



# The Effect of Fatigue-reducing Interventions on the Fatigue Levels of Children with Cancer: A Meta-analysis Study

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## ABSTRACT

**Aim:** This research was conducted to analyze the effect of fatigue-reducing interventions on the fatigue levels of children with cancer.

**Materials and Methods:** This quantitative study based on the literature relating to those interventions to reduce fatigue in children with cancer was carried out. No time limits were defined for the literature review; instead, all available studies published until February 2019 were reviewed. Data were collected from Pubmed, Cochrane, EBSCO Host, ScienceDirect, Embase/Elsevier, and Web of Science databases. The keywords "child", "cancer", and "fatigue" were used during the search process. The effect sizes and group comparisons of each study were analyzed using The Comprehensive Meta-analysis statistical software package for meta-analysis.

**Results:** The total sampling number of the five studies included in the study was 500. As a result of the heterogeneity test, it was determined that these studies involving interventions to reduce the fatigue of children with cancer had heterogeneous characteristics. The result of a publication bias test found no publication bias. The average effect size at 95% significance level was calculated as 1.452 for the study by Li et al. (2018), 0.560 for the study by Ramezani et al. (2018), 7.606 for the study by Kudubeş et al. (2019), -0.995 for the study by Lam et al. (2018), and 0.544 for the study by Vieira et al. (2015).

**Conclusion:** In this study, fatigue-reducing interventions were found to affect fatigue level.

**Keywords:** Child, cancer, fatigue, fatigue-reducing interventions, meta-analysis

## Introduction

Children with cancer experience various symptoms due to the treatments that they receive. These symptoms include anemia, neutropenia, nausea, vomiting, alopecia, mucositis, and fatigue (1,2). Fatigue is one of the symptoms that plays a significant role in caring for pediatric oncology patients. The literature states that 51 to 86 percent of pediatric oncology patients have cancer-related fatigue (3,4).

Fatigue is a multidimensional concept which can bring about biopsychosocial and cognitive effects and

change subjectively in childhood cancer. It also affects the individual's well-being, capacity to accomplish self-care, relationship with his/her environment, and state of enduring illness-related problems (5). Fatigue is a symptom that prevents the individual from working regardless of the size of the activity and constantly distresses the patient regarding their cancer. Fatigue associated with cancer in children is a deep feeling of exhaustion which is affected by various conditions, causes a lack of attention, creates negative emotions, affects play, and makes it difficult to move the limbs or even open the eyes (6).

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There are many reasons why cancer-related fatigue is often ignored by health professionals. As fatigue is an individual experience, the person tries to solve it without sharing with others. Moreover, fatigue is seen as being part of the nature of the disease process by healthcare personnel. Therefore, during the planned treatment to prolong the patient's life, this symptom can easily be ignored. However, fatigue, which is a symptom perceived by the patient, needs to be correctly identified. Fatigue should be identified in detail in all stages of the disease and its treatment and it should be controlled and intervened with using a multidisciplinary approach (7,8).

The role and autonomy of nurses in symptom management of pediatric oncology patients is quite significant. The nurse is responsible for assessing the findings of fatigue symptoms that have an important effect on the child's quality of life (QoL) and the factors that affect them. In addition, it is emphasized that the nurse should plan appropriate fatigue-reducing interventions and provide relevant training to the children and their families (9-12). In the literature, it has been reported that fatigue training given to children suffering from cancer and their families reduces the fatigue levels of these patients compared to the pre-treatment period. In addition, training for symptom control relieves children, improves the life quality of these children, and provides trust in healthcare personnel (10-12). There are many intervention options to reduce the fatigue of those children with cancer. These options include managing the fatigue symptoms, regulating activity, ensuring adequate and balanced nutrition, regulating the sleep schedule, and coping with stress (9-12).

