Remortel B, Date P, Gangnon R, et al. Effect of a technology-supported physical activity intervention on health-related quality of life, sleep, and processes of behavior change in cancer survivors: A randomized controlled trial. Psychooncology. 2020 Nov 4;29(11):1917–26.

45. MUSANTI R. A Study of Exercise Modality and Physical Self-esteem in Breast Cancer Survivors. 2011;(33):352–62.

46. Dol KS. Effects of a yoga nidra on the life stress and self-esteem in university students. Complement Ther Clin Pract. 2019;35(December 2018):232–6.

47. Salmon P, Clark L, McGrath E, Fisher P. Screening for psychological distress in cancer: renewing the research agenda. Psychooncology. 2015 Mar;24(3):262–8.

48. Hill J, Holcombe C, Clark L, Boothby MRK, Hincks A, Fisher J, et al. Predictors of onset of depression and anxiety in the year after diagnosis of breast cancer. Psychol Med. 2011 Jul 14;41(7):1429–36.

49. Abd El-Kader SM, Al-Jiffri OH. Aerobic exercise improves quality of life, psychological well-being and systemic inflammation in subjects with alzheimer's disease. Afr Health Sci. 2016;16(4):1045–55.

50. Notaras M, van den Buuse M. Brain-Derived Neurotrophic Factor (BDNF): Novel Insights into Regulation and Genetic Variation. Neuroscientist. 2019;25(5):434–54.

51. Murawska-Ciałowicz E, Wiatr M, Ciałowicz M, de Assis GG, Borowicz W, Rocha-Rodrigues S, et al. Bdnf impact on biological markers of depression—role of physical exercise and training. Int J Environ Res Public Health. 2021;18(14):1–21.

52. Rethorst CD, Wipfli BM, Landers DM. The antidepressive effects of exercise: A meta-analysis of randomized trials. Sport Med. 2009;39(6):491–511.

53. Kandola A, Ashdown-Franks G, Hendrikse J, Sabiston CM, Stubbs B. Physical activity and depression: Towards understanding the antidepressant mechanisms of physical activity. Neurosci Biobehav Rev. 2019;107(June):525–39.

54. Barrio SC, Molinuelo JS, De Durana ALD, López FJC, Carballo ROB. Cáncer de mama y ejercicio físico: Estudio piloto. Rev Andaluza Med del Deport. 2012;5(4):134–9.

55. Caru M, Curnier D, Levesque A, Sultan S, Marcil V, Laverdière C, et al. Children's physical activity behavior following a supervised physical activity program in pediatric oncology. J Cancer Res Clin Oncol. 2020;146(11):3037–48.

56. Caru M, Curnier D, Levesque A, Sultan S, Marcil V, Laverdière C, et al. The impact of cancer on theory of planned behavior measures and physical activity levels during the first weeks following cancer diagnosis in children. Support Care Cancer. 2021 Feb;29(2):823–31.

57. Courneya KS, McKenzie DC, Gelmon K, MacKey JR, Reid RD, Yasui Y, et al. A multicenter randomized trial of the effects of exercise dose and type on psychosocial distress in breast cancer patients undergoing chemotherapy. Cancer Epidemiol Biomarkers Prev. 2014;23(5):857–64.

58. Ho RTH. Effects of dance movement therapy on Chinese cancer patients: A pilot study in Hong Kong. Arts Psychother. 2005;32(5):337–45.

59. Morielli AR, Usmani N, Boulé NG, Severin D, Tankel K, Nijjar T, et al. Exercise motivation in rectal cancer patients during and after neoadjuvant chemoradiotherapy. Support Care Cancer. 2016;24(7):2919–26.

60. Müller C, Krauth KA, Gerß J, Rosenbaum D. Physical activity and health-related quality of life in pediatric cancer patients following a 4-week inpatient rehabilitation program. Support Care Cancer. 2016;24(9):3793–802.

61. Osypiuk K, Ligibel J, Giobbie-Hurder A, Vergara-Diaz G, Bonato P, Quinn R, et al. Qigong Mind-Body Exercise as a Biopsychosocial Therapy for Persistent Post-Surgical Pain in Breast Cancer: A Pilot Study. Integr Cancer Ther. 2020;19.

62. Rey-Barth S, Pinsault N, Terrisse H, Eychenne C, Rolland C, Foote A, et al. A program centered on smart electrically assisted bicycle outings for rehabilitation after breast cancer: A pilot study. Med Eng Phys. 2022;100(January):103758.

63. Speed-Andrews AE, Stevinson C, Belanger LJ, Mirus JJ, Courneya KS. Pilot evaluation of an Iyengar yoga program for breast cancer survivors. Cancer Nurs. 2010;33(5):369–81.

64. Török S, Kökönyei G, Károlyi L, Ittzés A, Tomcsányi T. Outcome Effectiveness of Therapeutic Recreation Camping Program for Adolescents Living with Cancer and Diabetes. J Adolesc Heal. 2006;39(3):445–7.

65. Vallet C, André N, Gentet JC, Verschuur A, Michel G, Sotteau F, et al. Pilot evaluation of physical and psychological effects of a physical trek programme including a dog sledding expedition in children and teenagers with cancer. Ecancermedicalscience. 2015 Jul;9:558.

66. Awick EA, Phillips SM, Lloyd GR, McAuley E. Physical activity, self-efficacy and self-esteem in breast cancer survivors: a panel model. Psychooncology. 2017;26(10):1625–31.

67. Belanger LJ, Plotnikoff RC, Clark AM, Courneya KS. Prevalence, correlates, and psychosocial outcomes of sport participation in young adult cancer survivors. Psychol Sport Exerc. 2013;14(2):298–304.

68. Deisenroth A, Söntgerath R, Schuster AJ, von Busch C, Huber G, Eckert K, et al. Muscle strength and quality of life in patients with childhood cancer at early phase of primary treatment. Pediatr Hematol Oncol. 2016;33(6):393–407.

69. Patsou ED, Alexias GT, Anagnostopoulos FG, Karamouzis M V. Physical activity and sociodemographic variables related to global health, quality of life, and psychological factors in breast cancer survivors. Psychol Res Behav Manag. 2018 Sep;11:371–81.

70. Ranft A, Seidel C, Hoffmann C, Paulussen M, Warby AC, Van Den Berg H, et al. Quality of survivorship in a rare disease: Clinicofunctional outcome and physical activity in an observational cohort study of 618 long-term survivors of Ewing sarcoma. J Clin Oncol. 2017;35(15):1704–12.

Supplementary material

Section 2

Cross-sectional studies: Physical activity and fitness in young pediatric cancer survivors.

Study II

24-hour movement behaviours and psychological health in young pediatric cancer survivors. A compositional data analysis from the iBoneFIT project.

Study II

ABSTRACT

Purpose: Examine the associations of 24-hour movement behaviours (moderate-to-vigorous physical activity [MVPA], light physical activity [LPA, sedentary behaviour and sleep) with psychological well-being (happiness, optimism, positive affect, and self-esteem) and distress indicators (depression, anxiety and negative affect) in young pediatric cancer survivors.

Methods: This cross-sectional multicentre study included 116 participants (12.1±3.3 years old; 42% female) from the iBoneFIT framework. Psychological well-being and distress indicators were assessed by questionnaires and time spent in movement behaviours by accelerometer. Participants were classified according to their somatic maturity (pre or peri/post-pubertal depending on the estimated years from peak height velocity). The adjusted models' coefficients were used to predict the effect of reallocating time proportionally across behaviours on the outcomes.

Results: Concerning well-being, reallocating time to LPA from the remaining movement behaviours (MVPA, sedentary behaviour, and sleep time) was positively associated with happiness (B=1.545, p=0.022) in the pre-pubertal group. Additionally, reallocating time to sedentary behaviour was positively associated with positive affect (B=2.860, p=0.006), whereas reallocating time to sleep time was negatively associated (B=-4.090, p=0.005). In the peri/post-pubertal group, reallocating time to MVPA was positively associated with happiness and optimism (B=0.778, p=0.032 and B=0.920, p=0.008, respectively). Concerning psychological distress, reallocating time to LPA or sedentary behaviour was negatively associated with depression (B=-1.786, p=0.032 and B=-2.294, p=0.029, respectively), whilst reallocating time to sleep was positively associated with depression (B=4.707, p=0.002) in the pre-pubertal group. In the peri/post-pubertal

group, reallocating time to MVPA was negatively associated with depression and anxiety (B=-0.779, p=0.026 and B=-0.749, p=0.014, respectively).

Conclusions: Our results underline the importance of promoting LPA and MVPA in pre-pubertal cancer survivors as well as MVPA in peri/post-pubertal cancer survivors to improve their psychological health.

INTRODUCTION

Childhood cancer is a rare disease, but the incidence has increased by 13% over the past decades[1] and remains one of the primary causes of death among children in developed countries[2]. The advancements in medical interventions have concurrently propelled the survival rate of affected individuals beyond 85%[3], but this is not exempt from adverse effects derived from the disease itself and its treatment. Some of them include obesity, cardiovascular disease, impaired growth, an increased risk of secondary malignancies and psychological sequels[4–6]. Among the psychological side effects, young pediatric cancer survivors tend to experience more symptoms of anxiety, depression and somatization[7,8]. For example, a recent report showed that the prevalence of anxiety in young cancer survivors varied from 1% to 27%, and that of depression, from 2% to 40%[9]. Apart from the psychological suffering, this could lead to a poor physical health, loss of quality of life and problems at the individual, family, social and economic level[10,11]. Therefore, there is a need to study effective strategies that could improve these undesired psychological sequels.

Physical activity is known to have health benefits for children and adolescents, including the improvement of cognitive function, physical fitness, and learning ability[12]. Moreover, previous studies have shown that physical activity is associated with improvements in psychological well-being and distress[13,14]. In an international cohort of 432 adolescent cancer survivors, just one-third attained the physical activity recommendation established by the World Health Organization[15]. Research among adolescents has shown that sedentary behaviours may affect the psychological health of this population[16]. Thus, there is a necessity to limit sedentary behaviour and engage in at least 60 minutes of MVPA per day, as emphasized in the physical activity guidelines for pediatric cancer survivors[6,17,18]. Some studies suggest that specific cancers[19] and adverse psychological health indicators [20] can be prevented by modifying lifestyle factors,

including movement behaviours. The 24-hour movement behaviours encompass MVPA, LPA, sedentary behaviour, and sleep time throughout a day[21]. In this way, the duration of at least one movement behaviour is fundamentally correlated with the duration of another movement[22]. Since only one movement behaviour (such as MVPA) can be performed at a time, modifying the amount of time spent on it requires modifying one or more of the other movement behaviours[22,23]. The compositional data analysis approach examines how time is reallocated among various behaviours within a specified timeframe (e.g., 24 hours), effectively mitigating the risk of multicollinearity[22,24]. Previous studies have shown that the distributions of 24-hour movement behaviours are associated with anxiety and depression in apparently healthy children and adolescents. Specifically, reducing sedentary behaviour by 10 minutes and increasing 10 minutes of LPA was linked to lower levels of depression and anxiety[21]. Since young pediatric cancer survivors are less active and more sedentary than their healthy peers[6] and, due to cancer treatments, they have an increased risk of psychological sequels[4], investigating the association between movement behaviours and psychological health indicators is of scientific interest.

Therefore, the primary objective of this study was to examine the associations between 24-hour movement behaviours (i.e., MVPA, LPA, sedentary behaviour, and sleep time) with psychological well-being indicators (i.e., happiness, optimism, positive affect, and self-esteem) and psychological distress (i.e., depression, anxiety, and negative affect) using compositional data analysis in young pediatric cancer survivors.

METHODS

This cross-sectional study included 116 pediatric cancer survivors (12.1 ± 3.3 years old; 42% female) from the iBoneFIT project framework. The study design and methods have been comprehensively published elsewhere[25]. Briefly, iBoneFIT is a multicentre parallel group randomized controlled trial designed to

examine the effect of a 36-weeks online plyometric exercise-based program in bone health in young pediatric cancer survivors. Survivors were recruited from the Units of Pediatric Oncology and Haematology of the 'Virgen de las Nieves' (Granada) and 'Reina Sofia' (Cordoba) University Hospitals. Inclusion criteria were aged from 6 to 18 years, not currently receiving treatments for cancer, diagnosed at least one year prior to enrolment, and previous exposure to radiotherapy and/or chemotherapy. Data collection occurred in two waves due to COVID-19 restrictions: 1) October 2020 to February 2021; and 2) December 2021 to March 2022. All parents and survivors provided written informed consent and assent before entering the trial, respectively. The iBoneFIT project was approved by the Ethics Committee on Human Research of Regional Government of Andalusia (Reference: 4500, December 2019), followed the ethical guidelines of the Declaration of Helsinki (revised version 2013), and the randomized controlled trial was registered (https://www.isrctn.com/ISRCTN61195625). The checklist and flow chart for Strengthening the Reporting of OBservational Studies in Epidemiology (STROBE) was followed in the reporting of this study (**Supplemental digital content 1 and Online Resource Supplementary Figure 1**). Although we recruited 116 young pediatric cancer survivors in total, sample size slightly varies for some variables due to missing data (i.e., accelerometers did not record data, empty questionnaire).

Body composition, maturity, and clinical data

Height (cm) was assessed using a precision stadiometer (SECA 225, Hamburg, Germany) with measurements recorded to the nearest 0.1 cm. Body mass (kg) was measured using an electronic scale (SECA 861, Hamburg, Germany) with an accuracy of 100 g. Body mass index was calculated as body mass (kg)/height (m2). Additionally, age- and sex-specific body mass index Z-score and categories were calculated using international reference data for pediatric population[26]. The estimated years from peak height velocity were

utilized as a somatic maturational landmark[27]. Peak height velocity represents the period of maximum growth in stature and was predicted using a validated algorithm that takes into account age and height in children[27]. The estimated years from peak height velocity are determined by considering the time before and after this period. Furthermore, the time (in years) between diagnosis and testing, as well as the type of neoplasm, were obtained from the participants' clinical records.

Movement behaviours: Physical activity, sedentary behaviour and sleep time

Movement behaviours (i.e., MVPA, LPA, sedentary behaviour, and sleep time) were measured by wrist-worn accelerometer (ActiGraph GT3X, Pensacola, FL, USA). Participants wore the accelerometers in non-dominant wrist for seven consecutively days (24 hours/day) and they were instructed to maintain their daily routine without making any changes, except for removing the accelerometer during water-based activities like bathing and swimming. The accelerometers were set to a sampling rate of 90 Hz, and the raw data underwent processing according to the methodology outlined in a previous study[28]. The Euclidean Norm of raw acceleration minus one G, with negative values rounded to zero (ENMO), was computed along with the angle of the z-axis of the device to estimate physical activity and sleep time indicators[29]. Non-wear time was detected based on the standard deviation of the raw accelerations recorded in the three accelerometer axes as described elsewhere [30], and then imputed by means of the acceleration in the rest of the days at the same time window. Sleep time and wake periods were determined using an automated algorithm (a novel; estimating de van hees[29,30]). We applied specific thresholds to detect sedentary behaviour, and physical activity intensities, with thresholds set at ≥200 mg for MVPA; a range of 35-199 mg for LPA; and <35 mg for sedentary behaviour [31]. We considered a day valid when: 1) the accelerometer registered at least 23 hours/day

and 2) survivors wore the accelerometers on at least 16 hours/day since in this study the accelerometers were worn at both day and night[32] Daily average values for MVPA, LPA, sedentary behaviour, and sleep time were computed as the mean across both weekdays and weekends. Furthermore, participants recorded their daily routine in an accelerometer diary which included wake-up and sleep time and the time when they did not wear the accelerometer. Data processing was carried out using the R software program (version 4.2.2) in conjunction with the GGIR open-source package (version 2.8-2)[28].

Psychological health

Self-perceived questionnaires were used to assess psychological health, with the focus being on the dimensions that best explain children's and adolescents' mental health status[33]: psychological well-being (i.e., happiness, optimism, positive affect, and self-esteem) and psychological distress (i.e., depression, anxiety and negative affect).

Psychological well-being

The Subjective Happiness Scale (SHS), whose Spanish version has demonstrated sufficient test-retest reliability, internal consistency, and convergent validity, was used to measure happiness, which is defined as positive psychological functioning[34]. With four elements on a Likert scale from 1 to 7 (from less happiness to greater happiness), this tool is quite useful. The first three items' sum determined the score, which ranged from 3 (lowest happiness) to 21 (most happiness). The Positive Affect and Negative Affect Schedule for Children (PANAS-C) consisted of 20 items (10 for positive affect and 10 for negative affect), each with three possible responses (never, sometimes, and many times). Positive affect is defined as the perception of emotion in a good or positive way, and negative affect is defined as the tendency to experience negative feelings[35]. The final score ranges from 10 (lowest negative or positive affect) to 30 (highest

negative or positive affect), and it was computed as the total of 10 elements (for either positive or negative affect). The Life Orientation Test-Revised (LOT-R) was used to assess dispositional optimism which refers to how positively people see their future. It consisted of six items (out of 10) with five potential responses: entirely disagree, disagree, neither disagree nor agree, agree, and totally agree [36]. The lowest optimism score is 6, and the greatest optimism score is 30. The Rosenberg Self-Esteem scale was used to assess self-esteem, which is defined as the opinion of ourselves, whether favourably or negatively. This scale has been validated in studies involving children and adolescents[37]. Ten items on this scale measure overall self-esteem while accounting for positive and negative emotions. There are four possible responses (completely disagree, disagree, agree, and totally agree)[38], which the final score range from 10 (the lowest self-esteem) to 40 (the highest self-esteem).

Psychological distress

The Children Depression Inventory (CDI), which consists of 27 items assessing five domains (interpersonal problems, ineffectiveness, negative mood, anhedonia, and negative self-esteem), was used to measure depression, which is defined as a persistently low or apathetic mood. Responses can take one of three forms, depending on the intensity of the selected symptoms, and scores range from 0 to 2[39]. The score goes from 0 (the lowest level of depression) to 54 (the highest level of depression). The State-Trait Anxiety Inventory for Children (STAIC-T) was used to measure childhood anxiety, which is defined as the brain's state of awareness of concern or dread. This inventory has been extensively validated in Spanish children[40]. With 20 items and three possible answers (rarely, sometimes, and often), this tool measures anxiety on a scale of 20 (lowest anxiety level) to 60 (highest anxiety level).

Statistical analysis

The normal distribution of the variables was checked and verified using Shapiro-Wilk test, skewness and kurtosis values, visual check of histograms, Q-Q and box plots. Descriptive data were reported as means and standard deviations (SD) for continuous variables or frequencies (percentages) for categorical variables. The analyses were conducted using the statistical software R version 4.0.3 (R Foundation for Statistical Computing), and the significance level (alpha) was established at 0.05. Compositional data analysis was employed to explore the relationships between different combinations of movement behaviours and the psychological health indicators (Z-score) in young pediatric cancer survivors. This analytical approach explores the redistribution of time among different behaviours within a defined timeframe (e.g., 24 hours), effectively reducing the potential for multicollinearity[22,24]. We established a one-time-use composition comprising MVPA, LPA, sedentary behaviour, and sleep time. For this analysis, the sample was stratified into two groups based on somatic maturity: pre-pubertal (≤-1 year from peak height velocity) and peri/post-pubertal (>-1 year from peak height velocity)[41]. Subsequently, we computed isometric log ratios using a sequential binary partition method[22] and incorporated them as explanatory variables. The B coefficients indicate the magnitude and direction of the relationship between each behaviour in relation to another (e.g., MVPA relative to sedentary behaviour) concerning an outcome (e.g., self-esteem). The coefficients from the models were subsequently employed to forecast the impact of redistributing time proportionally among behaviours (e.g., increasing MVPA while decreasing the remaining behaviours) as well as pairwise adjustments (e.g., increasing MVPA while decreasing sedentary behaviour) on the outcomes. The results include plots illustrating the effects of redistributing time proportionally among behaviours and pairwise time reallocation. These findings can be interpreted as indicating the outcomes

associated with time allocation adjustments between behaviours for a hypothetical average survivor in our sample, with all outcomes being relative to the mean behaviour composition in the sample. Linear regression adjusted by key confounders (i.e., sex, estimated years from peak height velocity, years between diagnosis and testing, body mass index, and type of neoplasm) was used considering the association with the outcome and predictor variables.

RESULTS

Table 1 shows descriptive data of all participants and divided by somatic maturity groups. The ternary plots for the daily time-use for MVPA, LPA and sedentary behaviour are displayed in **Figure 1**. This figure showed that pre-pubertal cancer survivors seem to be less sedentary and more physically active compared to peri/post-pubertal cancer survivors.

