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Review Article

Physical Exercise Intervention for Children Undergoing Cancer Treatment: A Scoping Review

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Abstract

Aims: This research aimed to explore articles regarding physical exercise for children undergoing cancer treatment.
Method: The research method used is scoping review. The process of doing a scoping review involves several steps, including developing research questions, establishing criteria for inclusion, a comprehensive search strategy, literature screening and selection, organizing data, and compiling, summarizing, and presenting the findings. The inclusion criteria encompassed full-text papers, namely randomized controlled trials or quasi-experimental research, published in English during the past decade (2014–2023). Pubmed, CINAHL, Scopus, and Proquest are used as search engines and database searches. Selected articles were extracted into charting data, analyzed with descriptive approaches, and the results reported.
Results: The results found 14 articles, which were then categorized into three physical exercise programs, such as integrated physical exercise, technology-based physical exercise, and multimodal exercise. Outcomes obtained are cardiorespiratory fitness, motor performance, cancer-related fatigue, and quality of life.
Conclusion: The side effects of cancer treatment in children may be mitigated through the implementation of physical exercise programs. This scoping review can be a consideration for optimizing pediatric nursing services by adding physical exercise interventions to the rehabilitation protocol as a supportive treatment for children who are currently undergoing cancer treatment.

Keywords:
Cancer Treatment, Children, Exercise Intervention, Pediatric Oncology, Physical Exercise,

INTRODUCTION

Pediatric cancer is the primary cause of mortality in children. According to data from the International Agency for Research on Cancer, in 2020 there were 11,156 children in Indonesia between the ages of 0 and 19 who had cancer, or about 12 per 1,000 total children. Of those, 4,234 children died from the disease, or 4.8 per 100,000 children (1). However, from 50% in the 1970s to 80% in 2016, cure rates and child survival rates have grown because of major advancements in medications, diagnostics, and access to better treatments in recent decades (2,3).

Cancer treatment is highly variable and should be planned taking into account many factors such as the primary location of the tumor, metastatic areas, individual characteristics, tumor stage, or cell types in heterogeneous tumor tissues (4). In addition to reviewing the benefits of some

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types of cancer treatment, children undergoing cancer treatment experience the impact of clinical manifestations that reduce comfort and affect daily life during and shortly after treatment. Children with cancer are known to experience physical side effects during and after treatment procedures such as chemotherapy, radiotherapy, stem cell transplantation, or a combination of multiple regimens. The symptoms encompassed are nausea, vomiting, diarrhea, hair loss, diseases affecting the muscles and skeleton, inflammation of the mucous membranes, and chronic pain symptoms such as fibrosis caused by radiation, inflammation of the intestines, inflammation of the skin, swelling of the lymph nodes, nerve pain, and delayed bone growth (5,6,7).

The impact of prolonged cancer treatment has been found to significantly affect the lives of children with cancer. Persistent nausea and vomiting symptoms and chronic pain during treatment cause mood disturbances, anxiety, loss of confidence, low self-esteem, depression, and behavioral changes that result in children being unable to attend school after cancer treatment (8-12). Other consequences of cancer treatment, such as symptoms of cancer-related fatigue (CRF), result in reduced muscle strength, compromised balance, and diminished cardiorespiratory fitness (13,14,15).

Interventions that are both pharmaceutical and non-pharmacological can be used in supportive care. Certain symptoms, though, continue to be treated mostly with pharmaceuticals. The treatment of nausea and vomiting starts with medications belonging to the corticosteroid (methylprednisolone, dexamethasone), serotonin receptor antagonist (granisetron, ondansetron, palonosetron), dopamine receptor antagonist group (prochlorperazine, metoclopramide), and other categories (16).

The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology state that non-pharmacologic therapies are the primary prescription for supportive care in cancer patients. Non-pharmacological interventions that can be offered include energy conservation, nutritional management, bright white light therapy, physical therapy (such as acupuncture and massage), psychosocial interventions (such as cognitive behavioral therapy, psychoeducational therapy, and supportive expressive therapy), physical activity (such as cardiorespiratory endurance training, muscle endurance and strength training, yoga, qigong, and combination physical training), and biosocial interventions (17). Dietary modifications, acupuncture and acupressure, relaxation techniques including guided imagery and hypnosis, and behavioral therapy are among the non-pharmacological approaches advised for the treatment of nausea and vomiting symptoms (16).

