The Effects of Exercise Intervention on the Quality of Life According to QoL Score in Children with Cancer: A Systematic Review of Randomized Controlled Trials

Christianna Zarou1, Maria Micha1,2*, Flora Bacopoulou1,3, Antonis Kattamis1,4, Katerina Katsibardi1,5, Christina Kanaka-Gantenbein1,6

1School of Medicine, National and Kapodistrian University of Athens, Athens, Greece
2Unit of Developmental and Behavioral Pediatrics, First Department of Pediatrics, School of Medicine, UoA, “Aghia Sophia” Children’s Hospital, Athens, Greece
3Center for Adolescent Medicine and UNESCO Chair on Adolescent Health Care, First Department of Pediatrics, National and Kapodistrian University of Athens, Athens, Greece
4First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, Athens, Greece
5Oncology Unit, Department of Pediatric Hematology, “Aghia Sophia” Children’s Hospital, National and Kapodistrian University of Athens, Athens, Greece
6First Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, ”Aghia Sophia” Children’s Hospital, Athens, Greece
Email: *michamaria2@hotmail.com

Abstract
Diagnosing childhood cancer is very stressful for the child and his family. In fact, this condition emotionally affects both the child and the family, resulting in a decrease in mood and in resilience. This requires intervention to enhance the well-being and quality of life of the child throughout the duration of treatment. Exercise interventions aim to improve the mental health and the QoL of these children. The aim of this systematic review was to sum up the evidence from randomized control studies that examined the effectiveness of exercise intervention in the quality of life of children with cancer. The Web of Science, PubMed and Scopus databases were meticulously searched from articles that studied the effect of exercise intervention on QoL of children with cancer. The initial search retrieved 632 studies, of which only seven randomized controlled trials met the selection criteria. Four out of seven studies demonstrated statistically significant improvement in QoL score, fact that verifies the hypothesis that exercise intervention may enhance the positive emotions of children and cultivate their mental resilience needed by the healing process. The results of our review indicate that...
exercise improves the satisfaction of children with cancer and their mental and physical health.

**Keywords**
Children, Cancer, Exercise Intervention, Quality of Life, QoL Score

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1. **Introduction**

Childhood cancer is a chronic disease that affects not only the biology but also the well-being and the quality of life of those patients. Fortunately, an increasing number of children can nowadays successfully cope with their disease due to the recent advances in the field of pediatric oncology. The modern successful methods of treatment combined with the progress in diagnostic procedures have resulted in a higher survival rate among children with cancer. At the same time, these children must continue living with the experience and consequences of cancer and its treatment. The main post-treatment psychological effects can vary significantly ranging from worrying about the future to a more worrisome concern about their “sick appearance”, the belief that they now look different from their healthy peers (McDougal, 1997).

People with cancer are usually obliged to undergo long term inpatient care repeatedly. Many studies have highlighted various stressors related to inpatient care and treatment of cancer, like fear of death, unknown environment, lack of activities, aggressive interventions, etc. (Boyd & Hunsberger, 1998; Bastin, 2000; Coyne, 2006). Especially in pediatric oncology, pediatric cancer treatment can include many painful interventions. Most of the children treated for cancer have been diagnosed with severe post-treatment physical/organic problems such as sudden changes in weight and metabolism, difficulties in eating, hair loss (Enskar & Von Essen, 2008; Simonton et al., 1992), psychological difficulties and pain, discomfort, fatigue, lack of confidence and melancholy, which can lead to depression (McCaffrey, 2006), as well as patient’s QoL issues that occur more quickly and more frequently in these children than in children who have completed their treatment (Collins et al., 2000; Enskar & Von Essen, 2007; Hicks et al., 2003). It is also well established that children with chronic health problems have significantly worse QoL than their healthy peers (Varni et al., 2007). Besides, the period following cancer diagnosis constitutes a stressful and life-changing event. Patients have to deal with treatment procedures and side-effects of the illness, absence from everyday activities, separation from family and friends, change in appearance, and fear of dying, factors that make their psychological adjustment very difficult (Askins & Moore, 2008; Firoozi & Rahmat, 2013).

For this reason, emphasis should be placed on maintaining a balanced mental and physical health of children, so that positive behavioral and emotional factors are influenced. With regards to physical activity, White et al. (2005) find that
physical activity is highly recommended for children with cancer during their treatment. Bjork et al. (2006) concluded that children need exercise even during their hospitalization. Physical exercise can have a tremendously positive effect on the self-image of children with cancer, which is of paramount psychological importance (Bjork et al., 2006).

Thereby, the aim of this review was to identify and appraise the existing scientific evidence on the effects of exercise interventions on the quality of life of children with cancer according to QoL score. It should also be mentioned that the results which will be extracted from our article could be used for the design and implementation of an intervention that combines the most effective elements of the existing ones.

2. Methods

The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2010).

2.1. Selection Criteria

The standards for including or excluding a study were set according to the PICOS components. With regards to Population, studies had to be conducted solely on patients diagnosed with childhood cancer. Regarding Intervention, exercise intervention was included. With respect to Comparator, all types of active or inactive comparators were included. As far as Outcome is concerned, the primary outcome was improvement of quality of life measured with the QoL score. Lastly, with regards to Studies, RCTs with a matched control group were sought. Identified research protocols that did not present satisfactory data were also excluded. Additionally, studies had to be published solely in the English language by journals with a peer-review process.