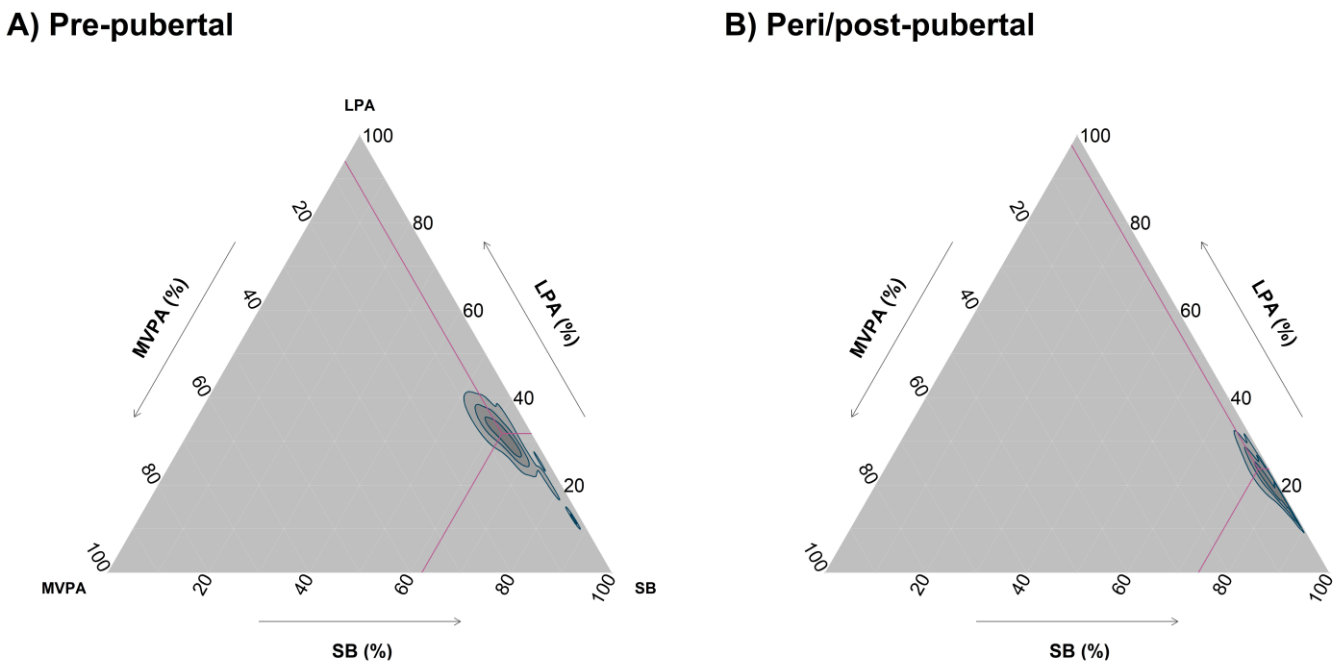


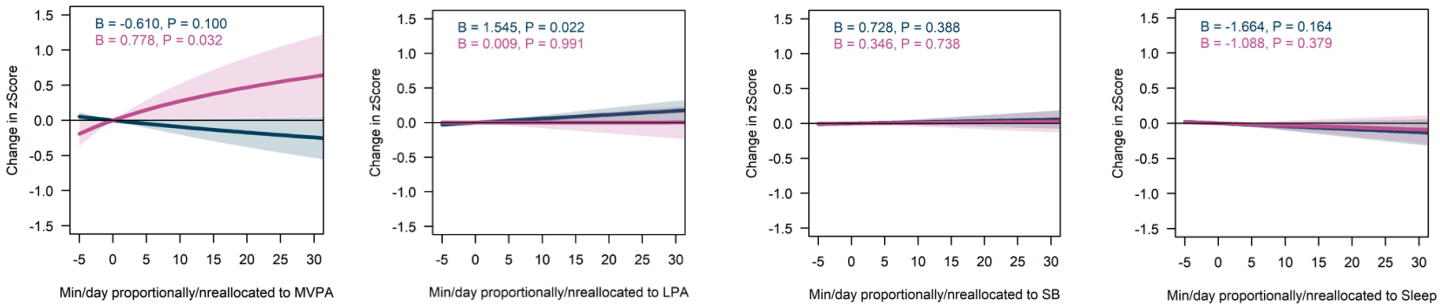
Figure 1 Ternary plots for the daily time-use in MVPA, LPA, and Sedentary behaviours (SB) by somatic maturity groups. For each group, the pink lines converge at their geometric means.

Estimated associations between movement behaviours and psychological well-being indicators.

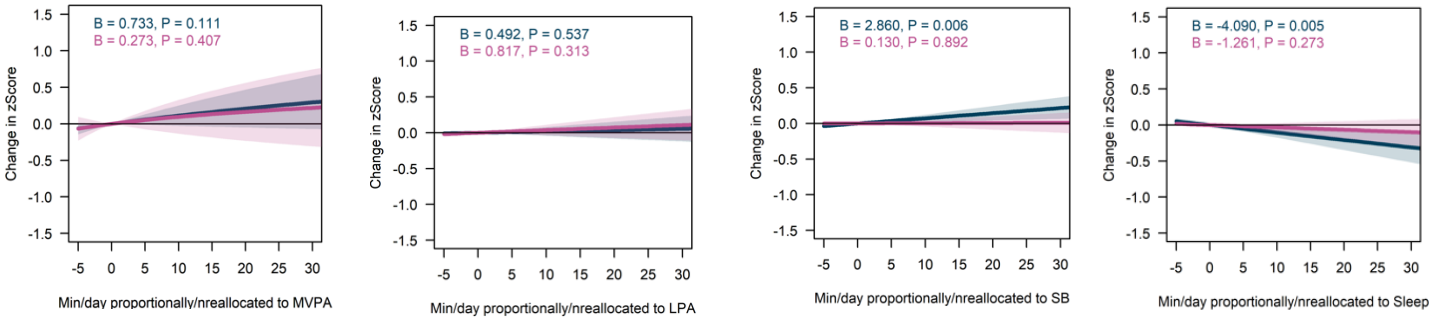
In the pre-pubertal group, reallocating time to LPA from the remaining movement behaviours (i.e., MVPA, sedentary behaviour and sleep time) was positively associated with happiness (B=1.545, p=0.022) (**Figure 2A**). Moreover, reallocating time to sedentary behaviour was positively associated with positive affect (B=2.860, p=0.006) (**Figure 2B**) and negatively associated when reallocating time to sleep time (B=-4.090, p=0.005) (**Figure 2B**). The dose-response curves of the pairwise reallocation plots indicated a negative association between replacing LPA or sedentary behaviour with MVPA in happiness (**Online Resource Supplementary Figure 2A**) and this association was positive when replacing sleep time with LPA (**Online Resource Supplementary Figure 2A**). In addition, replacing sleep time with MVPA, LPA or sedentary behaviour was positively associated with positive affect (**Online Resource Supplementary Figure 2B**).

In the peri/post-pubertal group, reallocating time to MVPA was positively associated with happiness and optimism (B=0.778, p=0.032 and B=0.920, p=0.008, respectively) (**Figures 2A and 2C**). The dose-response curves of the pairwise reallocation plots illustrated a significant positive association with happiness and optimism when replacing sedentary behaviour or sleep time with MVPA and, with optimism when replacing LPA with MVPA (**Online Resource Supplementary Figure 2A and 2C**).

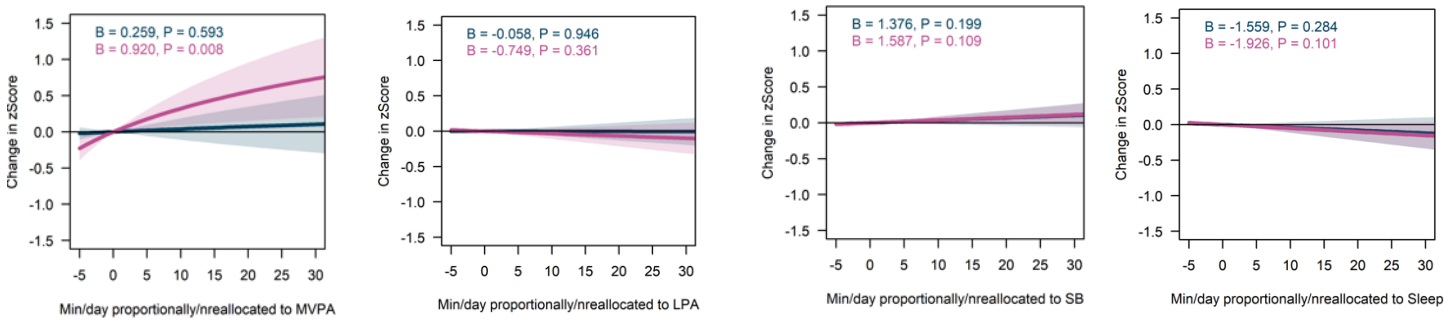
a) Happiness



b) Positive affect



c) Optimism



d) Self-esteem

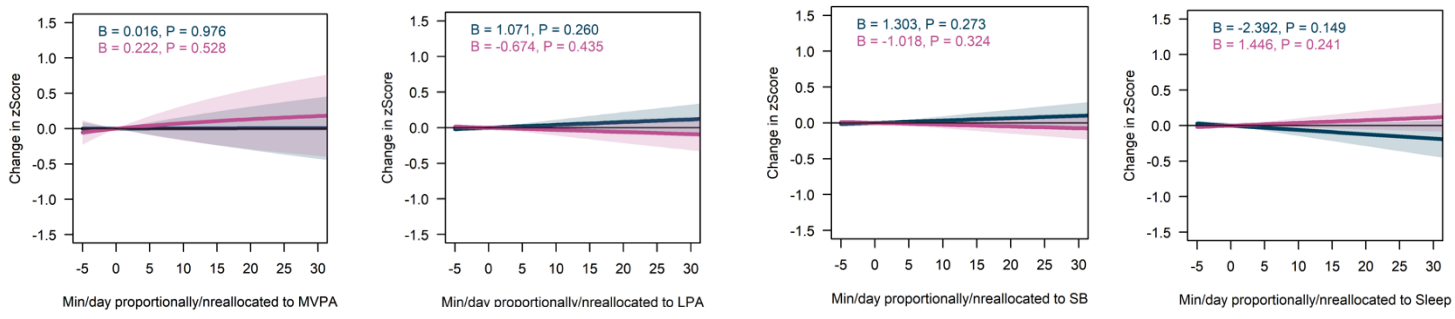


Figure 2 Dose-response curves relative to increase time on one movement behaviour while proportionally reducing the rest on psychological well-being indicators (happiness, positive affect, optimism and self-esteem) in young pediatric cancer survivors by somatic maturity groups. The lines represent the predicted change in psychological well-being indicators (Z-score) when the dominant behaviour is increased and the others are proportionately decreased. All models were adjusted for remaining movement behaviours, sex, estimated years from peak height velocity, years between diagnosis and testing, body mass index, and type of neoplasm.

Estimated associations between movement behaviours and psychological distress indicators.

In the pre-pubertal group, reallocating time to LPA or sedentary behaviour was negatively associated with depression (B=-1.786, p=0.032 and B=-2.294, p=0.029) (**Figure 3A**) whilst reallocating time to sleep was positively associated with it (B=4.707, p=0.002) (**Figure 3A**). The dose-response curves of the pairwise reallocation plots indicated a negative association between replacing sleep time with MVPA, LPA, or sedentary behaviour and depression (**Online Resource Supplementary Figure 3A**).

In the peri/post-pubertal group, reallocating time to MVPA was negatively associated with depression and anxiety (B=-0.779, p=0.026 and B=-0.749, p=0.014, respectively) (**Figures 3A and 3B**). The dose-response curves of the pairwise reallocation plots illustrated a significant negative association with depression replacing sedentary behaviour or sleep time with MVPA (**Online Resource Supplementary Figure 3A**). Similarly, replacing LPA, sedentary behaviour or sleep time with MVPA was negatively associated with anxiety (**Online Resource Supplementary Figure 3B**).

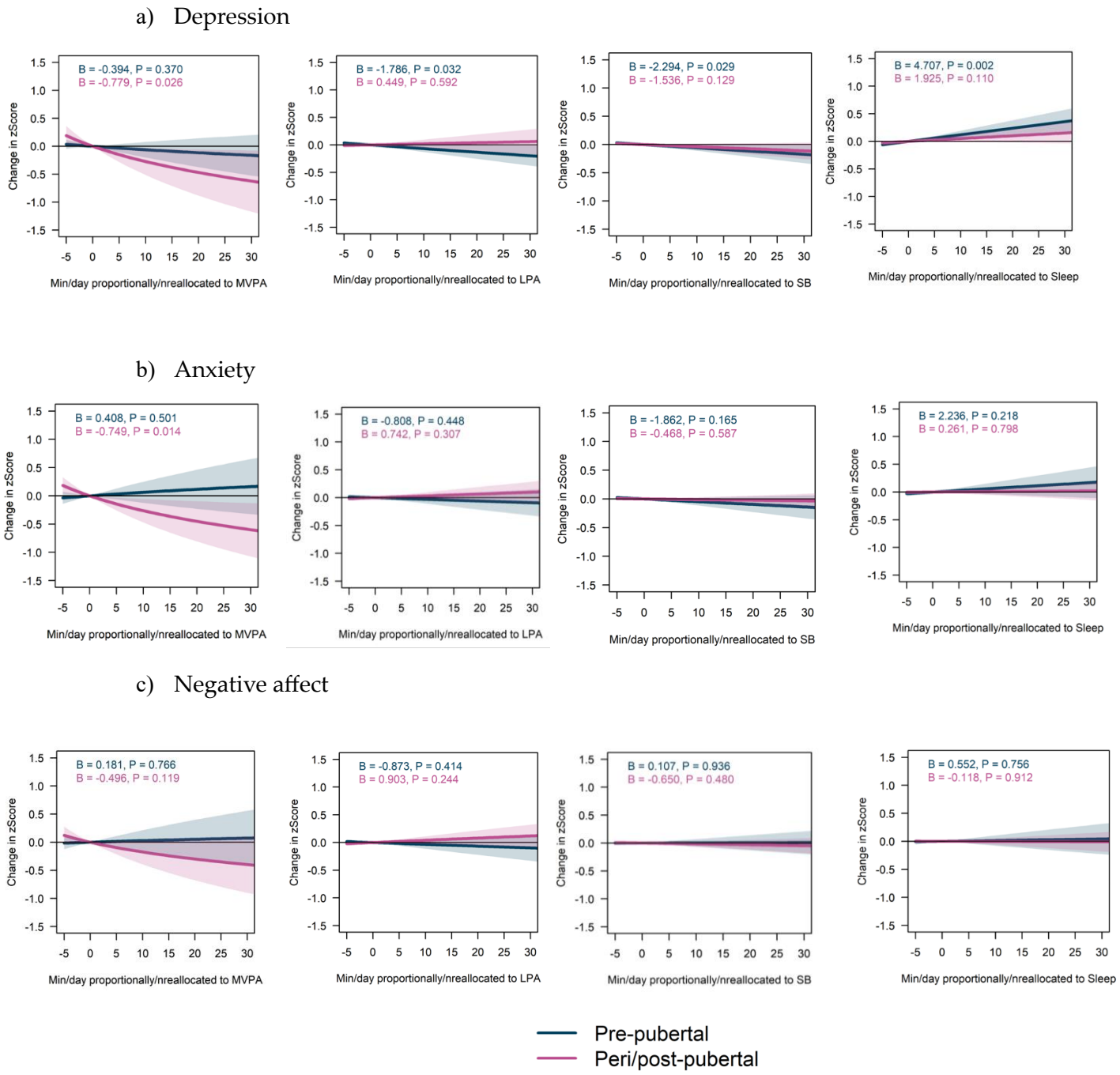


Figure 3 Dose-response curves relative to increase time on one movement behaviour while proportionally reducing the rest on psychological distress indicators (depression, anxiety and negative affect) in young pediatric cancer survivors by somatic maturity groups. The lines represent the predicted change in psychological distress indicators (Z-score) when the dominant behaviour is increased, and the others are proportionately decreased. All models were adjusted for remaining movement behaviours, sex, estimated years from peak height velocity, years between diagnosis and testing, body mass index, and type of neoplasm

DISCUSSION

The present study examined the association between 24-h movement behaviour with psychological health in young pediatric cancer survivors. Overall, reallocating time to LPA and MVPA from the remaining movement behaviours, seems to be the movement behaviours that could improve psychological well-being (i.e., happiness and positive affect) and distress (e.g., depression and anxiety) indicators in the pre-pubertal group and; ii) just reallocating time to MVPA from the remaining movement behaviours seems to be the most recommended movement behaviour to improve well-being (i.e.; happiness and optimism) and distress (i.e.; depression and anxiety) indicators in the peri/post pubertal group.

Estimated associations between movement behaviours and psychological well-being.

In our study, the increase of LPA through the decrease of MVPA, sedentary behaviour, and sleep time seems to improve the levels of happiness in the pre-pubertal group. These results are supported by the dose-response curves of the pairwise reallocation plots due to the replacement of sleep time with LPA appears to improve the levels of happiness whilst the replacement of LPA or sedentary behaviour with MVPA seems to reduce these levels and underline the importance of LPA rather than MVPA for these specific outcomes in this group. The scarcity of research limits establishing comparisons, but a cross-sectional study in children and adolescents with cerebral palsy is consistent with our results[42]. In the peri/post-pubertal group, reallocating time to MVPA showed positive associations with optimism and happiness. The importance of engaging in MVPA in this group is supported by the results of the dose-response curves of the pairwise reallocation plots. Research investigating the relationship between physical activity measured by accelerometer and happiness in women with breast cancer showed that MVPA is linked to these psychological health

indicators[43]. In addition, our results align with a cross-sectional study from a multi-national survey of adolescents and adults, which showed that an increase in the volume of physical activity (regardless of intensity) was associated with higher levels of happiness in European people[44].

In relation to positive affect, increasing sedentary behaviour seems to be the movement behaviour most related to having higher levels of positive affect in the pre-pubertal group, with no association between positive affect and the peri/post-pubertal group. Contrary to our results, a study though in healthy adolescents examining the association between positive affect and sedentary behaviour found that higher levels of positive affect were associated with lower levels of sedentary behaviour [45]. Nonetheless, the study also found that for some participants, increased sedentary behaviour led to increased positive affect. However, the authors suggest that despite this observation, the negative impact of sedentary behaviour is more significant than any mood-enhancing effect[45]. In addition, our results showed that spending more time sleeping instead of practising MVPA, LPA or sedentary behaviour and replacing sleep time with MVPA or sedentary behaviour also deteriorates positive affect levels in the pre-pubertal group. Contrary to our results, a study in adolescents and adults examining the effects of sleep deprivation on mental health showed that participants in the sleep deprivation group reported lower positive affect than the rest of the group[46]. Longitudinal studies are required to fully understand these unexpected findings on sleep deprivation and positive affect found in our study.

Estimated associations between movement behaviours and psychological distress indicators.

In our study, the increase in LPA and MVPA in the pre-pubertal group and MVPA in the peri/post pubertal group seems to reduce depression and anxiety indicators. Our results agree with a previous study[47] in adults and older adults

that showed that reallocating time to MVPA from sedentary behaviour was associated with lower levels of depression. In addition, we also observed that replacing LPA with MVPA also appears to reduce levels of anxiety. A cross-sectional study in adult survivors of colon cancer did not find an association between MVPA (measured using accelerometers) and depression, but associations were found with anxiety [48]. Another study conducted in adults and older adults[47] observed that substituting sedentary behaviour with MVPA may lead to the prevention of depressive symptoms. Concerning increasing sedentary behaviour through the decrease of the rest of the movement behaviours and replacing sleep time with MVPA, LPA or sedentary behaviour is associated with lower levels of depression in the pre-pubertal group. In contrast, the increase in sleep time from the rest of the movement behaviours seems to increase the levels of depression in this group. Contrary to our results, a longitudinal compositional data analysis found an association between the reallocation of sleep time (from screen time and MVPA) and reduced symptoms of depression in adolescents[49]. However, in our case, anxiety does not have significance in the pre-pubertal group maybe because the intensity must be higher to find.

Strength and limitations

This study is a cross-sectional study, so it does not enable us to establish causality for any of the associations. Therefore, longitudinal studies are required to confirm these findings. Furthermore, yet we adjusted the findings for major potential confounders full confounding cannot be disregarded. Included survivors were those who elected to enrol in an exercise intervention, so they may not be representative of all young pediatric cancer survivors, making our findings particularly vulnerable to selection bias. Regarding the strengths, a compositional data analysis was employed, as it is the most suitable method for explaining the interdependent nature of movement behaviour data.

Public health implication

Generally, studies in young pediatric cancer survivors have examined whether they meet physical activity recommendations or not [50]. Even though it might be difficult to limit sedentary behaviour and participate in at least 60 minutes of MVPA each week throughout the cancer continuum, our study found that increasing not only MVPA but also LPA could improve psychological health indicators in young cancer survivors. These results underscore the public health implications of our findings, particularly following the completion of pediatric cancer treatment.

CONCLUSION

Our findings on the estimated associations between movement behaviours and psychological health indicators underline the importance of increasing LPA and MVPA from the remaining movement behaviours in pre-pubertal cancer survivors and increasing MVPA from the remaining movement behaviours in peri/post-pubertal cancer survivors. Given that the psychological health of young pediatric cancer survivors is diminished, public health policies should promote physical activity in this population.