Nurses have a vital role in providing clients with both physical and psychological support as health professionals. Nurses have the ability to act as advocates for their clients, assist them in making decisions about the best kind of care based on their requirements, and support effective client-centered interventions that enhance their health-related quality of life (HRQOL) (18). Through therapeutic interventions that eliminate or reduce the physical and psychological distress that children experience, pediatric nurses also play a significant role in providing atraumatic care for children and families in a variety of healthcare settings (9). The atraumatic care provided can be in the form of recommendations or counseling regarding interventions that provide benefits and positive impacts on children. Physical exercise interventions are recommended as important supportive care for children undergoing cancer treatment. Support and assistance from pediatric nurses are essential in motivating children with cancer to actively engage in these physical exercise interventions (19).

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Nurses and other healthcare professionals can collaborate to create fitness programs for children undergoing cancer treatment, whether they are at home or in the hospital, to offer them high-quality treatment. Nurses can collaborate to develop engaging and inspiring physical exercise programs that are customized to the needs of the cancer-stricken child. This will increase the child's compliance with exercising regularly and enthusiastically (9,19). This research aims to gather information in order to enhance awareness and provide valuable insights to parents and children affected by cancer.

METHODS

Study Design

The scoping review method was used in this study because it aligns with the research objectives, which include examining available literature on physical exercise and pediatric cancer patients. Using the PCC format—P (Population), C (Concept), and C (Context)—this study first determined the research elements and identified the literature search keywords in order to find research articles using both qualitative and quantitative methods (20).

Sample

Children with cancer represent the population element in this study, physical exercise is the concept, and cancer treatment is the context. Inclusion criteria included articles available in full-text for full accessibility of research articles, articles with primary methods such as randomized controlled trials (RCT) or quasi-experimental (QET), English language articles, articles with 10 years of publication, and articles that had to discuss physical activity interventions for children with cancer.

Exclusion criteria applied were review articles such as literature reviews, theses, and theses, as well as the population of children with cancer aged 4-19 years with concomitant diseases or disorders, such as musculoskeletal disorders, history of respiratory failure, high risk of bleeding, thrombocytopenia, anemia, prognosis of cancer that has metastasized, has cognitive problems or learning difficulties, undergoing cancer management in the form of stem cell transplantation with a weak body condition, and cardiomyopathy disease because in these conditions the child's body condition is very weak and it is contraindicated for children who are on cancer treatment to be involved in the intervention.

Instrument

A thorough literature search was performed across multiple databases and search engines, such as Pubmed, CINAHL, Scopus, and ProQuest. The literature searched in these databases used English keywords using boolean phrases with Boolean Operators in the form of AND and OR. English keywords are children OR adolescents OR pediatric OR childhood AND cancer OR oncology AND exercise OR training.

Data Collection

The literature search was recorded following the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR). The PRISMA flowchart was utilized to delineate the amount of literature identified through the search results, the process of screening, the number of studies that fulfilled the eligibility criteria, and the number of studies that were included in the comprehensive review. Following the screening and selection of articles, the collected research articles must be reviewed and tested for eligibility using a critical evaluation instrument. JBI Appraisal Tools, a critical appraisal instrument by JBI, was used in this study.

Data Analysis

Selected articles get thorough reading and analysis. Moreover, the chosen articles will be displayed in a tabular manner to enhance the clarity of information presentation.