2.2. Search Strategy

The Web of Science, PubMed and Scopus electronic databases were searched by two reviewing investigators. Search terms used were the following: “Exercise” OR “exercise intervention” OR “physical intervention” AND “childhood cancer” AND “quality of life” OR “QoL score” OR “mental health”. Terms were searched for in each title and abstract, and in the keywords of each study, and were adapted accordingly to each electronic database. The researchers separately searched introduction sections and reference lists of papers that were to be included for supplementary studies consistent with the question of the review.

2.3. Data Extraction and Quality Evaluation

The data were collected independently by two researchers (C.Z. and M.M.). Data incorporated each study’s origin with respect to the country, its sample size, participants’ sex and age, measuring instruments used, intervention content, type of comparison, main results of each study and information required to assess risk of bias. Quality assessment of individual studies was conducted according to the
Cochrane Collaboration’s tool for assessing risk of bias (Higgins et al., 2011) by two researchers (C.Z. and M.M.).

3. Results

3.1. Study Flow and Included Studies

Initial search yielded 632 papers. The reviewing investigators concluded in 7 randomized control trials (Lam et al., 2018; Speyer et al., 2010; Senn-Malashonak et al., 2019; Cox et al., 2018; Stössel et al., 2020; Yildiz Kabak et al., 2019; Fiuza-Luces et al., 2017). The complete screening process is illustrated in Figure 1. Four trials were conducted in Europe, while the remaining two in Asia and the last of these in the USA. All studies were conducted in clinical populations with pediatric cancer. Among the seven studies, 338 subjects were recruited in total, aged 3 - 18 years. All interventions were based on physical session.

![Flow chart of the included studies](image-url)
3.2. Qualitative Evaluation of Studies

**Figure 2** illustrates the results of the quality evaluation of the involved studies based on the Cochrane Collaboration’s tool for assessing risk of bias (Higgins et al., 2011). Among the 7 included studies, two reported not using randomization for the allocation of the participants into the intervention and control groups, fact which led to a high risk of selection bias. For the remaining 5 studies, the risk of selection bias was low and unclear. The risk of attrition bias due to missing or excluded from analysis data was unclear for four of the studies. The reporting bias was assessed as unclear and considered as high in three of the studies.

3.3. Results of Exercise Intervention on QoL

From the included studies, four evaluated the effect of exercise intervention on QoL in children with cancer. Positive, statistically significant effects ($p < 0.001$)
were reported by Lam Katherine (Lam et al., 2018). Similar significant results were found by Stössel et al. (2020), Yildiz Kabak et al. (2019) and Speyer et al., (2010). Specifically, in Stössel et al. (2020), is presented improvement in self-esteem, strength and endurance in children with cancer. In Yildiz Kabak et al. (2019), the exercise program promoted the psychosocial condition and the QoL of these children. The physical activity used in Lam et al. (2018), was beneficial for the stress experienced by children and improved QoL and hope of them. In Speyer et al. (2010), a high intensity exercise program increased QoL domain complexities. The study of Senn-Malashonak et al. (2019), Cox et al. (2018) and Fiuza-Luces et al. (2017), did not have significant effects on the studied domain.

3.4. Limitations

This systematic review bears certain limitations. Firstly, an apparent lack of studies evaluating the effects of the exercise on QoL in children with cancer, and lack of rigorous conducted RCTs exist. In addition the majority of the studies included small sample sizes; among the studies, the different recruited control groups, and the observed high risk of overall bias constitute important limitations of this review. Therefore, these restrictive factors make the analysis of the results at a quantitative level not achievable.

4. Discussion

In this systematic review study, research material has been gathered, providing evidence for the efficacy of innovative methods in improving the QoL of children with cancer. More than half of the examined interventions resulted in significantly positive results and high value effect sizes; thus, proving the effectiveness of these therapies and validating their use and standardization in future clinical methodology and psychological treatment approach in pediatric oncology. Four out of the seven studies were able to demonstrate significant results on improving the QoL of their patients; others in specific sub-domains and others in the total generic score of the examined outcome. Taking into account the sum of evidence presented and analyzed in this review, we can see that physical activity and exercise interventions have a big effect especially on self-esteem, social and physical functioning, anxiety and stressful feelings which are critical domains of HR QoL. This positive effect of exercise and physical activity on these sub-domains and QoL in general, justifies their high spread and preference over other social or more psychological therapies. The inherent energetic and optimistic psychology of children makes them ideal candidates for these types of physical practice and kinetic interventions.

There is solid evidence that auxiliary interventions that complement the overall palliative care benefit children receiving cancer treatment in general and especially in uncomfortable and aching procedures. This area of expertise is of essential and fundamental importance to children fighting cancer, as well as, to
their relatives. This paper concludes that physical activity can have a beneficial effect on their overall quality of life and alleviate their psychological burden. Overall, the results demonstrate that children and adolescents’ mental health issues when facing cancer are addressable, while interventions with physical activity, and are essential in addressing various issues that degrade their wellbeing and fast rehabilitation.

In conclusion, this systematic review demonstrates that children with cancer can benefit from exercise interventions aiming to improve their mental health and QoL. Exercise helps children create new routines and work for a different and active life during this difficult period (West et al., 2015). After, all these interventions should enhance positive emotions and resilience, be preventive and child-centered (Engelen et al., 2012).

5. Conclusion
The effectiveness of exercise interventions on QoL in children with cancer was investigated in this review. The results of our review, although not all statistically significant, indicate that exercise interventions are beneficial for children with cancer. These children and their families are a growing population requiring more patient-centered, time flexible interventions which may enhance self-bonding and patients’ positive emotions. Overall, this study supports the usefulness of conducting further randomized controlled studies to test the effectiveness of this treatment program for this challenging chronic disease.

Conflicts of Interest
The authors declare no conflicts of interest regarding the publication of this paper.

References