REFERENCES

1. Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. Lancet Oncol. 2017;18(6):719-731. doi:10.1016/S1470-2045(17)30186-9
2. Filbin M, Monje M. Developmental origins and emerging therapeutic opportunities for childhood cancer. Nat Med. 2019;25(3):367-376. doi:10.1038/s41591-019-0383-9
3. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17-48. doi:10.3322/caac.21763
4. Erdmann F, Frederiksen LE, Bonaventure A, et al. Childhood cancer: Survival, treatment modalities, late effects and improvements over time. Cancer Epidemiol. 2021;71. doi:10.1016/j.canep.2020.101733
5. Henderson TO, Nathan PC. Childhood cancer survivors: Considerations for surgeons in the transition from pediatric to adult care. Semin Pediatr Surg. 2015;24(2):93-99. doi:10.1053/j.sempedsurg.2015.01.007

6. Antwi GO, Jayawardene W, Lohrmann DK, Mueller EL. Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies. Support Care Cancer. 2019;27(9):3183-3194. doi:10.1007/s00520-019-04788-z

7. Brinkman TM, Recklitis CJ, Michel G, Grootenhuis MA, Klosky JL. Psychological symptoms, social outcomes, socioeconomic attainment, and health behaviors among survivors of childhood cancer: Current state of the literature. J Clin Oncol. 2018;36(21):2190-2197. doi:10.1200/JCO.2017.76.5552

8. Michel G, Rebholz CE, Von Der Weid NX, Bergstraesser E, Kuehni CE. Psychological distress in adult survivors of childhood cancer: The Swiss childhood cancer survivor study. J Clin Oncol. 2010;28(10):1740-1748. doi:10.1200/JCO.2009.23.4534

9. Marchak JG, Christen S, Mulder RL, et al. Recommendations for the surveillance of mental health problems in childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol. 2022;23(4):e184-e196. doi:10.1016/S1470-2045(21)00750-6

10. Patel V, Saxena S, Lund C, et al. The Lancet Commission on global mental health and sustainable development. Lancet. 2018;392(10157):1553-1598. doi:10.1016/S0140-6736(18)31612-X

11. Mental GBD, Collaborators D. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Psychiatry. 2022;9(2):137-150. doi:10.1016/S2215-0366(21)00395-3

12. Janssen I, LeBlanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act. 2010;7(1):40. doi:10.1186/1479-5868-7-40

13. Rodriguez-Ayllon M, Cadenas-Sánchez C, Estévez-López F, et al. Role of Physical Activity and Sedentary Behavior in the Mental Health of Preschoolers, Children and Adolescents: A Systematic Review and Meta-Analysis. Sport Med. 2019;49(9):1383-1410. doi:10.1007/s40279-019-01099-5

14. Biddle SJH, Ciaccioni S, Thomas G, Vergeer I. Physical activity and mental health in children and adolescents: An updated review of reviews and an analysis of causality. Psychol Sport Exerc. 2019;42(September 2018):146-155. doi:10.1016/j.psychsport.2018.08.011

15. Grydeland M, Bratteteig M, Rueegg CS, et al. Physical Activity Among Adolescent Cancer Survivors: The PACCS Study. Pediatrics. 2023;152(3). doi:10.1542/peds.2023-061778

16. Hoare E, Milton K, Foster C, Allender S. The associations between sedentary behaviour and mental health among adolescents: a systematic review. Int J Behav Nutr Phys Act. 2016;13(1):108. doi:10.1186/s12966-016-0432-4

17. Wurz A, Mclaughlin E, Lategan C, et al. The international Pediatric Oncology Exercise Guidelines (iPOEG). Transl Behav Med. 2021;11(10):1915-1922. doi:10.1093/tbm/ibab028

18. Götte M, Gauß G, Dirksen U, et al. Multidisciplinary Network ActiveOncoKids guidelines for providing movement and exercise in pediatric oncology: Consensus-based recommendations. Pediatr Blood Cancer. 2022;69(11):1-9. doi:10.1002/pbc.29953

19. Friedenreich CM, Ryder-Burbidge C, McNeil J. Physical activity, obesity and sedentary behavior in cancer etiology: epidemiologic evidence and biologic mechanisms. Mol Oncol. 2021;15(3):790-800. doi:10.1002/1878-0261.12772

20. Pearce M, Garcia L, Abbas A, et al. Association between Physical Activity and Risk of Depression: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2022;79(6):550-559. doi:10.1001/jamapsychiatry.2022.0609

21. Faria FR de, Barbosa D, Howe CA, Canabrava KLR, Sasaki JE, Amorim PR dos S. Time-use movement behaviors are associated with scores of depression/anxiety among adolescents: A compositional data analysis. PLoS One. 2022;17(12 December):1-12. doi:10.1371/journal.pone.0279401

22. Chastin SFM, Palarea-Albaladejo J, Dontje ML, Skelton DA. Combined effects of time spent in physical activity, sedentary behaviors and sleep on obesity and cardio-metabolic health markers: A novel compositional data analysis approach. PLoS One. 2015;10(10). doi:10.1371/journal.pone.0139984

23. Curtis RG, Dumuid D, Olds T, et al. The association between time-use behaviors and physical and mental well-being in adults: A compositional isotemporal substitution analysis. J Phys Act Heal. 2020;17(2):197-203. doi:10.1123/jpah.2018-0687

24. Dumuid D, Stanford TE, Martin-Fernández JA, et al. Compositional data analysis for physical activity, sedentary time and sleep research. Stat Methods Med Res. 2018;27(12):3726-3738. doi:10.1177/0962280217710835

25. Gil-Cosano JJ, Ubago-Guisado E, Sánchez MJ, et al. The effect of an online exercise programme on bone health in paediatric cancer survivors (iBoneFIT): Study protocol of a multi-centre randomized controlled trial. BMC Public Health. 2020;20(1):1-13. doi:10.1186/s12889-020-09607-3

26. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-294. doi:10.1111/j.2047-6310.2012.00064.x

27. Moore SA, McKay HA, Macdonald H, et al. Enhancing a somatic maturity prediction model. Med Sci Sports Exerc. 2015;47(8):1755-1764. doi:10.1249/MSS.0000000000000588

28. Migueles JH, Rowlands A V., Huber F, Sabia S, Van Hees VT. GGIR: A Research Community–Driven Open Source R Package for Generating Physical Activity and Sleep Outcomes From Multi-Day Raw Accelerometer Data. J Meas Phys Behav. 2019;2(3):188-196. doi:10.1123/jmpb.2018-0063

29. Van Hees VT, Sabia S, Anderson KN, et al. A novel, open access method to assess sleep duration using a wrist-worn accelerometer. PLoS One. 2015;10(11):1-13. doi:10.1371/journal.pone.0142533

30. van Hees VT, Renström F, Wright A, et al. Estimation of daily energy expenditure in pregnant and Non-Pregnant women using a Wrist-Worn Tri-Axial accelerometer. PLoS One. 2011;6(7). doi:10.1371/journal.pone.0022922

31. Hildebrand M, Hansen BH, van Hees VT, Ekelund U. Evaluation of raw acceleration sedentary thresholds in children and adults. Scand J Med Sci Sport. 2017;27(12):1814-1823. doi:10.1111/sms.12795

32. Rowlands A V., Mirkes EM, Yates T, et al. Accelerometer-assessed physical activity in epidemiology: Are monitors equivalent? Med Sci Sports Exerc. 2018;50(2):257-265. doi:10.1249/MSS.0000000000001435

33. Antaramian SP, Scott Huebner E, Hills KJ, Valois RF. A dual-factor model of mental health: Toward a more comprehensive understanding of youth functioning. Am J Orthopsychiatry. 2010;80(4):462-472. doi:10.1111/j.1939-0025.2010.01049.x

34. Extremera N, Fernández-Berrocal P. The Subjective Happiness Scale: Translation and Preliminary Psychometric Evaluation of a Spanish Version. Soc Indic Res. 2014;119(1):473-481. doi:10.1007/s11205-013-0497-2

35. Sandín B, Chorot P, Lostao L, Joiner TE, Santed MA, Valiente RM. The PANAS Scales of Positive and Negative Affect: Factor Analytic Validation and Cross-cultural Convergence. Psicothema. 1999;11(1).

36. Scheier MF, Charles S, Bridges MW. Distinguishing optimism from neuroticism: A reevaluation of the Life Orientation Test. J Pers Soc Psychol. 1994;67(6):1063-1078. https://doi.org/10.1037//0022-3514.67.6.1063

37. Mäkinen M, Lindberg N, Komulainen E, Puukko-Viertomies LR, Aalberg V, Marttunen M. Psychological well-being in adolescents with excess weight. Nord J Psychiatry. 2015;69(5):354-363. doi:10.3109/08039488.2014.986194

38. Martín-Albo J, Núñez JL, Navarro JG, Grijalvo F. The Rosenberg self-esteem scale: Translation and validation in university students. Span J Psychol. 2007;10(2):458-467. doi:10.1017/S1138741600006727

39. del Barrio MV, Moreno C, López R. El Children's Depression Inventory (CDI; Kovacs , 1992). Su aplicación en población española. Clínica y Salud. 1999;10(3):393-416.

40. Rodrigo G, Lusiardo M. Spanish version of the Revised Children's Manifest Anxiety Scale in Uruguay: reliability and concurrent validity. Psychol Rep. 1989;65(1):94. doi:10.2466/pr0.1989.65.1.94

41. Faigenbaum, AD., Lloyd, DG. and Oliver J. Essentials of youth fitness. Am Coll Sport Med. Published online 2020.

42. Maher CA, Toohey M, Ferguson M. Physical activity predicts quality of life and happiness in children and adolescents with cerebral palsy. Disabil Rehabil. 2016;38(9):865-869. doi:10.3109/09638288.2015.1066450

43. Vallance JK, Friedenreich CM, Wang Q, et al. Depression, happiness, and satisfaction with life in women newly diagnosed with breast cancer: Associations with device-

measured physical activity and sedentary time. Psychooncology. 2023;32(8):1268-1278. doi:10.1002/pon.6180

44. Richards J, Jiang X, Kelly P, Chau J, Bauman A, Ding D. Don't worry, be happy: Cross-sectional associations between physical activity and happiness in 15 European countries. BMC Public Health. 2015;15(1):1-8. doi:10.1186/s12889-015-1391-4

45. Cushing CC, Mitchell TB, Bejarano CM, Walters RW, Crick CJ, Noser AE. Bidirectional associations between psychological states and physical activity in adolescents: A mHealth pilot study. J Pediatr Psychol. 2017;42(5):559-568. doi:10.1093/jpepsy/jsw099

46. Talbot LS, McGlinchey EL, Kaplan KA, Dahl RE, Harvey AG. Sleep Deprivation in Adolescents and Adults: Changes in Affect. Emotion. 2010;10(6):831-841. doi:10.1037/a0020138

47. del Pozo Cruz B, Alfonso-Rosa RM, McGregor D, Chastin SF, Palarea-Albaladejo J, del Pozo Cruz J. Sedentary behaviour is associated with depression symptoms: Compositional data analysis from a representative sample of 3233 US adults and older adults assessed with accelerometers. J Affect Disord. 2020;265(January):59-62. doi:10.1016/j.jad.2020.01.023

48. Vallance JK, Boyle T, Courneya KS, Lynch BM. Accelerometer-assessed physical activity and sedentary time among colon cancer survivors: associations with psychological health outcomes. J Cancer Surviv. 2015;9(3):404-411. doi:10.1007/s11764-014-0409-8

49. Sampasa-Kanyinga H, Colman I, Dumuid D, et al. Longitudinal association between movement behaviours and depressive symptoms among adolescents using compositional data analysis. PLoS One. 2021;16(9 September):1-19. doi:10.1371/journal.pone.0256867

50. Bull FC, Al- SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Published online 2020:1451-1462. doi:10.1136/bjsports-2020-102955

Supplementary material

Section 2

Cross-sectional studies: Physical activity and fitness in young pediatric cancer survivors.

Study III

Is higher physical fitness associated with better psychological health in young pediatric cancer survivors? A cross-sectional study from the iBoneFIT project.

Rodriguez-Solana A, Gracia-Marco L, Llorente-Cantarero FJ, et al. Is higher physical fitness associated with better psychological health in young pediatric cancer survivors? A cross-sectional study from the iBoneFIT project. Scand J Med Sci Sports. 2023;00:1-11. doi:10.1111/sms.14345

Study 3

ABSTRACT

Aim: To examine the associations of self-perceived and objectively-measured physical fitness with psychological well-being and distress indicators in young pediatric cancer survivors.

Materials and Methods: A total of 116 participants (12.1 ± 3.3 years, 56.9% boys) from the iBoneFIT project participated in this cross-sectional study. Objectively-measured physical fitness (muscular fitness) was obtained by handgrip strength and standing long jump tests for the upper and lower body, respectively. Self-perceived physical fitness was obtained by the International Fitness Scale (IFIS). Positive and negative affect were assessed by the positive affect schedule for children (PANAS-C), happiness by Subjective Happiness Scale (SHS), optimism by Life Orientation Test-Revised (LOT-R), self-esteem by the Rosenberg Self-Esteem Scale (RSE), anxiety by State–Trait Anxiety Inventory for Children (STAIC-R), and depression by Children Depression Inventory (CDI). Multiple linear regressions adjusted by key covariates were performed to analyze associations.

Results: No associations were found between objectively-measured muscular fitness and any of the psychological well-being and distress indicators ($p > 0.05$). Self-perceived overall fitness and flexibility were positively associated with positive affect ($\beta \geq 0.258$, $p < 0.05$). Self-perceived cardiorespiratory fitness, speed/ agility, and flexibility were negatively associated with depression ($\beta \geq -0.222$, $p < 0.05$). Finally, self-perceived cardiorespiratory fitness was also negatively associated with anxiety and negative affect ($\beta \geq -0.264$, $p < 0.05$).

Conclusions: Perceived physical fitness, but not objectively physical fitness, seems to be inversely related to psychological distress variables and to less extent positively related to psychological well-being. The findings from this study highlight the importance of promoting self-perceived fitness in the pediatric oncology population.

INTRODUCTION

Childhood cancer is a rare disease but one of the leading causes of death in the childhood population in developed countries.[1] The incidence has increased over the last decades by 13%,[2] despite this, the survival rate of this population has also increased beyond 85%.[3] The main side effects of pediatric cancer and its treatment are obesity, cardiovascular disease, impaired growth, and secondary malignancy. [4–6]. Moreover, the psychological sequels are very common in pediatric cancer survivors. For example, a 20% prevalence in anxiety[7] and 2%–40% [8] in depression has been reported in young pediatric cancer survivors, which also affects school absenteeism and fear to future recurrence.[6,9,10]

Childhood and adolescence play a key role in the psychological development. Good mental health is considered a dual-factor construct that comprehends the presence of psychological well-being along with the absence of psychological distress.[11] Psychological well-being is associated with positive thoughts and feelings (i.e., positive affect, happiness, optimism, and self-esteem) while psychological distress is related to negative thoughts and feelings (i.e., anxiety, depression, and negative affect).[12,13] Therefore, strategies to improve psychological health side effects in childhood cancer survivors seem to be required.

Physical fitness is considered an important tool for improving psychological health. Fitness can be measured either self-perceived by self-reported questionnaires or objectively-measured by testing in laboratory or field conditions. The most well-known self-perceived fitness tool is the International Fitness Scale (IFIS),[14] which assesses different fitness components: cardiorespiratory fitness, muscular fitness, speed/agility, and flexibility. Likewise, there are many fitness tests battery to assess fitness in laboratory or field conditions. One of the most used fitness test is the ALPHA battery (Assessing Levels of Physical Activity), which consists of evaluating

cardiorespiratory fitness, muscular fitness, and speed/agility through different reliable and valid tests.[15]

Physical fitness may be associated with better psychological health because people who are physically fit tend to look and feel better, and that makes them associate it with better physical and mental health. In addition, improved fitness can increase some hormones that contribute to mood elevation, such as serotonin.[16] Previous evidence in apparently healthy youths showed that those with better fitness showed also better psychological health.[13,14] In non-healthy young population, fitness has also been considered as a powerful marker of health associated with psychological well-being and distress.[15,16] Previous studies not only in healthy children and adolescents but also in adults with lung cancer observed that greater fitness reduces psychological distress[17,18] and improves psychological well-being indicators.[16,19] However, there is a need for studies to understand the potential contribution of fitness on psychological health variables in young pediatric cancer survivors, whose psychological health is compromised due to the disease itself and the required treatments.

Therefore, the aim of this study was to examine the associations of self-perceived (i.e., overall fitness, cardiorespiratory fitness, muscular fitness, speed/agility, and flexibility) and objectively-measured fitness components (i.e., upper and lower body) with psychological well-being indicators (i.e., positive affect, happiness, optimism, and self-esteem) and psychological distress (i.e., anxiety, depression, and negative affect) in young pediatric cancer survivors.

MATERIALS AND METHODS

Study design and participants

A cross-sectional study was conducted within iBoneFIT project framework (https://profith.ugr.es/pages/investigacion/proyectos/ibonefit). A detailed description of the study design and methods has been published

elsewhere.[20] In brief, this study included data from 116 children and adolescents' survivors of pediatric cancer (12.1 ± 3.3 years old; 56.9% boys) from Cordoba and Granada (Spain). Participants of this multicentre study were recruited and measured during Autumn and Winter and in two waves due to COVID-19 restrictions: first, from October to February 2020/2021; and second, a year apart from December to March 2021/2022. This study was approved by the Ethics Committee on Human Research of Regional Government of Andalusia (Reference: 4500, December 2019) and the randomized controlled trial was registered (https://www.isrctn.com/ISRCT N6119 5625). A signed informed consent was obtained from all participants prior to data collection.

Body composition, maturity, and clinical data

Height (cm) was evaluated with a precision stadiometer (SECA 225, Hamburg, Germany) to the nearest 0.1 cm. An electronic scale (SECA 861, Hamburg, Germany) with an accuracy of 100 g was used to measure body mass (kg). Body mass index was calculated as body mass (kg)/height (m2). Years from peak height velocity was used as a somatic maturational landmark.[21] Peak height velocity is the period of maximum growth in stature, and years from peak height velocity are considered in terms of time before and after the peak height velocity. It was predicted using age and height in a validated algorithm in children.[21] In addition, the time (years) between diagnosis to testing and the type of neoplasm was obtained from clinical records.

Physical fitness

The ALPHA fitness test battery was used to assess fitness objectively. These fitness tests have been demonstrated to be valid, reliable, and health-related in children and adolescents.[15] Cardiorespiratory fitness and speed/agility were expected to be measured by 20 m shuttle run and 4 × 10 m shuttle run tests. However, due to the pandemic situation during the evaluation time, the use of

face masks was mandatory by the National Health Authorities. After internal discussions, we finally decided to exclude the cardiorespiratory fitness and speed/agility test because the available evidence at that time showed impaired performance using FFP2/N95 face masks,[22] and more importantly, to ensure the safety of our participants. Muscular fitness for the upper and lower body was assessed with the handgrip strength (TKK 5101 Grip D, Takey, Tokyo Japan) and standing long jump tests, respectively. The handgrip was performed twice on each hand and the best value was chosen and averaged, while the best of two attempts was retained for the standing long jump. The ALPHA fitness test battery protocol was followed and a 1-minute rest was allowed between handgrip measures of the same hand.

Self-perceived fitness was assessed by using the IFIS, which is known to be valid in young populations.[14] This tool is composed of 5-items (i.e., overall fitness, cardiorespiratory fitness, muscular fitness, speed/agility, and flexibility) about the fitness perception of the participants compared with their friends. It includes 5 possible answers (i.e., very bad, bad, acceptable, good, and very good).

Psychological health

Psychological health was assessed through self-perceived questionnaires based on the following dimensions and focusing on the factors that best explain the mental health status of children and adolescents[11]: psychological well-being (i.e., positive affect, happiness, optimism, and self-esteem) and psychological distress (i.e., anxiety, depression, and negative affect).

Self-esteem, which refers to how we assess our-self whether positively or negatively, was evaluated with the Rosenberg Self-Esteem scale that it is validated in children and adolescents.[23] This scale has 10 items that assess global self-esteem considering both positive and negative feelings with 4 possible answers (i.e. totally disagree, disagree, agree, and totally agree).[24] The final score

ranges from 10 (lowest self-esteem) to 40 (highest self-esteem). Dispositional optimism, which refers to how favorably people view their future, was evaluated with the Life Orientation Test-Revised (LOT-R) using 6 items (out of 10) with 5 possible answers (totally disagree, disagree, neither disagree nor agree, agree, and totally agree).[25] The score ranges from 6 (lowest optimism) to 30 (highest optimism). Happiness, which refers to positive psychological functioning, was assessed by the Subjective Happiness Scale (SHS) whose Spanish version has shown appropriate test–retest reliability, internal consistency, and convergent validity. [26] This tool includes 4 items in a Likert scale ranging from 1 to 7 (from less happiness to more happiness) The score was calculated as the sum of the 3 first items with a range from 3 (lowest happiness) to 21 (highest happiness).

Positive affect, which is defined as the perception of emotion in a good or positive way, and negative affect, defined as the tendency to experience negative feelings, was measured with the Positive Affect Schedule for children (PANAS-C) in 20 items (10 for positive affect; 10 negative affect) with 3 possible answers (never, sometimes and many times).[27] The final score was calculated as the sum of 10 items (for either negative or positive affect) and it ranges from 10 (lowest negative or positive affect) to 30 (highest negative or positive affect).

Childhood anxiety, which refers to the brain's state of alertness to worry or fear, was assessed with the State–Trait Anxiety Inventory for Children (STAIC-T). This inventory has been extensively validated in Spanish children. [28] This tool collects 20 items with 3 possible answers (rarely, sometimes, and often) and a score range from 20 (lowest anxiety level) to 60 points (highest anxiety level). Depression, which means a low or apathetic mood over time, was measured with the Children Depression Inventory (CDI), which consists of 27 items assessing 5 domains (interpersonal problems, ineffectiveness, negative mood, anhedonia, and negative self-esteem) with three types of answer depending on the intensity

of the selected symptoms, rated with a score of 0–2.29 The score ranges from 0 (lowest depression level) to 54 (highest depression level).

Statistical analysis

Descriptive characteristics of the study sample were computed as mean and standard deviation or percentages for continuous and categorical variables, respectively. All variables were checked for normality using both graphical (normal probability plots) and statistical (Kolmogorov–Smirnov test) procedures. There was no interaction between sex and fitness variables in relation to psychological health variables and therefore, the analyses were performed including boys and girls together.

Partial correlations adjusted by key confounders (i.e., sex, years from peak height velocity, years between diagnosis and testing, body mass index, and type of neoplasm) were used to examine how the fitness components or psychological health indicators correlated to each other. The associations between fitness (i.e., objectively-measured and self-perceived) with psychological health (i.e., well-being and distress) were performed using multiple linear regression and adjusted by the previous covariates.

Additionally, differences in psychological well-being and psychological distress by fitness levels (low fitness vs. high fitness) were obtained by one-way analysis of covariance and adjusting for the same set of covariates. This analysis was performed for those significant associations reported in the multiple linear regressions. Children were grouped in the "low fitness" group when they perceived very bad and bad fitness levels in the IFIS (equivalent to <P10th) and in the "high fitness" group when they perceived good-very good fitness level (equivalent to ≥P30th).[30] In this specific analysis, we excluded children who answered "average" to have both end extremes (i.e., low and high).

All the analyses were performed using the IBM SPSS Statistics for Windows version 22.0 (IBM Corp), and the level of significance was set to $p < 0.05$.

RESULTS

Table 1 shows descriptive data on anthropometric characteristics, demographic characteristics, somatic maturation, clinical data, fitness, and psychological health variables in all participants and by sex.

Table S1 shows partial correlation coefficients between the fitness components. Overall, objectively-measured muscular fitness correlated with self-perceived overall fitness, muscular fitness, and speed/agility (r from 0.202 to 0.353, all $p < 0.05$). Moreover, most self-perceived fitness indicators correlated to each other (r from 0.256 to 0.550, all $p < 0.05$), except for the associations between flexibility with muscular strength ($r = 0.084$, $p = 0.397$) and speed/agility ($r = 0.185$, $p = 0.061$) and cardiorespiratory fitness with muscular strength ($r = 0.163$, $p = 0.099$) **Table S2** shows partial correlation coefficients between the psychological health indicators. All psychological well-being and distress indicators correlated to each other (r from −0.252 to 0.671, all $p < 0.05$), except for the association between negative and positive affect ($r = −0.132$, $p = 0.194$).

Table 1. Descriptive characteristic of the study sample by sex.