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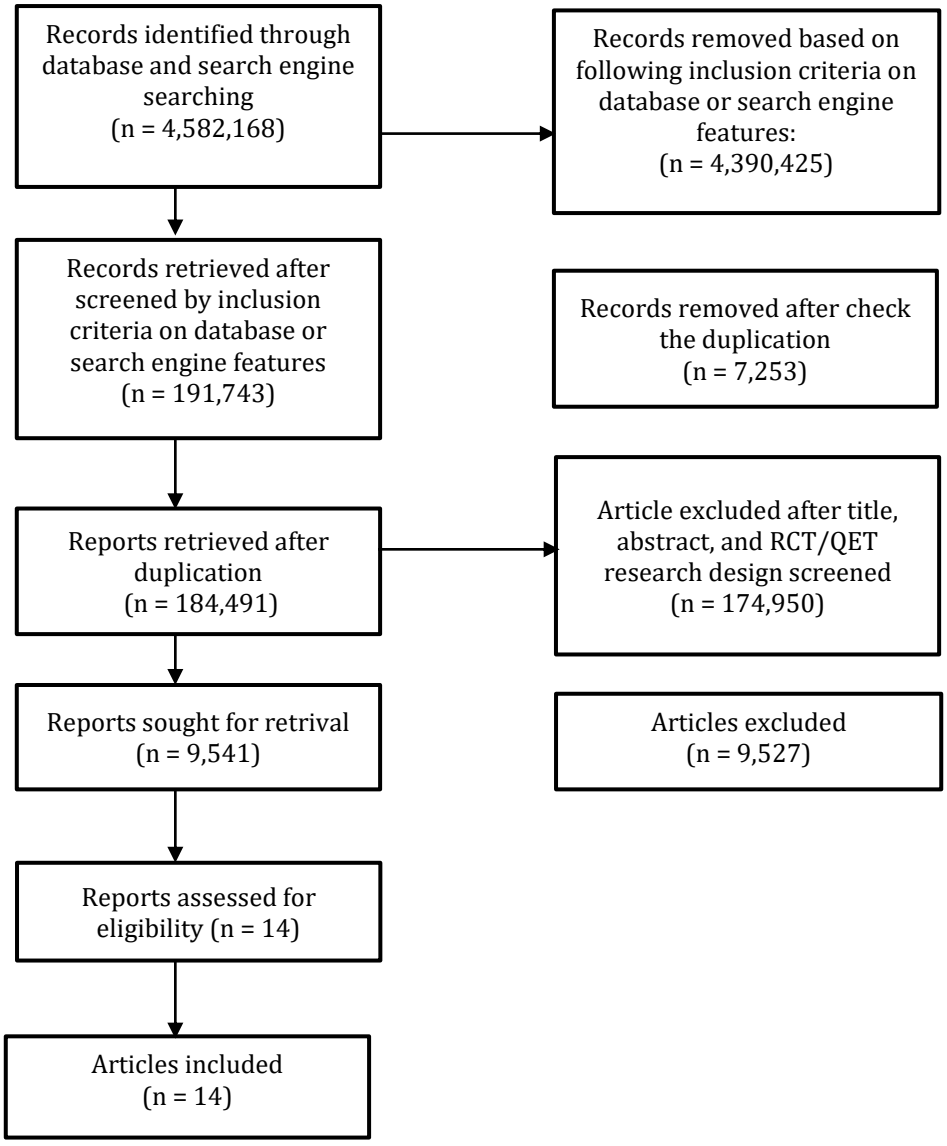

Figure 1. Diagram PRISMA-ScR

RESULTS

A total of 14 articles regarding physical activity interventions for children undergoing cancer treatment were acquired. The articles used in the study were articles published in the range of 2016–2023, with quantitative research designs in the form of randomized controlled trials (11 articles) and quasi-experimental studies (3 articles). The research was carried out in Egypt, Australia, Finland, Germany, France, the Netherlands, China, Spain, Turkey, Poland, and Denmark. A total of 813 participants were involved, and the sex ratio of males and females was about 3:2. The participants' ages ranged from 4 to 18 years, with an average age of 12 years. Leukemia was the most prevalent form of childhood cancer (37.3%, n = 303).

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Table 1. Data Extraction of Physical Exercise Intervention for Children Undergoing Cancer Treatment Articles

Author, Year, Country	Sample size	Method	Result
Mohamed, et al (2020) Mesir	19	Randomized controlled trial	**Muscle strength outcome:** Comparing group B's endurance and muscle strength training participants to group A's cardiorespiratory endurance training participants, there were statistically significant differences (P < 0.05) in muscular strength observed in the following muscle groups: elbow flexors, shoulder abductors, hip flexors, knee extensors, and ankle flexors, on both sides. **HRQOL outcome:** There was no notable disparity in HRQOL between the participants in group A who engaged in cardiorespiratory endurance training and the participants in group B who engaged in muscular endurance and strength training.
Gaser, et al (2022) Jerman	41	Randomized controlled trial	**Outcome of Activity of Daily Living (ADL):** ADL achievement improved significantly (p < 0.05) in both groups. **Outcome of physical activity level:** There was not a noticeable disparity in the amounts of physical activity between the two groups. **Motor performance outcome:** Motor performance decreased in all motor skills in both groups
Saultier, et al (2021) Prancis	80	Randomized controlled trial	**Motor performance outcome:** - The intervention group experienced notable improvements in the results of the six-minute walk distance test and upper muscular strength. - The degree of flexibility, balance, lower muscle