	N	Total	N	Boys	N	Girls
Age (years)	116	12.1 ± 3.3	66	12.0 ± 3.2	50	12.2 ± 3.
Weight (kg)	116	46.6 ± 18.0	66	47.1 ± 17.4	50	46.0 ± 19.0
Height (cm)	116	147.5 ± 17.1	66	148.8 ± 17.8	50	145.6 ± 16.0
Body mass index (kg/m^2)	116	20.7 ± 4.7	66	20.5 ± 4.1	50	20.9 ± 5.3
Years from peak height velocity	116	-0.7 ± 2.7	66	-1.3 ± 2.5	50	0.0 ± 2.9
Years from diagnosis to testing	110	6.4 ± 3.9	62	6.4 ± 3.9	48	6.6 ± 3.8

Type of neoplasm (%)						
Soft	70	60.9	41	63.1	29	58
Solid	45	39.1	24	36.9	21	42
Objectively-measured fitness						
Absolute upper-body muscular strength (kg)	116	18.1 ± 8.6	66	19.4 ± 10.0	50	16.3 ± 5.9
Relative lower-body muscular strength (cm)	115	118.1 ± 33.1	65	127.1 ± 35.8	50	106.4 ± 25.0
Self-reported fitness (Very low, low, average, high, very high; %)						
Overall fitness	114	1, 10, 32, 41, 16	64	2, 8, 34, 39, 17	50	0, 12, 30, 44, 14
Cardiorespiratory fitness	114	3, 18, 40, 29, 10	64	2, 15, 42, 30, 11	50	4, 22, 38, 28, 8
Muscular strength	114	13, 42, 28, 17	64	14, 36, 33, 17	50	13, 42, 28, 17
Speed / agility	114	2, 18, 30, 31, 19	64	3, 19, 25, 34, 19	50	0, 18, 36, 26, 20
Flexibility	114	9, 18, 34, 32, 7	64	10, 17, 42, 28, 3	50	8, 20, 24, 36, 12
Psychological well-being						
Positive affect (PANAS-C)	111	24.7 ± 3.3	62	24.8 ± 3.5	49	24.5 ± 3.0
Happiness (SHS)	110	22.5 ± 4.5	62	23.1 ± 4.3	48	21.8 ± 4.7
Optimism (LOT-R)	111	21.9 ± 4.2	62	22.3 ± 4.3	49	21.5 ± 4.1
Self-esteem (RSE)	111	27.7 ± 2.4	62	27.8 ± 2.4	49	27.4 ± 2.3
Psychological distress						
Anxiety (STAIC-R)	111	32.3 ± 6.6	62	31.7 ± 6.4	49	33.1 ± 6.8
Depression (CDI)	113	10.2 ± 5.9	65	10.5 ± 6.0	48	9.8 ± 5.8
Negative affect (PANAS-C)	111	17.9 ± 3.4	62	17.8 ± 3.4	49	18.1 ± 3.5

Values are mean ± standard deviation or percentages.

PANAS-C: Positive and Negative Affect Scale for Children (score ranges from 10-30), SHS: Subjective Happiness Scale (score ranges from 3-21), LOT-R: Life Orientation Test- Revised (score ranges from 6-30), RSE: The Rosenberg Self-Esteem Scale (score ranges from 10-40), STAIC-R: State-Trait Anxiety Inventory for Children (score ranges from 20-60), CDI: Children Depression Inventory (score ranges from 0-54). Analyses adjusted for sex, years from peak high velocity, years between diagnosis and testing, body mass index and type of neoplasm.

Table 2 shows multiple linear regression between fitness (i.e., objectively-measured and self-perceived) and psychological health (i.e., well-being and psychological distress dimensions) adjusted by sex, years from peak height velocity, years between diagnosis and testing, body mass index and type of neoplasm. Objectively-measured muscular fitness was not associated with any of the psychological well-being and psychological distress indicators analyzed (standardized beta, $\beta \leq -0.271$, all $p > 0.05$). Self-perceived overall fitness and flexibility were positively related to positive affect ($\beta \geq 258$, all $p < 0.05$). Self-perceived cardiorespiratory fitness, speed/agility, and flexibility were negatively associated with depression ($\beta \geq -0.222$, $p < 0.05$). Self-perceived cardiorespiratory fitness was also negatively associated with anxiety and negative affect ($\beta \geq -0.264$, $p < 0.05$). No significant associations were observed in the remaining self-perceived fitness and psychological health variables studied (all $p > 0.05$).

Table 2. Multiple linear regression models analysing the associations between physical fitness (i.e., objectively measured and self-reported) and psychological health (i.e., well-being and distress indicators) in young pediatric cancer survivors.

	Psychological well-being				Psychological distress		
	Positive Affect (PANAS-C)	Happiness (SHS)	Optimism (LOT-R)	Self-Esteem (RSE)	Anxiety (STAIC-R)	Depression (CDI)	Negative Affect (PANAS-C)
Objectively-measured †:.							
Absolute upper-body muscular strength (kg)	-0.102	-0.226	-0.188	-0.271	0.048	0.061	0.069
Relative lower-body muscular strength (cm)	0.115	-0.081	-0.060	-0.122	0.024	-0.146	0.166
Self-reported (IFIS):							
Overall Fitness	0.266*	0.185	0.181	0.135	-0.098	-0.206	-0.051
Cardiorespiratory Fitness	0.131	0.092	0.132	0.172	-0.317*	-0.236*	-0.264*
Muscular strength	0.188	0.178	0.182	0.106	-0.087	-0.144	-0.048
Speed/agility	0.167	0.147	0.103	0.146	-0.112	-0.222*	-0.118
Flexibility	0.258*	0.086	0.135	0.161	-0.087	-0.265*	0.054

PANAS-C: Positive and Negative Affect Scale for Children, SHS: Subjective Happiness Scale, LOT-R: Life Orientation Test-Revised. RSE: The Rosenberg Self-Esteem Scale, STAIC-R: State-Trait Anxiety Inventory for Children, CDI: Children Depression Inventory, IFIS: International Fitness Scale.

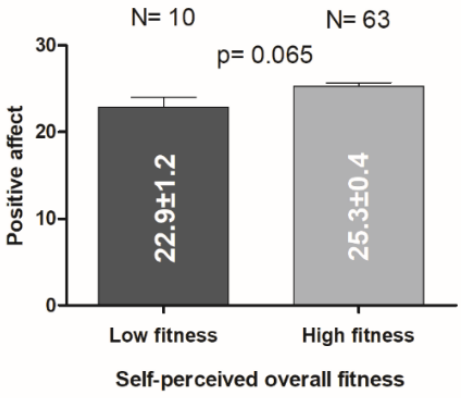
† Cardiorespiratory fitness and speed/agility tests were not performed during COVID-19 pandemic because of the available evidence at that time showing impaired performance using FFP2/N95 face masks [64], and more importantly, to ensure the safety of our participants.

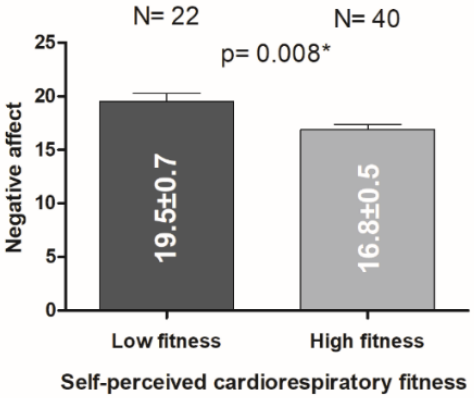
Values represent standardized coefficient. Statistically significant values are highlighted in bold.

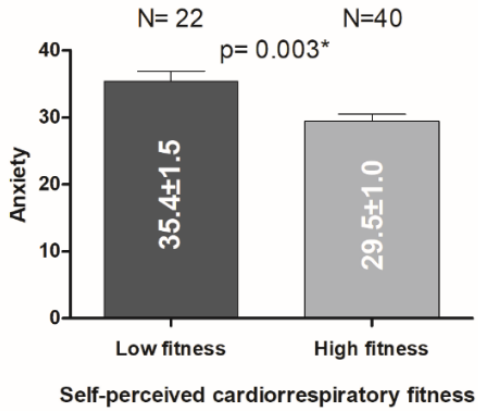
* $p < 0.05$ denotes statistically significant.

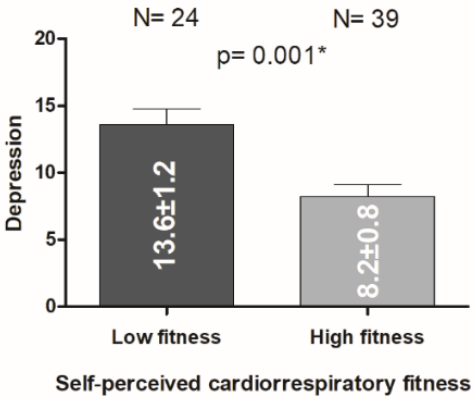
We explored whether those children categorized as "high fitness" presented greater psychological health than their peers grouped as "low fitness."

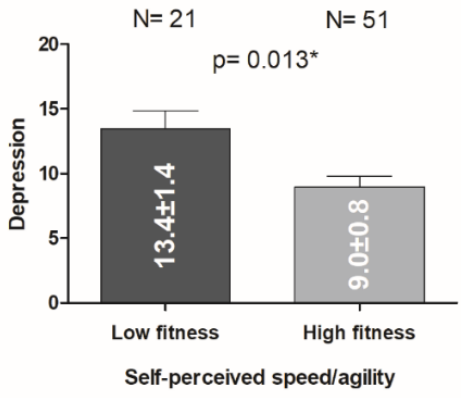
For this purpose, only significant associations previously described were analyzed (see **Figure 1**). We observed that high-fit participants in cardiorespiratory fitness presented lower anxiety, negative affect, and depression levels (all $p <= 0.008$) compared with those peers in the low-fit group. Moreover, high-fit participants in speed/agility had lower depression levels ($p = 0.013$) compared with low-fit participants. Finally, participants categorized in the high-fit group in flexibility had greater positive affect ($p = 0.010$) than those in the low-fit group.

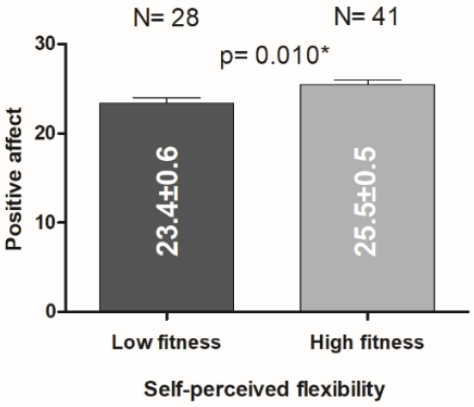

N= 10
N= 63
p= 0.065
Positive affect
30
20
10
0
22.9±1.2
25.3±0.4
Low fitness
High fitness
Self-perceived overall fitness


N= 22
N= 40
p= 0.008*
Negative affect
25
20
15
10
5
0
19.5±0.7
16.8±0.5
Low fitness
High fitness
Self-perceived cardiorespiratory fitness


N= 22
N=40
p= 0.003*
Anxiety
40
30
20
10
0
35.4±1.5
29.5±1.0
Low fitness
High fitness
Self-perceived cardiorrespiratory fitness


N= 24
N= 39
p= 0.001*
Depression
20
15
10
5
0
13.6±1.2
8.2±0.8
Low fitness
High fitness
Self-perceived cardiorrespiratory fitness


N= 21
N= 51
p= 0.013*
Depression
20
15
10
5
0
13.4±1.4
9.0±0.8
Low fitness
High fitness
Self-perceived speed/agility


N= 28
N= 41
p= 0.010*
Positive affect
30
20
10
0
23.4±0.6
25.5±0.5
Low fitness
High fitness
Self-perceived flexibility

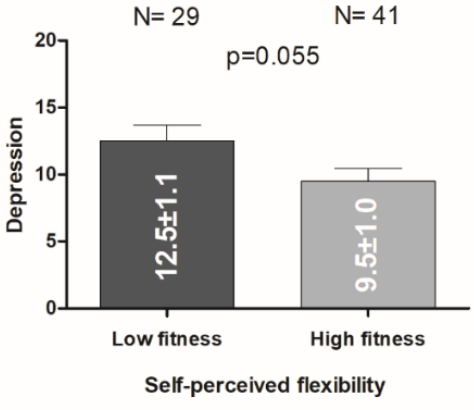

N= 29
N= 41
p=0.055
Depression
20
15
10
5
0
12.5±1.1
9.5±1.0
Low fitness
High fitness
Self-perceived flexibility

Figure 1. One-way analysis of covariance examining differences in psychological well-being and distress indicators (i.e., positive and negative affect, anxiety and depression) by self-reported fitness levels (low/high) and adjusted for sex, years from peak high velocity, years between diagnosis and testing, body mass index and type of neoplasm in young pediatric cancer survivors.

P shows differences between-groups (i.e., low fitness vs. high fitness). Low fitness group includes participants with very poor and poor fitness and high fitness includes participant with high and very high fitness in the IFIS. Values show as mean ± standard error.

DISCUSSION

The present study shows the associations between self-perceived and objectively-measured muscular fitness and psychological well-being and psychological distress indicators in young pediatric cancer survivors. The main findings of this study are: (i) self-perceived overall fitness and flexibility were positively associated with positive affect; and (ii) self-perceived cardiorespiratory fitness, speed/agility, and flexibility were negatively associated with anxiety, depression, and negative affect, respectively. No significant associations were observed between objectively-measured muscular fitness and any of the psychological well-being and psychological distress indicators analyzed.

Psychological well-being

In our study, self-perceived overall fitness and flexibility were positively associated with positive affect. The lack of studies investigating this association between cancer population and healthy youths[31] limits the comparisons among studies. Looking at intervention studies, Kolden et al.[32] including flexibility exercises) improved positive affect, albeit in breast cancer patients.[32] A plausible explanation could be due to the exercise capacity on reducing cortisol levels,[33] which in turn, could improve the psychological well-being.

In this line, two main systematic reviews and meta-analyses showed that physical activity has a potential role on improving psychological health and

physical fitness in children and adolescents.[31,34] In relation to the objective measures of fitness, no associations were found between upper-and lower-body muscular fitness with any of the psychological well-being indicators. Although there is no evidence focusing on cancer survivors (either pediatric or non-pediatric), a recent systematic review and meta-analyses in children and adolescents depicted that muscular fitness was positively related to psychological well-being indicators (i.e., self-esteem, self-concept, and physical self-perceptions). [31,35] These associations between muscular fitness and self-esteem may be due to the increase in lean mass resulting from resistance training and also because of the neurochemical effects of fitness in the brain that elevate mood.[16] However, in our study, these associations were not found nor even using the same tool, perhaps due to the different populations studied and the treatment-and cancer-related sequels as shown by their different levels of self-esteem (e.g., Rodriguez-Ayllon et al.[36]: mean ± SD of 33.1 ± 4.7 vs. 27.66 ± 2.37 in the present study). In addition, some studies have found that adolescents with higher fitness levels tend to exercise in a social context, which may increase feelings of total acceptance. [37] Cancer survivors, being a vulnerable population, tend to exercise individually, which may explain the lack of significant results between objectively-measured and some indicators of psychological health. In this study, we could not measure cardiorespiratory fitness objectively, but previous evidence in adolescents with overweight/obesity found that improving cardiorespiratory fitness was associated with better self-esteem, which may be due to changes in brain structure and brain signaling.[38] The lack of studies investigating these associations in oncology population makes it hard to explain the potential mechanisms behind the lack of association found in this manuscript, but it might be plausible that cardiorespiratory fitness does not influence psychological well-being outcomes in the same manner as it does with psychological distress indicators. Future studies with longitudinal design and using objective measures of fitness are needed in this population.

Psychological distress

We found that self-perceived cardiorespiratory fitness, the most consistent fitness component, was negatively associated with psychological distress indicators such as anxiety, depression, and negative affect. Moreover, speed/agility, and flexibility were also negatively associated with depression, that is, the better the perception of the speed/agility, and flexibility levels, the lower the depression levels. As with psychological well-being indicators, studies investigating this association in young pediatric cancer survivors are lacking, and therefore, other populations are used to discuss our findings. Our findings agree with those reported by a systematic review and meta-analysis by Cadenas-Sanchez et al.[31] who observed that adolescents who presented lower cardiorespiratory fitness reported elevated depressive symptoms. The plausible explanation might shed light on the role of aerobic and resistance training on psychological health through increasing oxygen transport and brain blood flow.[31] Although we could not measure cardiorespiratory fitness objectively, a previous study in childhood survivors of acute lymphoblastic leukemia found cardiorespiratory fitness to protect against depression,[39] which is in line with our perceived fitness findings. Regarding objective fitness, no associations were found between muscular fitness and any of the psychological distress indicators, supporting the lack of association that we observed when using self-perceived muscular fitness instead. Our findings are partially in agreement with a recent systematic review and meta-analyses in which the authors did not observe a significant association between muscular fitness and depression (pooled correlation −0.047, 95% confidence intervals: −0.110, 0.016); but they observed a pooled significant correlation between muscular fitness and anxiety (pooled correlation −0.176, 95% confidence intervals: −0.306, −0.040). Additionally, research in children with overweight/obesity showed that upper body muscular fitness and negative affect were inversely associated.[36] Differences between our

findings and the previous evidence could be due to the lower fitness and higher psychological distress levels in our sample with cancer survivors, than in those children apparently healthy or with overweight/obesity. As an example, we have observed that the negative affect (using the same questionnaire) was lower in children with overweight/ obesity than in pediatric cancer survivors (ActiveBrains: 16 ± 3.4 vs. iBoneFit: 17.9 ± 3.4).

Strengths and limitations

To our knowledge, this is the first study using both objective and self-perceived fitness assessments to examine its association with psychological health in this population. Moreover, our findings have been controlled for covariates that are known to affect psychological health in this population. Nevertheless, there are some limitations that should be noted. Firstly, being a cross-sectional study, it does not allow us to infer causality for any of the association factors, so further longitudinal studies are needed to confirm these findings. Moreover, although we have controlled for potential confounders, there may be other variables that could interfere with these associations. Some objective fitness tests (cardiorespiratory and speed/agility) could not be carried out due to the mandatory use of face masks (due to covid-19 pandemic) as these could affect the measures. Nevertheless, the participants and their families were grateful not to do these tests due to increased contagion risk and the uncertain consequences this could have had in this sensitive population.

CONCLUSIONS

Overall, our study indicates that higher self-perceived overall fitness and flexibility are associated with better psychological well-being (i.e., positive affect). Moreover, greater self-perceived cardiorespiratory fitness, speed/ agility, and flexibility but not muscular fitness (neither self-perceived nor objectively-

measured) is associated with lower psychological distress (i.e., anxiety, depression, and negative affect). The findings from this study highlight the importance of promoting self-perceived fitness in the pediatric oncology population.

PERSPECTIVE

Assessing psychological health after childhood cancer is important as it affects many areas such as school attendance and adherence to physical activity. Psychological health variables have hardly been studied nor related to exercise in young pediatric cancer survivors; however, some studies have looked at levels of anxiety and depression in this population. Likewise, fitness is usually measured only objectively; however, validated questionnaires are available that allow a quick assessment that facilitates the collection of this data. Given that some articles have observed that good fitness levels are related to better psychological health in healthy young, more studies examining both psychological well-being and distress in young pediatric cancer survivors are needed.

REFERENCES

1. Filbin M, Monje M. Developmental origins and emerging therapeutic opportunities for childhood cancer. Nat Med. 2019;25(3):367-376. doi:10.1038/s41591-019-0383-9

2. Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. Lancet Oncol. 2017;18(6):719-731. doi:10.1016/S1470-2045(17)30186-9

3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7-33. doi:10.3322/caac.21708

4. Erdmann F, Frederiksen LE, Bonaventure A, et al. Childhood cancer: survival, treatment modalities, late effects and improvements over time. Cancer Epidemiol. 2021;71(May 2020):101733. doi:10.1016/j.canep.2020.101733

5. Henderson TO, Nathan PC. Childhood cancer survivors: considerations for surgeons in the transition from pediatric to adult care. Semin Pediatr Surg. 2015;24(2):93-99. doi:10.1053/j.sempedsurg.2015.01.007

6. Antwi GO, Jayawardene W, Lohrmann DK, Mueller EL. Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies. Support Care Cancer. 2019;27(9):3183-3194. doi:10.1007/s00520-019-04788-z

7. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. Psychiatr Clin North Am. 2009;32(3):483-524. doi:10.1016/j.psc.2009.06.002

8. Marchak JG, Christen S, Mulder RL, et al. Recommendations for the surveillance of mental health problems in childhood, adolescent, and young adult cancer survivors: a report from the international late effects of childhood cancer guideline harmonization group. Lancet Oncol. 2022;23(4):e184-e196. doi:10.1016/S1470-2045(21)00750-6

9. Tonsing KN, Ow R. Quality of life, self-esteem, and future expectations of adolescent and young adult cancer survivors. Health Soc Work. 2018;43(1):15-21. doi:10.1093/hsw/hlx047

10. Ness KK, Mertens AC, Hudson MM, et al. Limitations on physical performance and daily activities among long-term survivors of childhood cancer. Ann Intern Med. 2005;143(9):639-648. doi:10.7326/0003-4819-143-9-200511010-00007

11. Antaramian SP, Scott Huebner E, Hills KJ, Valois RF. A dual-factor model of mental health: toward a more comprehensive understanding of youth functioning. Am J Orthopsychiatry. 2010;80(4):462-472. doi:10.1111/j.1939-0025.2010.01049.x

12. Rodriguez-ayllon M, Cadenas-sanchez C, Esteban-cornejo I, Migueles JH. Physical fitness and psychological health in overweight/obese children: a cross-sectional study from the ActiveBrains project. J Sci Med Sport. 2018;2020(21):179-184.

13. Kubzansky LD, Huffman JC, Boehm JK, et al. Positive psychological well-being and cardiovascular disease. J Am Coll Cardiol. 2018;72(12):1382-1396. doi:10.1016/j.jacc.2018.07.042

14. Ortega FB, Ruiz JR, España-Romero V, et al. The international fitness scale (IFIS): usefulness of self-reported fitness in youth. Int J Epidemiol. 2011;40(3):701-711. doi:10.1093/ije/dyr039

15. Ruiz JR, Castro-Piñero J, España-Romero V, et al. Field-based fitness assessment in young people: the ALPHA health-related fitness test battery for children and adolescents. Br J Sports Med. 2011;45(6):518-524. doi:10.1136/bjsm.2010.075341

16. Ortega FB, Ruiz JR, Castillo MJ, Sjöström M. Physical fitness in childhood and adolescence: a powerful marker of health. Int J Obes (Lond). 2008;32(1):1-11. doi:10.1038/sj.ijo.0803774

17. Ruggero CJ, Petrie T, Sheinbein S, Greenleaf C, Martin S. Cardiorespiratory fitness may help in protecting against depression among middle school adolescents. J Adolesc Health. 2015;57(1):60-65. doi:10.1016/j.jadohealth.2015.03.016

18. Chen HM, Tsai CM, Wu YC, Lin KC, Lin CC. Randomised controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-

related symptoms in patients with lung cancer. Br J Cancer. 2015;112(3):438-445. doi:10.1038/bjc.2014.612

19. Smith JJ, Eather N, Morgan PJ, Plotnikoff RC, Faigenbaum AD, Lubans DR. The health benefits of muscular fitness for children and adolescents: a systematic review and meta-analysis. Sports Med. 2014;44(9):1209-1223. doi:10.1007/s40279-014-0196-4

20. Gil-Cosano JJ, Ubago-Guisado E, Sánchez MJ, et al. The effect of an online exercise programme on bone health in paediatric cancer survivors (iBoneFIT): study protocol of a multi-Centre randomized controlled trial. BMC Public Health. 2020;20(1):1-13. doi:10.1186/s12889-020-09607-3

21. Moore SA, McKay HA, Macdonald H, et al. Enhancing a somatic maturity prediction model. Med Sci Sports Exerc. 2015;47(8):1755-1764. doi:10.1249/MSS.0000000000000588

22. Fikenzer S, Uhe T, Lavall D, et al. Effects of surgical and FFP2/ N95 face masks on cardiopulmonary exercise capacity. Clin Res Cardiol. 2020;109(12):1522-1530. doi:10.1007/s00392-020-01704-y

23. Mäkinen M, Lindberg N, Komulainen E, Puukko-Viertomies LR, Aalberg V, Marttunen M. Psychological well-being in adolescents with excess weight. Nord J Psychiatry. 2015;69(5):354-363. doi:10.3109/08039488.2014.986194

24. Martín-Albo J, Núñez JL, Navarro JG, Grijalvo F. The Rosenberg self-esteem scale: translation and validation in university students. Span J Psychol. 2007;10(2):458-467. doi:10.1017/ S1138741600006727

25. Scheier MF, Charles S, Bridges MW. Distinguishing optimism from neuroticism: a reevaluation of the life orientation test. J Pers Soc Psychol. 1994;67(6):1063-1078. doi:10.1037//0022-3514.67.6.1063

26. Extremera N, Fernández-Berrocal P. The subjective happiness scale: translation and preliminary psychometric evaluation of a Spanish version. Soc Indic Res. 2014;119(1):473-481. doi:10.1007/s11205-013-0497-2

27. Sandín B, Chorot P, Lostao L, Joiner TE, Santed MA, Valiente RM. The PANAS scales of positive and negative affect: factor analytic validation and cross-cultural convergence. Psicothema. 1999;11(1):37-51.

28. Rodrigo G, Lusiardo M. Spanish version of the revised Children's manifest anxiety scale in Uruguay: reliability and concurrent validity. Psychol Rep. 1989;65(1):94. doi:10.2466/pr0.1989.65.1.94

29. del Barrio MV, Moreno C, López R. El Children's Depression Inventory (CDI; Kovacs, 1992). Su aplicación en población española. Clin Salud. 1999;10(3):393-416.

30. Sánchez-López M, Martínez-Vizcaíno V, García-Hermoso A, Jiménez-Pavón D, Ortega FB. Construct validity and test-retest reliability of the international fitness scale (IFIS) in Spanish children aged 9–12 years. Scand J Med Sci Sports. 2015;25(4):543-551. doi:10.1111/sms.12267

31. Cadenas-Sanchez C, Mena-Molina A, Torres-Lopez LV, et al. Healthier Minds in Fitter Bodies: A Systematic Review and Meta-Analysis of the Association between Physical Fitness and Mental Health in Youth. Vol 51. Springer International Publishing; 2021. doi:10.1007/s40279-021-01520-y

32. Kolden GG, Strauman TJ, Ward A, et al. A pilot study of group exercise training (GET) for women with primary breast cancer: feasibility and health benefits. Psychooncology. 2002;11(5):447-456. doi:10.1002/pon.591

33. Sirgy MJ. Positive balance: a hierarchical perspective of positive mental health. Qual Life Res. 2019;28(7):1921-1930. doi:10.1007/s11136-019-02145-5

34. Rodriguez-Ayllon M, Cadenas-Sánchez C, Estévez-López F, et al. Role of physical activity and sedentary behavior in the mental health of preschoolers, children and adolescents: a systematic review and meta-analysis. Sports Med. 2019;49(9):1383-1410. doi:10.1007/s40279-019-01099-5

35. Bou-Sospedra C, Adelantado-Renau M, Beltran-Valls MR, Moliner-Urdiales D. Independent and combined influence of physical fitness components on self-esteem in adolescents: DADOS study. Ann Hum Biol. 2022;48(7–8): 550-556. doi:10.1080/03014460.2022.2032337

36. Rodriguez-Ayllon M, Cadenas-Sanchez C, Esteban-Cornejo I, et al. Physical fitness and psychological health in overweight/ obese children: a cross-sectional study from the ActiveBrains project. J Sci Med Sport. 2018;21(2):179-184. doi:10.1016/j.jsams.2017.09.019

37. Drenowatz C, Greier K, Ruedl G, Kopp M. Association between club sports participation and physical fitness across 6-to 14-year-old austrian youth. Int J Environ Res Public Health. 2019;16(18):33-92. doi:10.3390/ijerph16183392

38. Goldfield GS, Adamo KB, Rutherford J, Murray M. The effects of aerobic exercise on psychosocial functioning of adolescents who are overweight or obese. J Pediatr Psychol. 2012;37(10):1136-1147. doi:10.1093/jpepsy/jss084

39. Lemay V, Caru M, Samoilenko M, et al. Prevention of long-term adverse health outcomes with cardiorespiratory fitness and physical activity in childhood acute lymphoblastic leukemia survivors. J Pediatr Hematol Oncol. 2019;41(7):E450-E458. doi:10.1097/MPH.0000000000001426

Supplementary material

Section 3

Randomized control trial: Effects of a exercise program on psychological health in young pediatric cancer survivors

Study IV

The effects of a 36-week online plyometric exercise-based program on psychological health in young pediatric cancer survivors

Study IV

ABSTRACT

Aim: To examine the impact of a 36-week online plyometric exercise-based program on psychological health (i.e., well-being and distress) in young pediatric cancer survivors.

Materials and methods: 116 participants (aged 12.1 ± 3.3 years; 42% female) from the iBoneFIT multicenter randomized control trial (Ref. ISRCTN61195625) were randomized to an intervention or a control group. The intervention group received an online exercise intervention based on plyometric jumps and dietary counseling regarding calcium and vitamin D, while the control group only received dietary counseling. Psychological health was divided into psychological well-being (i.e., self-esteem, optimism, happiness, and positive affect) and psychological distress (i.e., depression, anxiety, and negative affect) which were measured with questionnaires. Data were analyzed using a constrained baseline longitudinal mixed model adjusted for baseline differences between groups. Effect size values of 0.2 to 0.5 are considered small, 0.5 to 0.8 are considered medium, and greater than 0.8 are considered large.

Results: The exercise intervention in the between-group analysis improved psychological distress, with the difference being -1.09 (95% CI: -2.11 to -0.08; P=.035) and with small effect sizes in all included outcomes; and negative affect -1.08 [95% CI: -2.11 to -0.04], P=.041). No significant results were found in the rest of the psychological health indicators. In the within-group analysis, the exercise intervention show significant results in the score of psychological distress -7.80% [mean score -1.57 (-2.46 to -0.67), p=<0.001] compared with the control group of -2.34% [mean score -0.47 (-2.46 to -0.67), p=0.382]; and anxiety in

the intervention group with 8.89% [mean score -2.87 (-4.74 to -1.00), p=0.001] compared with a change of -4.06% of the control group [mean score -1.31 (-3.08 to 0.45), p=0.184].

In the per-protocol analysis, the significant result between-group was found in the score of psychological distress -1.20 (-2.26 to -0.14); p=0.028). In the within-groups analysis, the significant results were found in the score of psychological distress in the intervention group with a change of -8.33% [mean score -1.68 (-2.66 to -0.70), p< 0.001] compared with the control group of -2.38% [mean score -0.48 (-1.33 to 0.37), p=0.373]; in depression, with a change in the intervention group of -10.47% [mean score -1.05 (-2.08 to -0.01), p=0.048] compared with the control group of -4.49% [mean score -0.45 (-1.31 to 0.41), p=0.434]; and, in anxiety, in the intervention group with a change of -9.58% [mean score -3.11 (-5.18 to -1.04), p=0.002] compared with the control group of -4.25% [mean score -1.38 (-3.18 to 0.42), p=0.166].

Conclusion: This exercise program seems to reduce the score of psychological distress, while no significant effects were observed on psychological well-being in young pediatric cancer survivors. However, it is important to note that the intervention group experiences greater changes than the control group in most psychological health variables.

INTRODUCTION

Despite childhood cancer being a rare disease, it remains one of the leading causes of death among children in developed countries and its incidence has increased by 13% over the past decades[1]. Medical intervention advancements have simultaneously propelled the survival rate of affected individuals beyond 85%[2]. However, cancer and its treatments still entail side effects for cancer survivors. Pediatric cancer survivors often experience psychological side effects, alongside adverse social and socioeconomic consequences, resulting in compromised psychological well-being and diminished quality of life[3,4]. For example, young pediatric cancer survivors display more symptoms of depression (prevalence ranging from 2%-40%) and anxiety (prevalence ranging from 1%-27%) than their siblings and the general population[5].

Physical activity has numerous health benefits such as reducing premature mortality, improving physical fitness, and improving cognitive function[6,7]. While previous studies show that physical activity may be safe and feasible in childhood cancer patients[8], emerging studies suggest an important gap in the literature regarding the harms of conducting evidence-based risk-benefit analyses on the prescription of physical exercise during cancer treatment[9,10]. Furthermore, childhood cancer patients tend to have lower levels of physical activity than their healthy peers [11].

Among the few clinical trials that have investigated the effects of physical activity on psychological health in children before and after cancer treatments: some focused on quality of life[12–16]; others on self-esteem[13–15,17,18]; and a few on depression[12,13]. Regarding quality of life, two studies found significant results after a physical activity program [14,15], while three others did not [12,13]. For self-esteem, three studies found significant results[14,15,17] while two did not [13,18]. As for depression, neither of the two studies found significant results [12,13]. Due to the lack of consistency in the results of these studies, further research is needed to

better understand the role of physical activity on psychological health in children before and after cancer treatments. Therefore, this is the first study examining the effects of a 36-weeks online plyometric exercise-based program on psychological health (including both psychological well-being and distress indicators) in young pediatric cancer survivors.

METHODS

A concise overview of the materials and methods is presented. The trial protocol and statistical analysis plan can be found in Supplement 1, while all methodological specifics are outlined in the eMethods section of Supplement 2.

Study design

The current study examines the effect of a 36-week online plyometric exercise-based program on psychological health in young pediatric cancer survivors. This study has been carried out within the iBonefit and REBOTA-Ex projects, with the former funding the first part of the intervention and the latter the last part, as well as adding bone biomarkers [19]. This was approved by the Ethics Committee on Human Research of Regional Government of Andalusia (Reference: 4500, December 2019) complied with the Declaration of Helsinki (revised version 2013), and was registered in isrctn.com (Reference: isrctn61195625, 2 April 2020). The reporting guidelines of the Consolidated Standards of Reporting Trials (CONSORT) were followed in **Supplementary Table S1**. All research processes were conducted by the premises of the Singapore Statement on Research Integrity[20].

Participants

A total of 116 young pediatric cancer survivors (aged 12.1 ± 3.3 years; 42% female) in this multicenter randomized control trial were recruited by the pediatric oncology and haematology sections at the university hospitals "Virgen de las Nieves" (Granada) and "Reina Sofia" (Cordoba). The inclusion criteria

were: participants diagnosed at least one year before enrolment, with previous exposure to radiotherapy and/or chemotherapy, and not currently receiving cancer treatments. Because of COVID-19 restrictions, data was collected in two waves: 1) from October 2020 to February 2021, and 2) from December 2021 to March 2022. Participants were randomized to an exercise or a control group. The flow chart of the study is shown in **Figure 1**.

For the sample size of the iBoneFIT project, the femoral neck areal bone mineral density was used due to its important role in osteoporosis diagnosis. Additionally, the sample size was determined to consider age group subgroups analysis (6-11 years and 12-18 years). At least 116 participants were required (58 in each group), with an 80% power, an α level of 0.05, and an estimated effect size of 0.25 for changes in femoral neck areal bone mineral density. This estimate includes an addition of 10% for multivariable analysis and 20% for occasional losses and refusals.

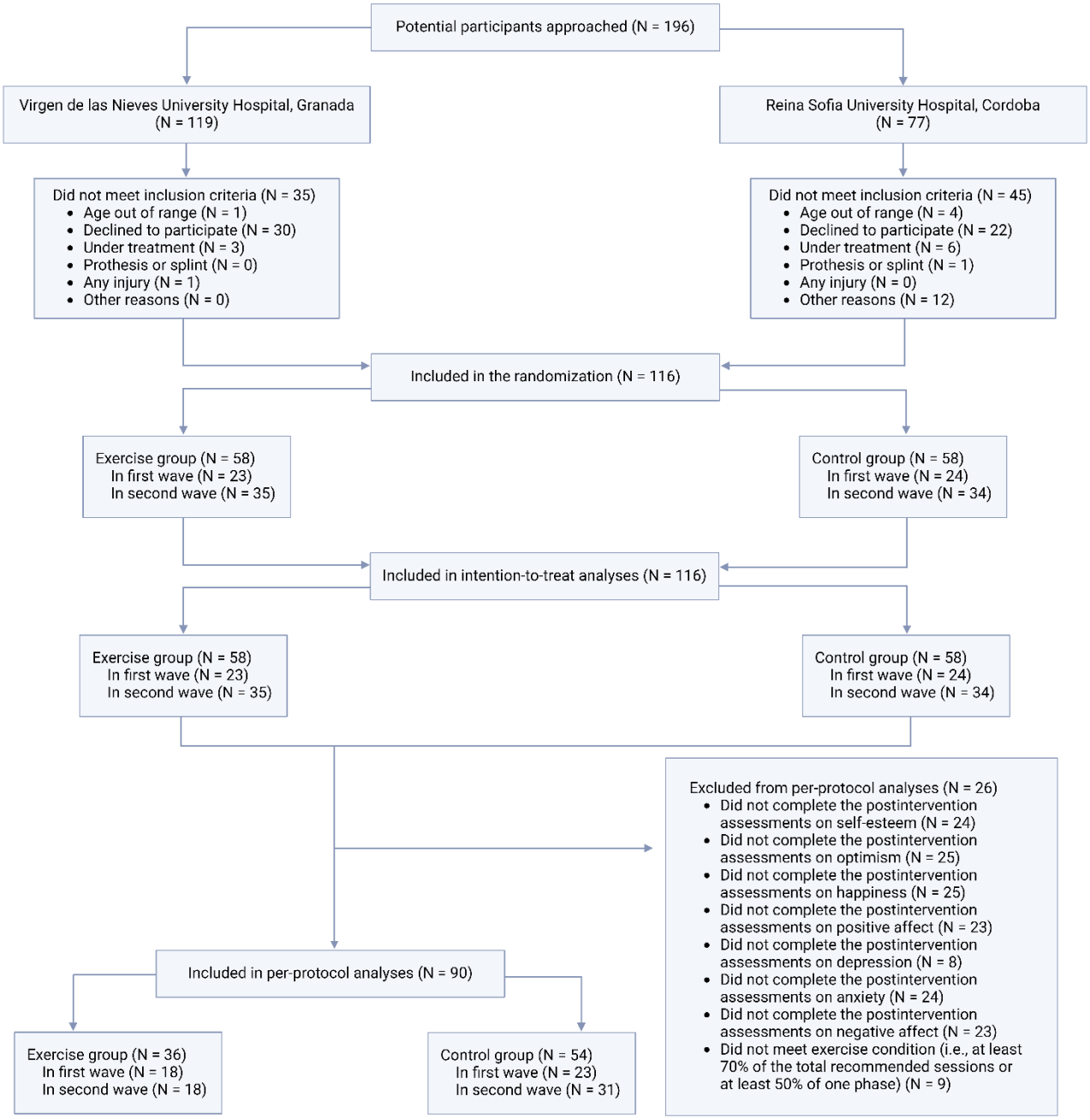


Figure 1. Flow chart of the participants of the study

Randomization and Blinding

Randomization was performed by an external partner (V. M-V) stratified by age and sex by using SAS software, version 9.1 (SAS Institute Inc). Assignments were hidden from the assessors until all tests were completed, after which participants were divided into an exercise or a control group (1:1). While outcome assessors were blinded to group assignments, participants could not be blinded to their assignments due to the nature of the exercise intervention.

Intervention and Control group

Participants in the control group continued with their usual routines. Participants in the intervention group were instructed to engage a 36-weeks online exercise program. Participants or their parents were added to a WhatsApp group where the training video was sent, accessible through a website (https://t.ly/iNqS6). The website incorporated five behaviour change techniques and gamification to maintain and increase the motivation of the participants during the exercise intervention. The program consisted of three phases, with three to four days per week dedicated to progressive plyometric jump exercises, each lasting approximately fifteen minutes. The duration and intensity of the exercise were adjusted depending on the phase and week of the program. The first phase consists of eight weeks focused on body mass-based squats; the second phase on 12 weeks of squat jumps, and the third phase on 16 weeks of countermovement jumps. Participants performed 7296 squats/leaps (2000 squats plus 5296 jumps) across 136 sessions. Information on vitamin D and calcium dietary counseling was given to both exercise and control groups. After that, the control group was offered the same online plyometric exercise-based program.

Adherence

Adherence was monitored using a diary, which participants or their parents had to send to the Whatsapp group once a month. At each phase of the intervention, a minimum of 50% adherence was required.

Psychological Health Measurements

Psychological health of the participants was measure using self-perceived questionnaires focus on two dimensions[21].: psychological well-being (i.e., self-esteem, optimism, happiness, and positive affect) and psychological distress (i.e., depression, anxiety, and negative affect).

Psychological well-being

Self-esteem was assessed using the Rosenberg Self-Esteem scale, which reflects our opinion of ourselves, whether favorably or negatively. This scale has been validated in studies involving children and adolescents[22]. It consists of ten items, each with four possible responses: completely disagree, disagree, agree, and totally agree. These items encompass both positive and negative emotions, resulting in a final score ranging from 10 (the lowest self-esteem) to 40 (the highest self-esteem).

Dispositional optimism was evaluated with the Life Orientation Test-Revised (LOT-R), which refers to how positively people see their future[23]. It consisted of six items (out of 10) with five responses options: entirely disagree, disagree, neither disagree nor agree, agree, and totally agree, with a scores ranging from 6 (the lowest optimism) to 30 (the greatest optimism).

Happiness was measured using the Subjective Happiness Scale (SHS), which is defined as positive psychological functioning[24]. It consisted of four items rated on a Likert scale from 1 to 7 (from less happiness to greater happiness). The sum of the first three items determined the score, which ranged from 3 (lowest happiness) to 21 (most happiness). Positive affect and negative affect were assessed using the Positive Affect and Negative Affect Schedule for Children (PANAS-C).

Positive affect was assessed with the Positive Affect Schedule for children (PANAS-C) and refers to perceiving emotions in a good or positive way [25]. It consisted of 20 items (10 for positive affect and 10 for negative affect), each with

three possible responses (never, sometimes, and many times). The final score ranges from 10 (lowest negative or positive affect) to 30 (highest negative or positive affect) calculated as the sum of the 10 items corresponding to either positive or negative affect.

The psychological well-being score was calculated by summing the self-esteem, optimism, happiness, and positive affect scores, and then dividing this total by the number of these outcomes.

Psychological distress

Depression was evaluated with the Children Depression Inventory (CDI), which is characterized by a persistently low or apathetic mood[26]. It consists of 27 items assessing five domains (interpersonal problems, ineffectiveness, negative mood, anhedonia, and negative self-esteem). Depending on the severity of the selected symptoms, responses can take one of three forms, ranging from 0 to 2. The score ranges from 0 (the lowest level of depression) to 54 (the highest level of depression).

Anxiety was assessed with the State-Trait Anxiety Inventory for Children (STAIC-T), which is defined as the brain's state of awareness of concern or dread[27]. It consisted of 20 items and three possible answers (rarely, sometimes, and often), with a score ranging from 20 (lowest anxiety level) to 60 (highest anxiety level).

Negative affect, as positive affect, was measured by the Positive Affect Schedule for children (PANAS-C) and is defined as the inclination to experience negative feelings.

The psychological distress score was calculated by summing the depression, anxiety, and negative affect scores, and then dividing this total by the number of these outcomes.

Demographic, Anthropometric and Clinical Variables

To examine the stature (cm) a precision stadiometer (SECA 225, Hamburg, Germany) with dimensions recorded to the nearest 0.1 cm was used. Body mass (kg) was measured with an electronic scale with an accuracy of 100 g (SECA 861, Hamburg, Germany). Body mass index (BMI) was determined as body mass (kg)/height (m2) and dichotomized as: normoweight (lowest to 24.9 kg/m2) and overweight/obesity (25 kg/m2 to highest). The somatic maturational landmark of years from peak height velocity was utilized[28]. The years from peak height velocity are measured in terms of time before and after peak height velocity, which represents the period of maximal stature growth. A tested approach was employed to predict this in children based on their age and height[28]. In addition, clinical data was obtained from clinical records.

Statistical Analysis

The analyses were conducted using both the intention-to-treat and per-protocol analysis, with the intention-to-treat analysis being the primary method. Mixed models were used to estimated means at constrained baseline and 36-week post-intervention follow-up in the psychological health indicators (i.e., well-being and distress) in this study. All the analyses were performed using the R software program (version 4.2.2) in conjunction with the GGIR open-source package (version 2.8-2)[29]. effect size values of 0.2 to 0.5 are considered small, 0.5 to 0.8 are considered medium, and greater than 0.8 are considered large[30,31].

RESULTS

The flow chart of the participants is shown in **Figure 1**. A total of 116 participants were included in the intention-to-treat analysis and randomized to a control (58 participants) or an intervention group (58 participants). In addition, of the 116 participants, 90 were included in the per-protocol analysis (36 in the

intervention group and 54 in the control group). There were not found any adverse events associated with the intervention. The total adherence rate of participants in the intervention of the iBoneFIT project was 83.1%, with phase-specific rates of 92.3% in the first phase, 87.7% in the second, and 69.4% in the third.

The descriptive characteristics of the participants included in this study by intention-to-treat analysis are presented in **Table 1**. Within the 116 participants (42.2% female), the mean (SD) age was 12.1 (3.3) years, with a mean of body mass of 46.6 (18.0) and a mean of stature of 147.5 (17.1); the mean (%) of normoweight was 64.7 and of overweight/obesity was 35.3; the mean (SD) of the years from peak height velocity was -0.8 (2.7); and 60.9% of the participants had a soft type of neoplasm and 39.1% a solid type of neoplasm.

The descriptive characteristics of the participants included in this study by per-protocol is in **Table 1**. The mean (SD) age of the 90 participants (42 % female) was 12.2 (3.4) years, with a mean body mass of 20.8 (4.8) and a mean stature of 147.4 (17.0); the mean (%) of normoweight was 18.6 and of overweight/obesity was 25.3%; the mean (SD) of years from peak height velocity was -0.7 (2.8); and 51% of the participants had a soft type of neoplasm and 39% a solid type of neoplasm.

Table 1. Descriptive characteristics of the participants included in the study (intention-to-treat analysis).