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Author, Year, Country	Sample size	Method	Result
			strength, trunk muscle endurance, and abdominal muscle endurance showed an increase. **Outcome of self-esteem:** The intervention group had significant differences when compared to the control group. **HRQOL outcome:** There was a significant difference in the intervention group compared to the control group
Lam, et al (2018) China	70	Randomized controlled trial	**CRF Outcome:** At 9 months, the intervention group had significantly reduced levels of CRF in comparison to the control group. **Physical activity level outcome:** At 9 months, the intervention group was observed to have increased physical activity levels compared to the control group. **Self-efficacy outcome:** At 9 months, the intervention group was observed to have an increased level of self-efficacy compared to the control group. **Grip strength outcome:** At 9 months, the intervention group was observed to have improved grip strength scores on both the right and left compared to the control group. **HRQOL outcome:** The monitored intervention group had improved HRQOL scores compared to the control group within 9 months
Fiuza-Luces, et al (2016) Spanyol	49	Randomized controlled trial	**Muscle strength outcome:** The intervention group showed a substantial enhancement in leg/bench press and lateral row performance following the 5RM test, in comparison to the control group ($p < 0.001$). **Cardiorespiratory fitness outcome:**

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Author, Year, Country	Sample size	Method	Result
			The intervention and control groups did not exhibit any notable disparity in their cardiorespiratory fitness levels. **Outcome body mass and BMI:** No significant variations in body mass or BMI were identified in the intervention and control groups. **Outcome of the ability to perform ADLs:** No significant difference in the improvement of ADL level ability was found in the intervention and control groups. **HRQOL outcome:** No significant difference in the improvement of HRQOL was found in the intervention and control groups.
Jung, et al (2021) Jerman	72	Randomized controlled trial	**CRF Outcome:** The intervention group had a significant decrease in CRF following the intervention, as observed during the 3-month and 6-month follow-up assessments, in comparison to the control group.
Kabak, et al (2019) Turki	26	Randomized controlled trial	**Outcome of clinical status:** There were no notable differences in the alterations of clinical status between the intervention group and the control group. **Depression outcome:** The intervention group exhibited a significant difference in the decrease of depressive symptoms ($p < 0.05$) when compared to the control group. **Outcome of pain and fatigue:** The intervention group exhibited a notable reduction in pain intensity throughout hospitalization, which was statistically significant ($p < 0.05$) when compared to the control group.

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Author, Year, Country	Sample size	Method	Result
			Child HRQOL outcome: The intervention group exhibited a statistically significant improvement in child HRQOL compared to the control group ($p < 0.05$). **HRQOL outcomes of parents**: Both the parents in the intervention group and the control group observed a decrease in their HRQOL.
Ouyang, et al (2019) China	114	Quasi Experimental	**Physical activity outcome:** Both the intervention and control groups experienced a significant increase in moderate-high intensity physical activity ($p < 0.001$). **Cancer distress symptom outcome:** The intervention group showed a substantial reduction in the score for cancer psychological symptoms compared to the control group ($p < 0.001$). The Global Distress Index score of the intervention group exhibited a statistically significant reduction compared to the control group ($p < 0.001$). The intervention group demonstrated a statistically significant decrease in physical symptoms ($p = 0.01$).
Nielsen, et al (2020) Denmark	170	Quasi Experimental	**Cardiorespiratory fitness outcome:** There was an increase in VO_2 max as an indicator of cardiorespiratory fitness in the intervention group compared to the control group after 6 months ($p = 0.01$). **Physical function outcome:** There was an improvement in physical function in the intervention group compared to the control group after 3 months and 6 months ($p < 0.0001$).

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Author, Year, Country	Sample size	Method	Result
Götte, et al (2018) Jerman	40	Quasi Experimental	**Outcome of the number of daily steps:** There was an increase in the number of daily steps achieved in the intervention group (p = 0.04). **Outcome active minutes:** There was no significant change in both groups. **HRQOL outcome:** There was an increase in HRQOL scores in the intervention group compared to the control group (p < 0.01).
Stössel et al (2020) Australia	35	Randomized controlled trial	The intervention group showed significant differences in many variables between the pre- and post-intervention stages, such as: - Leg strength - Walking performance - Fatigue - Self-esteem - Muscle strength and endurance capacity based on individual reports
Hamari, et al (2019) Finlandia	36	Randomized controlled trial	No significant differences were observed in fatigue, motor function, or physical activity levels between the intervention and control groups.
Kowaluk & Wozniewski (2019) Polandia	21	Randomized controlled trial	**Cardiorespiratory fitness outcome:** Following the 14th month, a difference in the cardiorespiratory fitness levels became evident between the intervention and control groups. **Activity intensity outcome:** Following the 14th month, the intervention group showed a higher level of exercise intensity compared to the control group. **Energy output outcome:** Following the 14th month, the energy output of the intervention group surpassed that of the control group. **Physical activity level outcome**: Following the 14th month, the