	N	Total	N	Intervention	N	Control
Sex (female/male, %)	116	42.2	58	37.9	58	46.6
Age (years)	116	12.1 (3.3)	58	11.7 (3.2)	58	12.5 (3.5)
Body mass (kg)	116	46.6 (18.0)	58	46.9 (17.9)	58	46.3 (18.3)
Stature (cm)	116	147.5 (17.1)	58	147.2 (16.7)	58	147.7 (17.5)
Body mass index (kg/m2)	116	20.7 (4.7)	58	20.9 (4.6)	58	20.5 (4.7)
Body mass index (categories, %)						
Normoweight	75	64.7	34	58.6	41	70.7
Overweight/obesity	41	35.3	24	41.4	17	29.3
Years from peak height velocity	116	-0.8 (2.7)	58	-1.0 (2.6)	58	-0.5 (2.8)
Years from diagnosis to testing	113	6.4 (3.8)	55	5.9 (3.8)	58	6.9 (3.8)
Type of neoplasm (%)						
Soft	70	60.9	34	59.6	36	62.1
Solid	45	39.1	23	40.4	22	37.9
Psychological well-being						
Self-esteem	111	27.7 (2.4)	56	28.0 (2.3)	55	27.3 (2.4)
Optimism	111	22.0 (4.2)	56	22.4 (3.8)	55	21.5 (4.6)
Happiness	110	22.5 (4.5)	55	23.5 (4.1)	55	21.6 (4.8)
Positive affect	111	24.7 (3.3)	56	25.2 (2.8)	55	24.2 (3.7)
Psychological distress						
Depression	113	10.2 (5.9)	58	9.2 (5.1)	55	11.4 (6.5)
Anxiety	111	32.3 (6.6)	56	32.0 (6.1)	55	32.6 (7.1)
Negative affect	111	17.9 (3.4)	56	18.0 (3.1)	55	17.9 (3.8)

Data are presented as mean (standard deviation) or as frequencies (percentages), as indicated.

Self-esteem was measured with the Rosenberg Self-Esteem Scale (RSE) (score range from 10 to 40); Optimism with the Life Orientation Test-Revised (LOT-R) (score range from 6 to 30); Happiness with the Subjective Happiness Scale (SHS) (score range from 3 to 21); Positive and Negative affect with the Positive and Negative Affect Scale for Children (PANAS-C) (score range from 10 to 30); Depression with the Children Depression Inventory (CDI) (score range from 0 to 54); Anxiety with the State–Trait Anxiety Inventory for Children (STAIC-R) (score range from 20 to 60).

Changes in psychological health

Table 2 shows the changes (0-36 weeks) within and between groups in the psychological health indicators (i.e., well-being and distress) analyzed through intention-to-treat analysis. A graphical illustration of the estimated means at constrained baseline and 36-week post-intervention follow-up in the psychological health indicators (i.e., well-being and distress) by intention-to-treat analysis are shown in **Figure 2 and Figure 3** and by per-protocol in **Supplementary figure S2. Supplementary figure S3** shows the parallel line plot for the baseline value to their 36-week value in psychological health (i.e., well-being and distress) for each participant, and **Supplementary figure S4 and Supplementary figure S5** the estimated means at constrained baseline and 36-week post-intervention follow-up for the per-protocol analyses in the psychological well-being and distress, respectively.

Table 2. Within-group changes (baseline-36 weeks) and between-group differences in the psychological health indicators (Intention-to-treat analysis).

	Within-group changes						Between-group changes		
	Intervention			Control					
	Change (95% CI)	Change (%)	*P*	Change (95% CI)	Change (%)	*P*	MD (95% CI)	Effect Size	*P*
Psychological well-being	0.29 (-0.40 to 0.99)	1.20	0.576	0.07 (-0.58 to 0.72)	0.29	0.967	0.23 (-0.53 to 0.98)	0.11	0.552
Self-esteem	0.80 (-0.04 to 1.65)	2.89	0.067	0.04 (-0.74 to 0.83)	0.14	0.991	0.76 (-0.10 to 1.62)	0.30	0.083
Optimism	0.58 (-0.71 to 1.86)	2.64	0.535	-0.50 (-1.72 to 0.71)	-2.28	0.588	1.08 (-0.34 to 2.50)	0.28	0.134
Happiness	0.15 (-1.11 to 1.40)	0.67	0.958	0.82 (-0.37 to 2.01)	3.64	0.235	-0.67 (-2.00 to 0.65)	0.17	0.316
Positive affect	0.08 (-0.81 to 0.97)	0.32	0.977	-0.29 (-1.12 to 0.54)	-1.18	0.689	0.36 (-0.61 to 1.33)	0.14	0.457
Psychological distress	-1.57 (-2.46 to -0.67)	-7.80	**< 0.001***	-0.47 (-1.32 to 0.37)	-2.34	0.382	-1.09 (-2.11 to -0.08)	0.40	**0.035***
Depression	-0.71 (-1.48 to 0.06)	-6.93	0.079	-0.47 (-1.24 to 0.29)	-4.59	0.311	-0.24 (-1.14 to 0.67)	0.10	0.607
Anxiety	-2.87 (-4.74 to -1.00)	-8.89	**0.001***	-1.31 (-3.08 to 0.45)	-4.06	0.184	-1.55 (-3.60 to 0.49)	0.27	0.135
Negative affect	-0.83 (-1.78 to 0.12)	-4.63	0.099	0.25 (-0.64 to 1.13)	1.39	0.789	-1.08 (-2.11 to -0.04)	0.38	**0.041***

Results are presented as mean change from baseline - post-intervention for each group and as mean difference between groups change. Statistically significant values are highlighted in bold. *p < 0.05 denotes statistically significant. Data were analysed using a constrained baseline longitudinal model. Abbreviations: MD, mean difference.

Self-esteem was measured with the Rosenberg Self-Esteem Scale (RSE) (score range from 10 to 40); Optimism with the Life Orientation Test-Revised (LOT-R) (score range from 6 to 30); Happiness with the Subjective Happiness Scale (SHS) (score range from 3 to 21); Positive and Negative affect with the Positive and Negative Affect Scale for Children (PANAS-C) (score range from 10 to 30); Depression with the Children Depression Inventory (CDI) (score range from 0 to 54); Anxiety with the State–Trait Anxiety Inventory for Children (STAIC-R) (score range from 20 to 60).

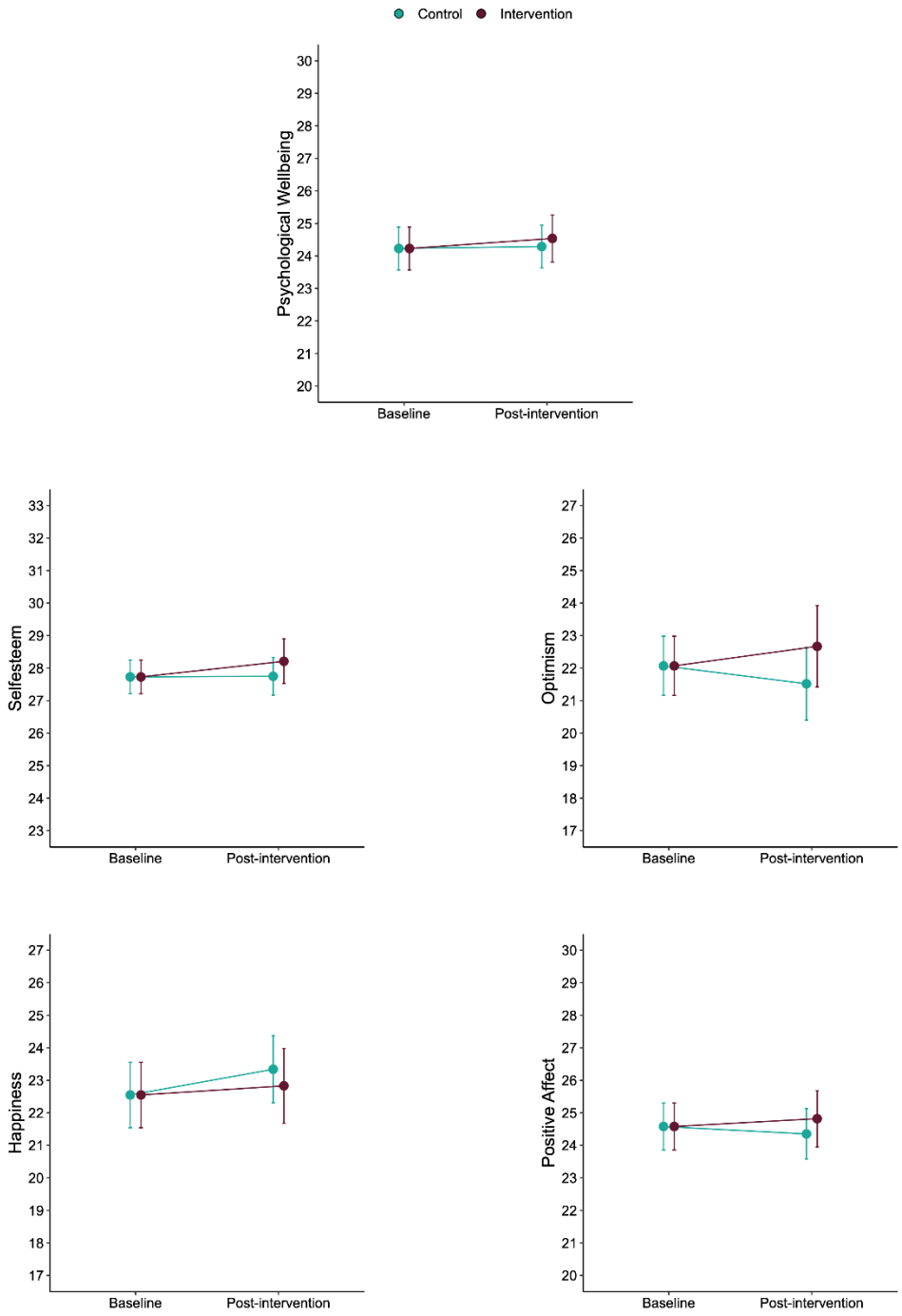


Figure 2. Estimated means at constrained baseline and 36-week post-intervention follow-up in the psychological well-being (Intention-to-treat analyses). Error bars represent 95% confidence intervals. Data were analysed using a constrained baseline longitudinal model.

Self-esteem was measured with the Rosenberg Self-Esteem Scale (RSE) (score range from 10 to 40); Optimism with the Life Orientation Test-Revised (LOT-R) (score range from 6 to 30); Happiness with the Subjective Happiness Scale (SHS) (score range from 3 to 21); Positive and

Negative affect with the Positive and Negative Affect Scale for Children (PANAS-C) (score range from 10 to 30).

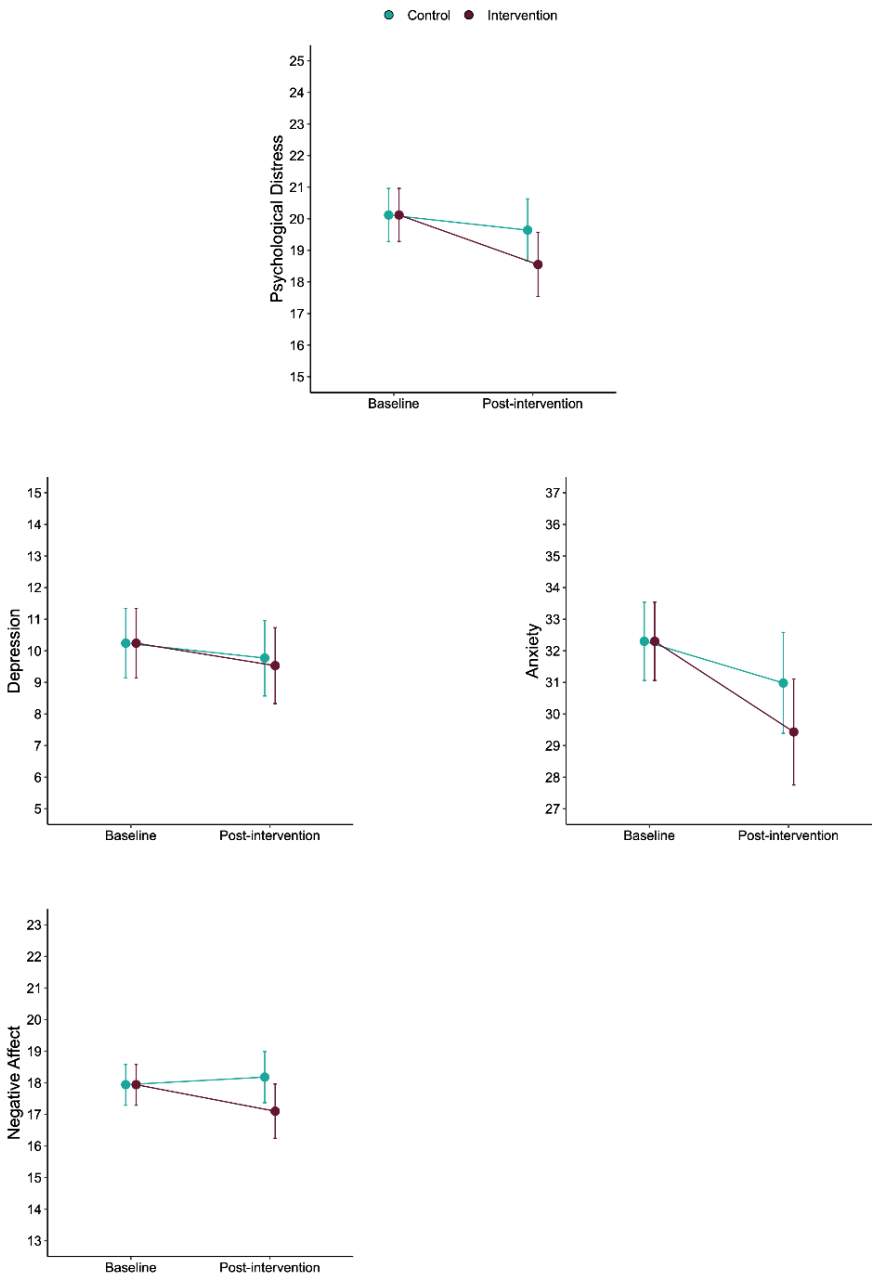


Figure 3. Estimated means at constrained baseline and 36-week post-intervention follow-up in the psychological distress (Intention-to-treat analyses). Error bars represent 95% confidence intervals. Data were analysed using a constrained baseline longitudinal model.

Positive and Negative affect with the Positive and Negative Affect Scale for Children (PANAS-C) (score range from 10 to 30). Depression was measured with the Children Depression Inventory

(CDI) (score range from 0 to 54); Anxiety with the State–Trait Anxiety Inventory for Children (STAIC-R) (score range from 20 to 60).

Change in psychological well-being

For the intention-to-treat analysis, the intervention did not have effect on the psychological well-being indicators (small effect sizes). Participants in the intervention group showed a not statistically significant change in the psychological well-being of 1.20% [mean score 0.29 (-0.40 to 0.99), p=0.576] compared with the control group of 0.29% [mean score 0.07 (-0.58 to 0.72), p=0.967], being a mean score difference between groups of 0.23 (-0.53 to 0.98; p=0.552). No effect was found with self-esteem, with a change of 2.89% in the intervention group [mean score 0.8 (-0.04 to 1.65), p=0.067] compared with a change of 0.14% in the control group [0.04 (-0.74 to 0.83), p=991], showing a mean score difference between groups of 0.76 (-0.10 to 1.62; p=0.083). In optimism, the intervention group showed a not statistically significant change of 2.64% [mean score 0.58 (-0.71 to 1.86), p=0.535] compared with the control group of -2.28% [mean score -0.50 (-1.72 to 0.71), p=0.588], with a mean score difference between groups of 1.08 (-0.34 to 2.50; p=0.134). In happiness, the not statistically significant change in the intervention group was 0.67% [mean score 0.15 (-1.11 to 1.40), p=0.958] compared with the control group of 3.64% [mean score 0.82 (-0.37 to 2.01), p=0.235], with a mean score difference between groups of -0.67 (-2.00 to 0.65; p=0.316). In positive affect, the intervention group showed a not statistically significant change of 0.32% [mean score 0.08 (-0.81 to 0.97; p=0.977)] compared with the control group of -1.18% [mean score -0.29 (-1.12 to 0.54), p=0.689], with a mean score difference between groups of 0.36 (-0.61 to 1.33; p=0.457).

For the per-protocol analysis, the intervention also did not have an effect on any of the psychological well-being indicators (small effect sizes). In psychological well-being, the intervention group showed a not statistically significant change of 1.24% [mean score 0.3 (-0.48 to 1.09), p=0.624] compared

with the control group of 0.25% [mean score 0.06 (-0.63 to 0.74), p=0.979], with a mean score different between groups of 0.25 (-0.56 to 1.05; p=0.541). In self-esteem, the not statistically significant change in the intervention group was 1.77% [mean score 0.49 (-0.41 to 1.39), p=0.405] compared with the control group of 0.07% [mean score 0.02 (-0.77 to 0.81), p=0.998], with a mean score difference between groups of 0.47 (-0.41 to 1.34; p=0.291). In optimism, the intervention group showed a not statistically significant change of 2.72% [mean score 0.60 (-0.81 to 2.02), p=0.568] compared with the control group of -2.49% [mean score -0.55 (-1.80 to 0.70), p=0.548], with a mean score difference between groups of 1.15 (-0.35 to 2.65; p=0.130). In happiness, the intervention group showed a not statistically significant change of 1.24% [mean score 0.28 (-1.14 to 1.70), p=0.888] compared with the control group of 3.50% [mean score 0.79 (-0.47 to 2.06), p=0.301], with a mean score difference between groups of -0.51 (-1.94 to 0.91; p=0.474). In positive affect, the not statistically significant change in the intervention group was 0.98% [mean score 0.24 (-0.69 to 1.17), p=0.816] compared with the control group of -0.94% [mean score -0.23 (-1.03 to 0.58), p=0.782), with a mean score difference between groups of 0.46 (-0.50 to 1.43; p=0.343).

Changes in psychological distress

Participants in the intervention group experienced a statistically significant change in psychological distress of -7.80% [mean score -1.57 (-2.46 to -0.67), p=<0.001] compared with the control group of -2.34% [mean score -0.47 (-2.46 to -0.67), p=0.382], with a mean score difference between groups of -1.09 (-2.11 to -0.08; p=0.035) with a small effect size in all psychological health indicators. In depression, the intervention group showed no statistically significant change of -6.93% [-0.71 (-1.48 to 0.06), p=0.079] compared with the control group of 4.59% [mean score -0.47 (-1.24 to 0.29), p=0.311], with a mean score difference between groups of -0.24 (-1.14 to 0.67; p=0.607). In anxiety, the intervention group showed a statistically significant change of 8.89% [mean score

-2.87 (-4.74 to -1.00), p=0.001] compared with a change of -4.06% of the control group [mean score -1.31 (-3.08 to 0.45), p=0.184], being a mean score difference between groups of -1.55 (-3.60 to 0.49; p=0.135). In negative affect, the intervention group experienced no statistically significant change of –4.63% [mean score -0.83 (-1.78 to 0.12), p=0.099] compared with the control group of 1.39% [mean score 0.25 (-0.64 to 1.13), p=0.789)], showing a mean score difference between groups of -1.08 (-2.11 to -0.04; p=0.041).

For the per-protocol analysis, in psychological distress, the intervention group showed a statistically significant change of -8.33% [mean score -1.68 (-2.66 to -0.70), p< 0.001] compared with the control group of -2.38% [mean score -0.48 (-1.33 to 0.37), p=0.373], with a mean score different between groups of -1.20 (-2.26 to -0.14); p=0.028). In depression, the statistically significant change in the intervention group was -10.47% [mean score -1.05 (-2.08 to -0.01), p=0.048] compared with the control group of -4.49% [mean score -0.45 (-1.31 to 0.41), p=0.434], with a mean score difference between groups of -0.60 (-1.72 to 0.53); p=0.295). In anxiety, the intervention group showed a statistically significant change of -9.58% [mean score -3.11 (-5.18 to -1.04), p=0.002] compared with the control group of -4.25% [mean score -1.38 (-3.18 to 0.42), p=0.166], with a mean score difference between groups of -1.73 (-3.90 to 0.44; p=0.116). In negative affect, the intervention group showed a not statistically significant change of -4.22% [mean score -0.76 (-1.79 to 0.27), p=0.191] compared with the control group of 1.22% [mean score 0.22 (-0.67 to 1.11), p=0.831], with a mean score difference between groups of -0.98 (-2.05 to 0.10); p=0.074).

DISCUSSION

The present study shows the effect of a 36-weeks online plyometric exercise-based program on psychological health in young pediatric cancer survivors. The main findings of this study are as follows: (i) in terms of

psychological well-being, despite the lack of significant results, after 36 weeks of an online plyometric exercise-based program, the intervention group experienced more positive changes than the control group in the score of psychological well-being, self-esteem, optimism and positive affect, while in happiness it was the control group that experienced more positive changes; (ii) regarding psychological distress, the intervention group reduces more the score of psychological distress, depression, anxiety and with no significant result, the negative affect.

Changes between group

In this randomized control trial, we observed no significant results between groups in psychological well-being after a 36-week online exercise program (both in intention-to-treat and per-protocol analysis). However, considering that psychological health was a secondary outcome in the iBoneFIT Project, it is important to underline that the effect size in self-esteem and optimism indicates a positive influence of the intervention on these outcomes. Nonetheless, it is possible that the sample size was not sufficient to find significant results. Concerning psychological distress, the score of psychological distress and negative affect were significant after the intervention.

Only a few studies examine the effect between groups of physical exercise intervention on the psychological health of children and adolescents before and after childhood cancer, with one of these studies focusing on self-esteem[32] and another on depression[12]. In Saultier et al.[32] the intervention was a 6-month exercise program based on combined physical activity (i.e., strength and muscle building, balance and proprioception training, and 15 multi-activity sessions) in 80 children during cancer treatment. The results showed significant improvement in the self-esteem of this population. So, this is in agreement with our trendy result. Although young pediatric cancer survivors were not examined in this study, in healthy children and adolescents, physical activity contributes to

improved health, making them feel healthier and more energetic, which can enhance self-esteem[33]. Additionally, physical activity helps promote a more positive body image, which is especially important during childhood and adolescence [33]. In the study by Dubnov et al.[12], the intervention was a 6-month supervised combined PA program (i.e., aerobic PA, strength, and endurance exercise) for children after cancer treatments. In line with our results, this study showed no significant results in depression. This may be because children still had a normal score for depression, so the potential for improvement is smaller.

Changes within group

For these results, we must consider that due to COVID-19, the levels of physical activity of children and adolescents generally decreased. This could explain that, although no significant result in psychological well-being, we observe that the results in the intervention group were greater than those in the control group, specifically in self-esteem and optimism (both in intention-to-treat and per-protocol). Contrary to our results, a prior study that examines the effect of a 6 month adapt combined physical activity in children with cancer shows significant results on self-esteem [14]. That may be because physical activity during cancer treatments can help those children experience a sense of normalcy and control over their bodies at a crucial time. Regarding psychological distress, our results show significant results in the score of psychological distress, depression, and anxiety in the intervention group while no significant results were found in the control group. It should be noted that psychological health may be affected by various factors, among which may be that some children were still having visits to doctors and were affected by those months of COVID-19 restrictions not having those visits. Additionally, this is a vulnerable population, so more research is needed examining the effect of physical activity on psychological health to understand how it affects this relationship.

Strength and limitations

This study has several strengths. First, it includes 116 participants from a vulnerable population. Since childhood cancer is a rare disease, recruiting such a sample presents a significant challenge. Second, the statistical analysis employed is innovative and beginning to gain traction in recent literature. Concerning the limitations, first, the online plyometric exercise-based program was unsupervised. and adherence was monitored using diaries checked once a month. Second, the sample size may be small for robust conclusions about psychological health. Third, due to the nature of the intervention, participant blinding was not possible. Future studies should consider a face-to-face group intervention, which has greater social interaction.

CONCLUSIONS

The findings of this randomized control trial indicate that a 36-weeks online plyometric exercise-based program appears to improve the score of psychological distress and negative affect, in the between-group analysis for the intention-to-treat, and only psychological distress in the per-protocol analysis. Regarding within-group analysis, significant improvements were observed in the psychological distress score and anxiety in the intention-to-treat analysis, as well as in the score of psychological distress, anxiety and depression in the per-protocol analysis. Although there were no significant results for other psychological health results, changes in the intervention group seemed to be greater than those in the control group, specifically in self-esteem and optimism.

REFERENCES

1. Steliarova-Foucher et al,. International incidence of childhood cancer, 2001–10: a population-based registry study. Lancet Oncol. 2017;18(6):719–31. DOI: 10.1016/S1470-2045(17)30186-9

2. Siegel et al,. Cancer statistics, 2023. CA Cancer J Clin. 2023 Jan 12;73(1):17–48. DOI: 10.3322/caac.21763

3. Brinkman et al,. Psychological symptoms, social outcomes, socioeconomic attainment, and health behaviors among survivors of childhood cancer: Current state of the literature. J Clin Oncol. 2018;36(21):2190–7. DOI: 10.1200/JCO.2017.76.5552

4. Maurice-Stam et al,. Longitudinal assessment of health-related quality of life in preschool children with non-CNS cancer after the end of successful treatment. Pediatr Blood Cancer. 2008 May 3;50(5):1047–51. DOI: 10.1002/pbc.21374

5. Marchak et al,. Recommendations for the surveillance of mental health problems in childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol. 2022;23(4):e184–96. DOI: 10.1016/S1470-2045(21)00750-6

6. Warburton et al,. Health benefits of physical activity. Curr Opin Cardiol. 2017 Sep;32(5):541–56. DOI: 10.1097/HCO.0000000000000437

7. Janssen et al,. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act. 2010;7(1):40.

8. Baumann et al,. Clinical exercise interventions in pediatric oncology: A systematic review. Vol. 74, Pediatric Research. 2013. p. 366–74. DOI: 10.1038/pr.2013.123

9. Ligibel et al,. Exercise, Diet, and Weight Management during Cancer Treatment: ASCO Guideline. J Clin Oncol. 2022;348(22). DOI: 10.1200/JCO.22.00687

10. Thomsen et al,. Harms of exercise training in patients with cancer undergoing systemic treatment: a systematic review and meta-analysis of published and unpublished controlled trials. eClinicalMedicine. 2023;59:101937. DOI: 10.1016/j.eclinm.2023.101937

11. Antwi et al,. Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies. Support Care Cancer. 2019 Sep 16;27(9):3183–94. DOI: 10.1007/s00520-019-04788-z

12. Dubnov-Raz et al,. Changes in fitness are associated with changes in body composition and bone health in children after cancer. Acta Paediatr Int J Paediatr. 2015;104(10):1055–61. DOI: 10.1111/apa.13052

13. van Dijk-Lokkart et al,. Effects of a combined physical and psychosocial intervention program for childhood cancer patients on quality of life and psychosocial functioning: results of the QLIM randomized clinical trial. Psychooncology. 2016 Jul;25(7):815–22. DOI: 10.1002/pon.4016 [doi]

14. Speyer et al,. Effect of adapted physical activity sessions in the hospital on health-related quality of life for children with cancer: A cross-over randomized trial. Pediatr Blood Cancer. 2010 Dec 1;55(6):1160–6. DOI: 10.1002/pbc.22698

15. Saultier et al,. A Randomized Trial of Physical Activity in Children and Adolescents with Cancer. Cancers (Basel). 2021 Jan 2;13(1):121. DOI: 10.3390/cancers13010121

16. Bogg et al,. Feasibility of an inpatient exercise intervention for children undergoing hematopoietic stem cell transplant. Pediatr Transplant. 2015;19(8):925–31. DOI: 10.1111/petr.12614

17. Caru et al,. The impact of cancer on theory of planned behavior measures and physical activity levels during the first weeks following cancer diagnosis in children. Support Care Cancer. 2021 Feb;29(2):823–31. DOI: 10.1007/s00520-020-05541-7 [doi]

18. Caru et al,. Children's physical activity behavior following a supervised physical activity program in pediatric oncology. J Cancer Res Clin Oncol. 2020;146(11):3037–48. DOI: 10.1007/s00432-020-03294-8

19. Gil-Cosano et al,. The effect of an online exercise programme on bone health in paediatric cancer survivors (iBoneFIT): Study protocol of a multi-centre randomized controlled trial. BMC Public Health. 2020;20(1):1–13. DOI: 10.1186/s12889-020-09607-3

20. Resnik et al,. The Singapore Statement on Research Integrity. Account Res. 2011 Mar 9;18(2):71–5.

21. Antaramian et al,. A dual-factor model of mental health: Toward a more comprehensive understanding of youth functioning. Am J Orthopsychiatry. 2010;80(4):462–72. DOI: 10.1111/j.1939-0025.2010.01049.x

22. Mäkinen et al,. Psychological well-being in adolescents with excess weight. Nord J Psychiatry. 2015;69(5):354–63. DOI: 10.3109/08039488.2014.986194

23. Scheier et al,. Distinguishing optimism from neuroticism: A reevaluation of the Life Orientation Test. J Pers Soc Psychol. 1994;67(6):1063–78.

24. Extremera et al,. The Subjective Happiness Scale: Translation and Preliminary Psychometric Evaluation of a Spanish Version. Soc Indic Res. 2014;119(1):473–81. DOI: 10.1007/s11205-013-0497-2

25. Sandín et al,. The PANAS Scales of Positive and Negative Affect: Factor Analytic Validation and Cross-cultural Convergence. Psicothema. 1999;11(1).

26. del Barrio et al,. El Children's Depression Inventory (CDI; Kovacs , 1992). Su aplicación en población española. Clínica y Salud. 1999;10(3):393–416.

27. Rodrigo et al,. Spanish version of the Revised Children's Manifest Anxiety Scale in Uruguay: reliability and concurrent validity. Psychol Rep. 1989;65(1):94.

28. Moore et al,. Enhancing a somatic maturity prediction model. Med Sci Sports Exerc. 2015;47(8):1755–64. DOI: 10.1249/MSS.0000000000000588

29. Migueles et al,. GGIR: A Research Community–Driven Open Source R Package for Generating Physical Activity and Sleep Outcomes From Multi-Day Raw

Accelerometer Data. J Meas Phys Behav. 2019;2(3):188–96. DOI: 10.1123/jmpb.2018-0063

30. Cohen et al,. A power primer. Psychol Bull. 1992;112(1):155–9. DOI: 10.1037/0033-2909.112.1.155

31. Cohen et al,. Statistical Power Analysis for the Behavioral Sciences. Vol. 112, Psychological Bulletin. Routledge; 2013. 155–159 p.

32. Saultier et al,. A Randomized Trial of Physical Activity in Children and Adolescents with Cancer. Cancers (Basel). 2021 Jan 2;13(1):121. DOI: 10.3390/cancers13010121

33. Ekeland et al,. Exercise to improve self-esteem in children and young people. Cochrane Database Syst Rev. 2004;2009(1). DOI: 10.1002/14651858.CD003683.pub2

Supplementary material

9

General discussion

General Discussion

The overall aim of the current International Doctoral Thesis was to study the role of physical activity, physical fitness, and movement behaviours on psychological health in young pediatric cancer survivors. This has been examined through three sections: Section 1: reviewing the literature about physical activity and self-esteem in the oncology population (**Study I**); Section 2: examining the association between physical activity and fitness and psychological health in young pediatric cancer survivors (**Studies II and III**); and Section 3: studying the effect of an exercise program on psychological health in young pediatric cancer survivors (**Study IV**).

It is well-established that physical activity provides health benefits[44]. According to previous research, different types of physical activity may help to reduce fatigue, anxiety, and depression both during and after cancer treatment[50,51]. Additionally, although some studies have shown positive associations between physical activity interventions and self-esteem during and after cancer treatment[65–67], these have not been thoroughly examined, and a systematic review and meta-analysis of all the studies that are currently available was required. Findings from our systematic review and meta-analysis (**Study I**) suggest that the type of physical activity, timing, and duration of the intervention may have a positive and small effect on self-esteem. Specifically, aerobic physical activity and mind-body exercise show positive effects on self-esteem with small and medium effects, respectively. In contrast, no evidence that combined physical activity or resistance training has such effects, maybe because of the lack of studies. These results are in line with our randomized control trial (**Study IV**) in the between-group results since self-esteem appeared to be unaffected by a 36-week online plyometric exercise-based program focused on weight-bearing impact exercise (classified as resistance training) among young pediatric cancer survivors. A study in adolescent males examining the effects of the frequency and

type of physical activity (i.e., endurance and strength) on self-esteem showed that the frequency of exercise, rather than the type, had a significant impact on self-esteem levels[68].

Study IV showed a significant effect of the intervention between groups on psychological distress score and negative affect. We also identified within group effects for the exercise group on the psychological distress score and anxiety, but no effects were found on psychological well-being. A systematic review and meta-analysis on the role of physical activity in the psychological health of children and adolescents partially agrees with our results showing significant associations between physical activity and lower levels of psychological distress, depression, and negative affect, and greater levels of happiness and psychological well-being[69]. For our results, it should be noted that this intervention took place during the COVID-19 pandemic, which imposed restrictions on mobility and outdoor activities. This may have impacted the psychological health of participants, as children and adolescents, though less studied compared to adults are in a critical developmental period for their psychological health[70]. Furthermore, given that our 36-week online plyometric exercise-based program was a video-recorded program primarily aimed at improving bone health, the impact on these psychological variables (which are secondary) may be more pronounced within groups than between groups.

Concerning the intensity of the interventions, our cross-sectional **Study II** estimates how reallocating time to each movement behaviour affects indicators of psychological health. Our results highlight the importance of increasing MVPA and LPA from the rest of movement behaviour to improve happiness and depression in pre-pubertal cancer survivors. Additionally, increasing MVPA from the remaining movement behaviours may improve happiness, optimism, depression, and anxiety in peri/post-pubertal cancer survivors. A prior study shows that, despite some non-compositional data analysis indicating an

association between movement behaviour and psychological health, the results from their compositional data analysis did not find any association[71].

In relation to physical fitness and psychological health, most studies have focused on objective measurements. However, few studies examine this relationship using self-perceived physical fitness, which may be easily measured with a questionnaire. Our cross-sectional **Study III** investigated the associations between objective and perceived physical fitness and psychological health in young pediatric cancer survivors. Our results underscore the importance of measuring not only objective measurements of physical fitness but also perceived physical fitness, due to the significant associations of this relationship. A previous study examining the link between self-perceived physical activity, fitness and psychosomatic health symptoms in adolescents with unhealthy lifestyles found that those who were perceived as more physically fit reported fewer psychosomatic symptoms. The authors described these symptoms as physical manifestations resulting from psychological factors such as anxiety and psychological distress[72].

Possible mechanisms linking physical activity and fitness to psychological health

Physical activity can enhance psychological well-being through psychosocial mechanisms like social interaction, improved appearance, and enhanced mood. In particular, it can bolster self-efficacy, which refers to an individual's self-confidence in performing specific activities[73]. This improvement initially impacts self-concept and subsequently boosts overall self-esteem[73]. Additionally, regularly engaging in physical activity and leading a healthy lifestyle can effectively redirect attention away from negative thoughts and rumination, leading to increased self-esteem[74]. As a result, having higher self-esteem is associated with a decreased occurrence of depressive behaviours[74]. In

this regard, a study exploring the benefits of aerobic physical activity in individuals with inflammatory disorders found that this kind of intervention was successful in lowering depression symptoms[75]. Regarding the beneficial impact of activities like yoga on mental health, it can be attributed to the cultivation of self-regulation and coping skills[73].

In relation to physical fitness, an increase in physical fitness, specifically through aerobic physical activity and resistance exercise, often leads to an improved body image, as it is typically associated with an increase in lean mass and a decrease in fat mass[20]. Additionally, this increase in physical fitness may influence the neurochemicals in the brain, such as serotonin and endorphins, which are known to elevate mood and improve psychological health[20].

Concerning physiological mechanisms, growing evidence supports the immune-nervous system connection with the psychological health. The immune system plays a key role in the development of mental disorders such as anxiety, mood changes, and depression[74]. Physical activity may reduce inflammation, which is explained by four mechanisms: modifications in cytokine release, reduction of visceral fat mass, down-regulation of toll-like receptors, and increased vagal tone[74]. Some studies have found that vagal nerve function can be improved through exercise interventions and mind-body practices, including techniques focused on breathing control and meditation[76]. This improvement may be attributed to a decrease in respiratory rate and a smaller inhalation/exhalation ratio, both of which directly stimulate the vagus nerve. Consequently, these changes lead to a reduction in heart rate, blood pressure, and other factors, activating an anti-inflammatory pathway and ultimately decreasing acute stress levels[76]. There is limited evidence supporting the role of exercise in anxiety and other stress-related conditions. Moreover, only a minority of studies provide conclusive results regarding the quality of aerobic physical

activity or resistance training. Mind-body exercise, and to a lesser extent, mindfulness practices, have shown some positive outcomes in this regard [76].

10

Conclusions

General conclusion

The overall conclusion of this International Doctoral Thesis underscores the importance of promoting exercise, physical activity, and fitness as an approach to enhancing psychological well-being and decreasing psychological distress. It also emphasizes the need to encourage self-perceived fitness among the pediatric oncology population.

Specific conclusions

	GAP	Conclusion
Section 1	Most systematic reviews and meta-analyses on the effect of physical activity interventions on psychological health in young pediatric cancer survivors focus on psychological distress (i.e., anxiety and depression). However, there is a lack of systematic review and meta-analysis on self-esteem in this population. In addition, there are very few studies examining the effect of physical activity on self-esteem in young pediatric cancer survivors.	Physical activity, specifically aerobic and mind-body, may positively impact self-esteem during and after cancer treatment. Additionally, cancer status and the length of the intervention play a significant role in determining this relationship (**Study I**).

Section 2	Most studies have focused on the association between objectively measured physical fitness and psychological health. However, little research has been conducted on the association between self-perceived physical fitness and psychological health. Nonetheless, there are increasingly more studies that use compositional data analysis to estimate the association between the reallocation of 24-hour movement behaviours (MVPA, LPA, sedentary behaviour, and sleep time) and other health parameters in various populations. However, there is a lack of this type of analysis in young pediatric cancer survivors to understand how reallocating one type of movement behaviour from the others influences psychological health.	Our results emphasize the importance of promoting LPA and MVPA in pre-pubertal cancer survivors, as well as MVPA in peri/post-pubertal cancer survivors, to enhance their psychological health (**Study II**). Perceived physical fitness, rather than objectively measured physical fitness, appears to be inversely related to psychological distress and, to a lesser extent, positively related to psychological well-being. These findings underscore the importance of promoting self-perceived fitness within the pediatric oncology population (**Study III**).
Section 3	The effect of physical activity interventions on psychological health in children and adolescents during and after cancer treatment is not clear due to the different psychological health indicators used by the studies.	Our results suggest that a 36-week online plyometric exercise-based program appears to improve psychological distress and negative affect scores in the between-group analysis for the intention-to-treat population. In the within-group analysis, significant improvements were found in psychological distress and anxiety scores. Although no significant results were found for other psychological health outcomes, changes in the intervention group appeared greater than those in the control group, especially in self-esteem and optimism (**Study IV**).

Table 3. Specific conclusions of the present International Doctoral Thesis

Overall limitations

The main findings of this International Doctoral Thesis should be considered with caution due to some limitations:

· This Thesis includes two cross-sectional studies, which limits our ability to establish causality for any of the associations. Additionally, although potential confounders were controlled for, other variables may still influence these associations

· The participants included in the project of this Thesis were young pediatric cancer survivors who chose to enrol in the exercise intervention, which may mean they are not representative of the entire young pediatric population. This selection bias could make our findings particularly vulnerable. Nevertheless, the distribution of cancer types in the study is similar to the total incidence in Spain according to the Spanish Registry of Children with Tumors.

· Only the depression questionnaire was completed with the investigator in the laboratory. The remaining questionnaires were answered at home, and often required parental support, especially for the younger participants.

· Due to the aim objective of the project to which this Thesis belongs is bone health, both the intervention and the tests are designed for this variable and not for the main variable of this Thesis which is psychological health.

· Due to COVID-19 restrictions, certain measurements, such as cardiorespiratory capacity and the speed/agility test, were not conducted due to the imprecise data that would have been obtained wearing face masks.

Overall strengths

This International Doctoral Thesis also has several strengths that should be highlighted:

· This Thesis contributes to the scientific literature by providing a meta-analysis of the effects of various types of physical activity interventions on self-esteem during and after cancer treatment.

· The use of objective and valid methods to assess physical activity, sedentary behaviour, and sleep time.

· The measures of physical fitness both objectively and perceived which offer a comprehensive understanding of how physical fitness impacts psychological health

·The inclusion of young pediatric cancer survivors, a vulnerable population whose psychological health may be affected by cancer treatments

· Given that childhood cancer is a rare disease, recruiting leads to significant challenges.

Future perspective

·Future research should focus on specific physical activity interventions designed to improve the psychological health of young pediatric cancer survivors, as such interventions are crucial for drawing further conclusions.

· Future studies in young pediatric cancer survivors would benefit of the inclusion of a healthy control group to compare their data on psychological health outcomes and test the effects of an exercise-based intervention.

· Future research should investigate the effect of an online exercise intervention on psychological health in young pediatric cancer survivors, with a follow-up to examine how these effects persist over time.

· To obtain more objective results on the psychological health of this population, future research might add further measurements such as the use of magnetic resonance imaging (MRI), to assess potential alterations in brain regions that may be associated with psychological health indicators, such as depression.

· To better understand the most effective timing of exercise interventions, future research should implement population-based exercise programs during cancer treatment. This approach will help identify which phases of treatment are most likely to benefit from such interventions.

11

References

References (introduction, methods, and discussion)

1. National Cancer Institute. What Is Cancer?
2. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12-49. doi:10.3322/caac.21820
3. Antaramian SP, Scott Huebner E, Hills KJ, Valois RF. A dual-factor model of mental health: Toward a more comprehensive understanding of youth functioning. *Am J Orthopsychiatry*. 2010;80(4):462-472. doi:10.1111/j.1939-0025.2010.01049.x
4. Kubzansky LD, Huffman JC, Boehm JK, et al. Positive Psychological Well-Being and Cardiovascular Disease. *J Am Coll Cardiol*. 2018;72(12):1382-1396. doi:10.1016/j.jacc.2018.07.042
5. Rodriguez-Ayllon M, Cadenas-Sanchez C, Esteban-Cornejo I, et al. Physical fitness and psychological health in overweight/obese children: A cross-sectional study from the ActiveBrains project. *J Sci Med Sport*. 2018;21(2):179-184. doi:10.1016/j.jsams.2017.09.019
6. Mäkinen M, Lindberg N, Komulainen E, Puukko-Viertomies LR, Aalberg V, Marttunen M. Psychological well-being in adolescents with excess weight. *Nord J Psychiatry*. 2015;69(5):354-363. doi:10.3109/08039488.2014.986194
7. Scheier MF, Charles S, Bridges MW. Distinguishing optimism from neuroticism: A reevaluation of the Life Orientation Test. *J Pers Soc Psychol*. 1994;67(6):1063-1078. https://doi.org/10.1037//0022-3514.67.6.1063
8. Extremera N, Fernández-Berrocal P. The Subjective Happiness Scale: Translation and Preliminary Psychometric Evaluation of a Spanish Version. *Soc Indic Res*. 2014;119(1):473-481. doi:10.1007/s11205-013-0497-2
9. Sandín B, Chorot P, Lostao L, Joiner TE, Santed MA, Valiente RM. The PANAS Scales of Positive and Negative Affect: Factor Analytic Validation and Cross-cultural Convergence. *Psicothema*. 1999;11(1).
10. del Barrio MV, Moreno C, López R. El Children's Depression Inventory (CDI; Kovacs , 1992). Su aplicación en población española. *Clínica y Salud*. 1999;10(3):393-416.
11. Rodrigo G, Lusiardo M. Spanish version of the Revised Children's Manifest Anxiety Scale in Uruguay: reliability and concurrent validity. *Psychol Rep*. 1989;65(1):94. doi:10.2466/pr0.1989.65.1.94
12. Silvestri PR, Baglioni V, Cardona F, Cavanna AE. Self-concept and self-esteem in patients with chronic tic disorders: A systematic literature

review. *Eur J Paediatr Neurol*. 2018;22(5):749-756. doi:10.1016/j.ejpn.2018.05.008

13. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep*. 1985;100(2):126-131. doi:10.1093/nq/s9-IX.228.365-f

14. HOWLEY ET. Type of activity: resistance, aerobic and leisure versus occupational physical activity. *Med Sci Sports Exerc*. 2001;33(Supplement):S364-S369. doi:10.1097/00005768-200106001-00005

15. Bo A, Mao W, Lindsey MA. Effects of mind–body interventions on depressive symptoms among older Chinese adults: a systematic review and meta-analysis. *Int J Geriatr Psychiatry*. 2017;32(5):509-521. doi:10.1002/gps.4688

16. Clarke AE, Janssen I. A compositional analysis of time spent in sleep, sedentary behaviour and physical activity with all-cause mortality risk. *Int J Behav Nutr Phys Act*. 2021;18(1):1-12. doi:10.1186/s12966-021-01092-0

17. Delfino LD. Reflections on the concept of sedentary behavior during the COVID-19 pandemic. *Universa Med*. 2022;41(2):101-103. doi:10.18051/univmed.2022.v41.101-103

18. Young DR, Hivert MF, Alhassan S, et al. Sedentary behavior and cardiovascular morbidity and mortality: A science advisory from the American Heart Association. *Circulation*. 2016;134(13):e262-e279. doi:10.1161/CIR.0000000000000440

19. Colley RC, Michaud I, Garriguet D. Reallocating time between sleep, sedentary and active behaviours: Associations with obesity and health in Canadian adults. *Heal Reports*. 2018;29(4):1-13.