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Author, Year, Country	Sample size	Method	Result
			intervention group had a higher level of activity compared to the control group.
Braam, et al (2018) Belanda	60	Randomized controlled trial	**Cardiorespiratory fitness outcome:** There were no statistically significant differences in the immediate intervention impacts on psychosocial functioning and physical fitness. **Muscle strength outcome:** After 12 months, the intervention group demonstrated substantially higher enhancements in lower body muscle strength (β = 56.5 Newton; 95% CI: 8.5; 104.5) compared to the control group. **Outcome of bone mineral density (BMD):** Both groups exhibited a significant increase in bone density over time when comparing changes within each group. **HRQOL outcome:** HRQOL demonstrated considerable improvement over time in both groups, as seen by the changes observed within each group. The impact of the intervention on Health-Related Quality of Life (HRQOL) was not significantly influenced by physical fitness and psychological functioning as mediators. **Psychosocial functioning outcome:** The implementation of the intervention was satisfactory, with an average attendance rate of 67% each session and a dropout rate of 22% (mostly owing to disease recurrence).

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DISCUSSION

A total of three types of physical exercise programs were created from the articles that were found: integrated physical exercise programs, technology-based physical exercise programs, and multimodal exercise programs. Based on the scoping review study's findings, Physical exercise interventions may function as a form of supportive care for children undergoing cancer treatment due to their beneficial impact on multiple aspects of their physical and mental well-being. The majority of the time, favorable outcomes that can have a positive impact on health are what indicate how successful physical exercise programs are for children undergoing therapy.

Integrated Physical Exercise Program

The research found that the comprehensive physical exercise program was highly effective in producing favorable results in enhancing the physical capabilities of children receiving cancer treatment. These improvements include enhancements in cardiovascular endurance, muscular strength, motor skills, and a reduction in CRF. Cardiorespiratory endurance training is a great method to increase cardiorespiratory fitness levels in an integrated physical exercise program. The objective of cardiorespiratory endurance training is to enhance the endurance of the cardiorespiratory system, hence improving the ability of the heart and lungs to deliver oxygen to the muscles throughout extended periods of physical exercise (6). Cardiorespiratory endurance exercise leads to a functional adaptation known as an augmentation in maximal cardiac output. This is achieved through the enlargement of cardiac dimensions, enhanced contractility, and increased blood volume. These changes enable greater ventricular filling and, consequently, a larger heart volume. Simultaneously with a rise in maximal cardiac output, there is an enhancement in muscle perfusion capacity, which enables a larger delivery of oxygen (21).

Muscle strength endurance training can stimulate the release of growth hormone (GH) and insulin-like growth factor-1 (IGF-1), which induces the process of repair and replacement of muscle constituent components at the cellular level in muscle cells, where muscle fibers fuse to form new muscle protein strands, or myofibrils (22). The repaired myofibrils undergo a rise in both thickness and quantity, leading to muscle growth and subsequent expansion (hypertrophy). Thick muscles have the capacity to contract and then relax to move bones and other body parts, allowing for the best possible performance of musculoskeletal physiological processes (23).

Multiple studies in this scoping review have demonstrated that supervised integrated physical activity regimens can effectively manage the symptoms of CRF. CRF symptoms, experienced by both parents and children with cancer, are the most incapacitating symptoms of cancer and the adverse effects of cancer treatment. The combined physical exercise intervention of cardiorespiratory endurance training and muscular endurance and strength training conducted by Jung et al. (24) provided positive benefits in significantly reducing CRF levels in children with cancer. In addition, a related study on integrated physical exercise by Lam et al. (25) was also found to significantly reduce CRF levels.

The activation of a regular integrated physical exercise program can induce the Hypothalamus-Pituitary-Adrenal axis (HPA axis) in the brain. Induction of the HPA axis can modulate stress and anxiety reactivity, increase the release of endorphins in the brain, which are beneficial for the regulation of pain perception and mood improvement, increase the release of serotonin levels, which are beneficial for mood improvement, sleep quality, digestive problems, relief of symptoms of nausea, wound repair, and bone health, increase body metabolism, and improve HRQOL related to health (26,27). The combination of an integrated physical exercise program

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with several other multimodal exercises may provide better psychosocial functioning outcomes in children undergoing cancer treatment.

Technology-based Physical Exercise Program

Technology-based physical exercise programs conducted through exergaming Nintendo Wiifit games by Stössel et al. (28) and Interactive Video Games (IVG) by Kowaluk & Wozniewski (29) provided similar positive outcomes on improving muscle strength and motor performance in children undergoing cancer treatment. This was attributed to the fun nature of the intervention protocol and researcher supervision during the intervention over a period of 3–6 months, which resulted in all children being more motivated. High motivation in cancer treatment children in this physical exercise program can increase the level of participation and compliance, so that children get optimal benefits from the physical exercise program. However, this is different from the Active Video Games (AVG) technology-based physical exercise intervention conducted by Hamari et al. (30), where there was no apparent difference in the level of physical activity, motor performance, or fatigue levels following the intervention. It explained that this intervention was not supervised by the research team, which led to a low level of compliance, so the effectiveness of this intervention was not achieved.

For all health and social care workers, supervision is essential to their work, and there ought to be a collective responsibility for ensuring the efficiency and security of their responsibilities. According to Rothwell et al. (31), Supervision is a process that involves an ongoing professional relationship between two or more staff members with different levels of expertise or experience. Its purpose is to enhance professional growth and reinforce knowledge and skills. Efficient supervision in research is essential for ensuring the best techniques and protocols for all parties involved, such as practitioners, service delivery managers, clinical supervisors, colleagues, clients, and other service users, as well as the entire profession. Research without good supervision will leave the effectiveness of health interventions unexamined and the risk of research bias greater.

Multimodal Exercise Program

A multimodal exercise program conducted by Braam et al. (32) found an increase in HRQOL scores, increased motivation to follow the intervention, and increased motivation to attend school in pediatric patients with cancer. Psychosocial training interventions are individually structured programs to improve socioemotional functioning and cope with disease-related effects. The intervention contains psychoeducation and cognitive-behavioral strategies, encompassing the articulation of emotions, self-perception, and effective stress management abilities. The intervention aimed to enhance psychosocial functioning as manifested in HRQOL, self-perception, behavioral issues, and depressive symptoms.

The psychosocial training intervention effectively reduced depression levels in children with cancer by promoting self-reflection, offering continuous encouragement to enhance participants' self-efficacy, and facilitating the learning process. Self-efficacy, as defined by social cognitive theory, refers to an individual's self-evaluation of their own competence in carrying out specific actions, such as physical exercise. It plays a crucial role in determining the probability of an individual's engagement or avoidance of these behaviors (33). In order to achieve the effectiveness of physical exercise, as measured by positive outcomes in increased muscle strength, improved bone composition, HRQOL, and increased motivation to attend school, participants must have improved self-efficacy.

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LIMITATION

A limitation of this study is that the analysis was restricted to articles published within the past decade. Although it aims to explore physical exercise interventions, this study would be more comprehensive if it reviewed more previous articles. Furthermore, the effectiveness of physical exercise interventions in managing physical disorders such as symptoms of nausea and vomiting and chronic pain remains limited. Therefore, researchers hope to conduct further research using appropriate instruments to assess the effectiveness of physical exercise interventions as part of supportive care efforts. Furthermore, a potential bias was identified as some articles could not be included in the quantitative synthesis due to a lack of necessary data. Therefore, the uncertainty of some studies related to the effectiveness of physical exercise interventions in children with cancer necessitates further attention.

CONCLUSION

Through this scoping analysis, three physical exercise programs for children undergoing cancer treatment were identified. These physical exercise programs include integrated physical exercise programs, technology-based physical exercise programs, and multimodal exercise programs. Through these physical exercise programs, researchers can explore physical exercise interventions and their effectiveness for children with cancer in providing positive outcomes in physical function and psychosocial function that are impaired due to cancer treatment. The positive outcomes obtained by children undergoing cancer treatment through these three physical exercise programs include cardiorespiratory fitness level, muscle strength and motor performance, CRF, and HRQOL. Nurses' support and assistance in providing atraumatic care is essential in motivating children with cancer to participate in regular physical exercise. Nurses are expected to work with multidisciplinary professionals in order to implement physical exercise programs while children with cancer are undergoing hospitalization. Nurses can also collaborate to develop engaging and motivating physical exercise programs that cater to the abilities of children with cancer, thereby promoting their consistent and active participation in physical exercise.

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