20. Ortega FB, Ruiz JR, Castillo MJ, Sjöström M. Physical fitness in childhood and adolescence: a powerful marker of health. *Int J Obes (Lond)*. 2008;32(1):1-11. doi:0803774 [pii]

21. Evans CH, White RD. *Exercise Stress Testing for Primary Care and Sports Medicine*. (Evans CH, White RD, eds.). Springer New York; 2009. doi:10.1007/978-0-387-76597-6

22. Nieman DC. The exercise test as a component of the total fitness evaluation. *Prim Care - Clin Off Pract*. 2001;28(1):119-135. doi:10.1016/S0095-4543(05)70010-5

23. Moore SA, McKay HA, Macdonald H, et al. Enhancing a somatic maturity prediction model. *Med Sci Sports Exerc*. 2015;47(8):1755-1764. doi:10.1249/MSS.0000000000000588

24. Keller K. National Center for Health Statistics. *Encycl Obes*. Published online 2017:23-24. doi:10.4135/9781412963862.n310

25. Huang J, Chan SC, Ngai CH, et al. Global incidence, mortality and temporal trends of cancer in children: A joinpoint regression analysis. *Cancer Med*. 2023;12(2):1903-1911. doi:10.1002/cam4.5009

26. Globocan 2020. Cancer Tomorrow. International Agency for Research on Cancer. WHO. Published 2020. https://gco.iarc.fr/tomorrow/en/dataviz/isotype?years=2040&age_end=3&single_unit=10000

27. *Las Cifras Del Cáncer En España 2024*.; 2024.

28. Red Española de Registros de Cáncer (REDECAN). Estimaciones De La Incidencia. Published online 2024.

29. National Cancer Institute. Childhood Cancers. 2024. https://www.cancer.gov/types/childhood-cancers

30. Erdmann F, Frederiksen LE, Bonaventure A, et al. Childhood cancer: Survival, treatment modalities, late effects and improvements over time. *Cancer Epidemiol*. 2021;71. doi:10.1016/j.canep.2020.101733

31. Henderson TO, Nathan PC. Childhood cancer survivors: Considerations for surgeons in the transition from pediatric to adult care. *Semin Pediatr Surg*. 2015;24(2):93-99. doi:10.1053/j.sempedsurg.2015.01.007

32. Antwi GO, Jayawardene W, Lohrmann DK, Mueller EL. Physical activity and fitness among pediatric cancer survivors: a meta-analysis of observational studies. *Support Care Cancer*. 2019;27(9):3183-3194. doi:10.1007/s00520-019-04788-z

33. Darlington ASE, Wakefield CE, van Erp LME, van der Graaf WTA, Cohn RJ, Grootenhuis MA. Psychosocial consequences of surviving cancer diagnosed and treated in childhood versus in adolescence/young adulthood: A call for clearer delineation between groups. *Cancer*. 2022;128(14):2690-2694. doi:10.1002/cncr.34257

34. Moore BD. Neurocognitive outcomes in survivors of childhood cancer. *J Pediatr Psychol*. 2005;30(1):51-63. doi:10.1093/jpepsy/jsi016

35. Mertens AC, Gilleland Marchak J. Mental health status of adolescent cancer survivors. *Clin Oncol Adolesc Young Adults*. Published online September 2015:87. doi:10.2147/COAYA.S49174

36. Wakefield CE, McLoone J, Goodenough B, Lenthen K, Cairns DR, Cohn RJ. The psychosocial impact of completing childhood cancer treatment: A systematic review of the literature. *J Pediatr Psychol*. 2010;35(3):262-274.

doi:10.1093/jpepsy/jsp056

37. Friend AJ, Feltbower RG, Hughes EJ, Dye KP, Glaser AW. Mental health of long-term survivors of childhood and young adult cancer: A systematic review. *Int J Cancer*. 2018;143(6):1279-1286. doi:10.1002/ijc.31337

38. Michel G, Rebholz CE, Von Der Weid NX, Bergstraesser E, Kuehni CE. Psychological distress in adult survivors of childhood cancer: The Swiss childhood cancer survivor study. *J Clin Oncol*. 2010;28(10):1740-1748. doi:10.1200/JCO.2009.23.4534

39. Brinkman TM, Recklitis CJ, Michel G, Grootenhuis MA, Klosky JL. Psychological symptoms, social outcomes, socioeconomic attainment, and health behaviors among survivors of childhood cancer: Current state of the literature. *J Clin Oncol*. 2018;36(21):2190-2197. doi:10.1200/JCO.2017.76.5552

40. Zeltzer LK, Recklitis C, Buchbinder D, et al. Psychological status in childhood cancer survivors: A report from the childhood cancer survivor study. *J Clin Oncol*. 2009;27(14):2396-2404. doi:10.1200/JCO.2008.21.1433

41. Wang YH, Li JQ, Shi JF, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Mol Psychiatry*. 2020;25(7):1487-1499. doi:10.1038/s41380-019-0595-x

42. Marchak JG, Christen S, Mulder RL, et al. Recommendations for the surveillance of mental health problems in childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. *Lancet Oncol*. 2022;23(4):e184-e196. doi:10.1016/S1470-2045(21)00750-6

43. Maurice-Stam H, Oort FJ, Last BF, Brons PPT, Caron HN, Grootenhuis MA. Longitudinal assessment of health-related quality of life in preschool children with non-CNS cancer after the end of successful treatment. *Pediatr Blood Cancer*. 2008;50(5):1047-1051. doi:10.1002/pbc.21374

44. Warburton DER, Bredin SSD. Health benefits of physical activity. *Curr Opin Cardiol*. 2017;32(5):541-556. doi:10.1097/HCO.0000000000000437

45. Janssen I, LeBlanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. *Int J Behav Nutr Phys Act*. 2010;7(1):40. doi:10.1186/1479-5868-7-40

46. Singh B, Olds T, Curtis R, et al. Effectiveness of physical activity interventions for improving depression, anxiety and distress: An overview of systematic reviews. *Br J Sports Med*. Published online 2023:1-10. doi:10.1136/bjsports-2022-106195

47. Maddocks M. Physical activity and exercise training in cancer patients. *Clin Nutr ESPEN*. 2020;40:1-6. doi:10.1016/j.clnesp.2020.09.027

48. Ligibel JA, Bohlke K, May AM, et al. Exercise, Diet, and Weight Management during Cancer Treatment: ASCO Guideline. *J Clin Oncol*. 2022;348(22). doi:10.1200/JCO.22.00687

49. Thomsen SN, Lahart IM, Thomsen LM, et al. Harms of exercise training in patients with cancer undergoing systemic treatment: a systematic review and meta-analysis of published and unpublished controlled trials. *eClinicalMedicine*. 2023;59:101937. doi:10.1016/j.eclinm.2023.101937

50. Fong DYT, Ho JWC, Hui BPH, et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. *BMJ*. 2012;344(jan30 5):e70-e70. doi:10.1136/bmj.e70

51. Li J, Li C, Puts M, et al. Effectiveness of mindfulness-based interventions on anxiety, depression, and fatigue in people with lung cancer: A systematic review and meta-analysis. *Int J Nurs Stud*. 2023;140:104447. doi:10.1016/j.ijnurstu.2023.104447

52. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors. *Med Sci Sport Exerc*. 2010;42(7):1409-1426. doi:10.1249/MSS.0b013e3181e0c112

53. Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. *CA Cancer J Clin*. 2022;72(3):230-262. doi:10.3322/caac.21719

54. Friedenreich CM, Ryder-Burbidge C, McNeil J. Physical activity, obesity and sedentary behavior in cancer etiology: epidemiologic evidence and biologic mechanisms. *Mol Oncol*. 2021;15(3):790-800. doi:10.1002/1878-0261.12772

55. Baumann FT, Bloch W, Beulertz J. Clinical exercise interventions in pediatric oncology: A systematic review. *Pediatr Res*. 2013;74(4):366-374. doi:10.1038/pr.2013.123

56. Hoare E, Milton K, Foster C, Allender S. The associations between sedentary behaviour and mental health among adolescents: a systematic review. *Int J Behav Nutr Phys Act*. 2016;13(1):108. doi:10.1186/s12966-016-0432-4

57. Faria FR de, Barbosa D, Howe CA, Canabrava KLR, Sasaki JE, Amorim PR dos S. Time-use movement behaviors are associated with scores of depression/anxiety among adolescents: A compositional data analysis. *PLoS One*. 2022;17(12 December):1-12. doi:10.1371/journal.pone.0279401

58. Ruggero CJ, Petrie T, Sheinbein S, Greenleaf C, Martin S. Cardiorespiratory fitness may help in protecting against depression among middle school adolescents. *J Adolesc Heal*. 2015;57(1):60-65. doi:10.1016/j.jadohealth.2015.03.016

59. Chen HM, Tsai CM, Wu YC, Lin KC, Lin CC. Randomised controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *Br J Cancer*. 2015;112(3):438-445. doi:10.1038/bjc.2014.612

60. Smith JJ, Eather N, Morgan PJ, Plotnikoff RC, Faigenbaum AD, Lubans DR. The health benefits of muscular fitness for children and adolescents: A systematic review and meta-analysis. *Sport Med*. 2014;44(9):1209-1223. doi:10.1007/s40279-014-0196-4

61. Gil-Cosano JJ, Ubago-Guisado E, Sánchez MJ, et al. The effect of an online exercise programme on bone health in paediatric cancer survivors (iBoneFIT): Study protocol of a multi-centre randomized controlled trial. *BMC Public Health*. 2020;20(1):1-13. doi:10.1186/s12889-020-09607-3

62. Tishya A. L. Wren, Ph.D.1, Heidi J. Kalkwarf, Ph.D.2, Babette S. Zemel, Ph.D.3 JM, Lappe, Ph.D.4, Sharon Oberfield, M.D.5, John A. Shepherd, Ph.D.6, Karen K. Winer MD., and Vicente Gilsanz, M.D. PD. on behalf of the BMD in CS, Group*. Longitudinal Tracking of DXA Bone Measures Over 6 Years in Children and Adolescents: Persistence of Low Bone Mass to Maturity. 2015;164(6):1280-1285. doi:10.1016/j.jpeds.2013.12.040

63. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *Br J Sports Med*. 2016;50(23):1428-1437. doi:10.1136/bjsports-2016-096651

64. Fikenzer S, Uhe T, Lavall D, et al. Effects of surgical and FFP2/N95 face masks on cardiopulmonary exercise capacity. *Clin Res Cardiol*. 2020;109(12):1522-1530. doi:10.1007/s00392-020-01704-y

65. Saultier P, Vallet C, Sotteau F, et al. A Randomized Trial of Physical Activity in Children and Adolescents with Cancer. *Cancers (Basel)*. 2021;13(1):121. doi:10.3390/cancers13010121

66. Kovačič T, Kovačič M. Impact of Relaxation Training According to Yoga in Daily Life ® System on Self-Esteem After Breast Cancer Surgery. *J Altern Complement Med*. 2011;17(12):1157-1164. doi:10.1089/acm.2010.0653

67. Leite B, de Bem Fretta T, Boing L, Coutinho de Azevedo Guimarães A. Can belly dance and mat Pilates be effective for range of motion, self-esteem, and depressive symptoms of breast cancer women? *Complement*

Ther Clin Pract. 2021;45:101483. doi:10.1016/j.ctcp.2021.101483

68. Romero I, Kaye A, Poulin C, Peterson ME. An Analysis of the Effects of Frequency and Type of Physical Activity on Self-Esteem in Adolescent Males. *Georg Sci Res J*. 2022;2(2):42-52. doi:10.48091/gsr.v2i2.42

69. Rodriguez-Ayllon M, Cadenas-Sánchez C, Estévez-López F, et al. Role of Physical Activity and Sedentary Behavior in the Mental Health of Preschoolers, Children and Adolescents: A Systematic Review and Meta-Analysis. *Sport Med*. 2019;49(9):1383-1410. doi:10.1007/s40279-019-01099-5

70. Marques de Miranda D, da Silva Athanasio B, Sena Oliveira AC, Simoes-e-Silva AC. How is COVID-19 pandemic impacting mental health of children and adolescents? *Int J Disaster Risk Reduct*. 2020;51(August):101845. doi:10.1016/j.ijdrr.2020.101845

71. Fairclough SJ, Tyler R, Dainty JR, et al. Cross-sectional associations between 24-hour activity behaviours and mental health indicators in children and adolescents: A compositional data analysis. *J Sports Sci*. 2021;39(14):1602-1614. doi:10.1080/02640414.2021.1890351

72. Baceviciene M, Jankauskiene R, Emeljanovas A. Self-perception of physical activity and fitness is related to lower psychosomatic health symptoms in adolescents with unhealthy lifestyles. *BMC Public Health*. 2019;19(1):1-11. doi:10.1186/s12889-019-7311-2

73. Lubans D, Richards J, Hillman C, et al. Physical Activity for Cognitive and Mental Health in Youth: A Systematic Review of Mechanisms. *Pediatrics*. 2016;138(3). doi:10.1542/peds.2016-1642

74. Mikkelsen K, Stojanovska L, Polenakovic M, Bosevski M, Apostolopoulos V. Exercise and mental health. *Maturitas*. 2017;106:48-56. doi:10.1016/j.maturitas.2017.09.003

75. Abd El-Kader SM, Al-Jiffri OH. Aerobic exercise improves quality of life, psychological well-being and systemic inflammation in subjects with alzheimer's disease. *Afr Health Sci*. 2016;16(4):1045-1055. doi:10.4314/ahs.v16i4.22

76. Gerritsen RJS, Band GPH. Breath of Life: The Respiratory Vagal Stimulation Model of Contemplative Activity. *Front Hum Neurosci*. 2018;12(February):1-25. doi:10.3389/fnhum.2018.00397

12

Curriculum vitae

Andrea Rodríguez Solana

SHORT CURRICULUM VITAE

Collaborating researcher in the PROFITH research group at the University of Granada (2019 - Present)

ABOUT ME

Date of birth	10-03-1997
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LANGUAGES

Spanish (native)
English (B2 level)

KEY WORDS

Psychological health
Cancer
Exercise
Physical activity
Children and adolescents

SKILLS

· Training and experience in peripheral quantitative computed tomography (pQCT)
· Course in X-ray Facilities for Medical Diagnosis
· Management of Scientific Databases

EDUCATION

2015-2019

Bachelor degree in Primary Education. Faculty of Education, University of Jaen, Spain

2019-2020

Master degree in Research on physical activity and sport. Faculty of Sport Sciences, University of Granada, Spain

2021-Present

PhD Program in Biomedicine at the University of Granada, Spain

CONTRACTS

2021-2024

Contract under the research project "Regulando el metabolismo óseo a través del ejercicio en supervivientes de cáncer pediátrico" Ref. PID2020-117302RA-I00. Ministry of Science and Innovation, Spain

RESEARCH STAYS

2024

Research Centre in Physical Activity, Health and Leisure (CIAFEL), Faculty of Sport Sciences (FADEUP)

· City and country: University of Porto, Portugal

· Duration: 3 months (1 January - 1 April)

· Funding: Programa: 10. Programa de Ayudas para Realizar "Estancias Breves en Centros de Investigación Nacionales y Extranjeros", University of Granada

PUBLICATIONS

Rodriguez-Solana A, Gracia-Marco L, Llorente-Cantarero FJ, Cadenas-Sanchez C, Marmol-Perez A, Gil-Cosano JJ, Moliner-Urdiales D, Ubago-Guisado E. Is higher physical fitness associated with better psychological health in young pediatric cancer survivors? A cross-sectional study from the iBoneFIT project. Scand J Med Sci Sports. 2023 Jul;33(7):1157-1167. doi: 10.1111/sms.14345. Epub 2023 Mar 7. PMID: 36843418. (IF: 4,645, Q1)

Marmol-Perez, A., Ubago-Guisado, E., Llorente-Cantarero, F.J., Vlachopoulos, D., **Rodriguez-Solana A**., et al. Determinants of bone parameters in young paediatric cancer survivors: the iBoneFIT project. Pediatr Res (2023). https://doi.org/10.1038/s41390-023-02645-8
(IF: 3.953, Q1)

Marmol-Perez A, Ubago-Guisado E, **Rodriguez-Solana A**, Gil-Cosano JJ, Martinez-Vizcaino V, Cavero-Redondo I, Ruiz JR, Gracia-Marco L. Effect of exercise on bone health in children and adolescents with cancer during and after oncological treatment: A systematic review and meta-analysis. Front Physiol. 2023 Mar 14;14:1088740. doi: 10.3389/fphys.2023.1088740. PMID: 37035662; PMCID: PMC10081564.
(IF: 4.755, Q1)

Marmol-Perez A, Migueles JH, Ubago-Guisado E, Gil-Cosano JJ, **Rodriguez-Solana A**, Redondo-Tébar A, Llorente-Cantarero FJ, Labayen I, Ortega FB, Ruiz JR, Gracia-Marco L. Every Move Counts to Improve Bone Health at Clinical Sites in Young Pediatric Cancer Survivors: The iBoneFIT Project. Med Sci Sports Exerc. 2024 Jun 1;56(6):1085-1093. doi: 10.1249/MSS.0000000000003397. Epub 2024 Jan 30. PMID: 38306313. (IF: 5.411, Q1)

BOOK CHAPTER

Gil-Cosano JJ, Gracia-Marco L, Rodriguez-Solana A, Pascual-Gázquez Juan F, Marmol-Perez A, Llorente-Cantarero FJ, Ubago-Guisado E. Estrategias de adherencia al ejercicio físico en la enfermedad oncológica infantil. En: Ejercicio físico y cáncer infantil. ¿Qué dice la ciencia?. Dykinson, Madrid. 2023. ICEE: 0,954. Category and Position: Education, Position 16 out of 94

PARTICIPATION IN RESEARCH PROJECTS

(100010434) "iBoneFIT: Improving bone health in paediatric cancer survivors" La Caixa Foundation. Dr. Luis Gracia Marco, 01/05/2019-30/04/2022

(PID2020-117302RA-I00), "Regulando el metabolismo óseo a través del ejercicio en supervivientes de cáncer pediátrico" Ministerio de Ciencia e Innovación. Dr. Luis Gracia Marco, 1/9/2021 - 31/08/2024

(PPJIB2023-073), "Machine learning Approaches for Joint Analysis on Randomized clinical trials data In young pediatric cancer survivors (MAJARI)". Ayudas del Plan Propio UGR 2023. Andrea Rodríguez Solana, 1/01/2024 – 31/12/2024

CONGRESS COMUNICATIONS AS FIRST AUTHOR

Rodríguez Solana A, Gil-Cosano JJ, Ubago Guisado E, Llorente Cantarero FJ, Pascual Gázquez JF, Ortega Acosta MJ, Gracia-Marco L. Asociación entre la condición física percibida y la salud mental en niños y adolescentes supervivientes de cáncer. Symposium EXERNET Red Española de Investigación en Ejercicio físico y Salud. Cuenca, October 22-23, 2021. Poster presentation

Rodríguez-Solana A, Ubago-Guisado E, J.J. Gil-Cosano, A. Marmol-Perez y L. Gracia-Marco L. Asociación entre la condición física y la depresión en niños y adolescentes supervivientes de cáncer. International Multidisciplinary Congress of Innovation and Research in Healthy Habits. Ceuta, May 12-14, 2022. Oral presentation.

Rodriguez-Solana A, Ubago Guisado E, Gil-Cosano JJ y Gracia-Marco L. Asociación entre la condición física, la autoestima y la ansiedad en niños/as y adolescentes supervivientes de cáncer. Congreso de Actividad Física en Edad Escolar. Cuenca, May 19-21, 2022. Oral presentation

Rodríguez-Solana A, Ubago-Guisado E, Redondo-Tebar A, Herrada-Robles M, Pascual-Gázquez JF, Gracia-Marco L. Actividad física, sedentarismo y sueño y salud psicológica en población infantil y adolescente superviviente de cáncer pediátrico. 69 Congreso Asociación Española de Pediatría. Granada, June 1-3, 2023. Oral presentation

Rodríguez-Solana, A., Ubago-Guisado, E., Redondo-Tébar, A., Cadenas-Sanchez, C., Marmol-Perez, A., Gil-Cosano, J. J., Llorente Cantarero, F. J., & Gracia-Marco, L. Efecto de la actividad física sobre la autoestima en población oncológica: una revisión sistemática y metaanálisis. Symposium EXERNET Red Española de Investigación en Ejercicio físico y Salud. Almería, October 20-21, 2023. Poster presentation

Rodríguez-Solana, A., Gracia-Marco, L., Migueles, J. H., Marmol-Perez, A., Cadenas-Sanchez, C., Gil-Cosano, J. J., Llorente-Cantarero, F. J., Delgado-Ferro, F., & Ubago-Guisado, E. Physical activity, sedentarism and sleep time and psychological health in young paediatric cancer survivors. A compositional data analysis from the iBoneFIT Project. International Congress "Exercise, Biomechanics and Nutrition". Setúbal, Portugal, June 4-5, 2024. Oral presentation

Rodríguez-Solana, A., Gracia-Marco, L., Marmol-Perez, A., Cadenas-Sanchez, C., Ortega, F. B., Gil-Cosano, J. J., Llorente-Cantarero, F. J., Pascual-Gázquez, J. F., Ortega Acosta, M. J., & Ubago-Guisado, E. The effects of an online exercise program on psychological health in young paediatric cancer survivors: the iBoneFIT multicenter randomized control trial. 2nd International Congress "Promoting Brain Health Through Exercise Across the Lifespan". Granada, September 19-20, 2024. Oral presentation.

RESEARCH ACTIVITIES

Training Activity: Herramientas para el Desarrollo de la Investigación. March 22-24, 2022. Duration: 9 hours. University of Granada

Training Activity: Diseño gráfico aplicado al ámbito científico. May 4-6, 9, and 10, 2022. Duration: 20 hours. University of Granada

Training Activity: Escritura de artículos científicos. April 26 and 28, and May 4 and 6, 2022. Duration: 20 hours in-person and 5 hours online. University of Granada

Training Activity: Introducción a la programación y análisis de datos en R. May 13-24, 2024. Duration: 24 hours in-person. University of Granada