A review of studies on reducing the fatigue levels of pediatric oncology patients has revealed that there are limited quantities of meta-analysis studies available. It has been found in these studies that exercise interventions, nutritional support, and training plans are available to reduce fatigue in pediatric oncology patients (12-14). However, the number of studies is limited and the majority of them relate to the adult population. This variation in study findings makes it difficult to come up with a straightforward conclusion on the matter. This situation requires the subject to be studied using sophisticated statistical methods. The meta-analysis approach is one of those statistical approaches (15,16). Meta-analysis is defined as the grouping of similar studies on a topic, theme or field of study under certain criteria and integrating and interpreting the quantitative findings of these studies (17). Meta-analysis differs from traditional statistical methods. While a significant difference is sought in traditional methods, in meta-analysis, the effect size of

this difference and the direction of this effect make up the focal point of the analysis (18,19). However, there are very few studies investigating the effect of fatigue-reducing interventions on the fatigue level of pediatric oncology patients using the meta-analysis method. In our country, no studies investigating this topic using the meta-analysis method have been found. That constituted the key starting point for this study's planning. The purpose of this study was to synthesize the results of studies investigating the effect of fatigue-reducing interventions on the fatigue levels of pediatric oncology patients using the meta-analysis method. The results of this study are thought to contribute to the planning of care for nurses, who play a major role in managing the symptoms and improving the QoL of pediatric oncology patients. It is also expected that this study will provide researchers with a new vision for future studies.

## **Materials and Methods**

This study aimed to analyze the effect of fatigue-reducing interventions on the fatigue levels of children with cancer.

### **Research Question**

What is the size of effect of fatigue-reducing interventions on the fatigue levels of children with cancer?

### **Literature Review**

Within the framework of this study, observational research on fatigue-reducing interventions in children with cancer were examined in order to evaluate the impact of these fatigue-reducing interventions on the fatigue rates of children with cancer. Since there was a limited number of meta-analysis studies on fatigue in pediatric oncology patients, no time limits were established; instead, all available studies published until February 2019, when the literature review was performed, were reviewed. Pubmed, Cochrane, EBSCO Host, ScienceDirect, Embase/Elsevier and Web of Science databases were searched. Printed publications accessed in this way were researched, but congress papers were not researched. During this search, the keywords "cancer", "child" and "fatigue" were used in Turkish and English. During the data collection phase, full-text research papers published on this subject were utilized.

### **Inclusion Criteria**

The following criteria were used for the inclusion of the accessed papers in the meta-analysis: (a) having a sampling of children with cancer, (b) having quantitative analysis data, (c) analyzing fatigue variables in children with cancer, (d) sufficient statistical data for calculating the size of the

effect, (e) analyzing at least one of the fatigue-reducing interventions, and (f) access to the full-text version of the study.

Figure 1 presents the flow diagram which summarizes the process of including studies in the meta-analysis. A total of 2,370 studies were obtained through the database search. Hundred and ten duplicate studies were removed. Two thousand two hundred and sixty studies were reviewed and 2,236 of them were removed based on their titles. Two researchers reviewed the abstracts of the remaining 24 studies according to inclusion and exclusion criteria, and their full-text copies were analyzed where appropriate. Nineteen studies which did not meet the requirements for inclusion were excluded. The lack of the fatigue variable or differences in the study population were among the reasons for removal. As a result, this study was based on a total of 5 previously published studies. Two researchers independently carried out the collection of these studies for meta-analysis. When the selection process for the two researchers was later measured, it was found that there was a 100 percent agreement on the researchers' paper selection. The studies included in the review have been planned according to the "PRISMA Flow Diagram Directive". There is a representation of this in Figure 1 (20).

### Coding of the Studies

A form of data coding has been used to gather data from the 5 studies included. The researchers developed the form using the related literature (21,22). The data coding form was used to obtain the statistical data and the characteristics of the sample method, measurement, measuring devices, type of publication, etc. needed to measure the effect size from each sample. The title of the report, author, year of publication, form of the report, design, sample size, findings and conclusion were coded for each study using "Cohen's d effect size". Comparing the coding of the first researcher with second researcher ensured reliability of the coded results. A value of positive effect size would indicate that fatigue-reducing interventions affect fatigue in children with cancer positively, whereas a negative value would indicate that fatigue-reducing interventions affect fatigue in children with cancer negatively. It can therefore be concluded that if the effect size is zero (0) or close to zero, the fatigue-reducing interventions do not have any effect on fatigue.

### Statistical Analysis

The study employed the Group Difference method, one of the group comparison meta-analysis types. The

comparisons of the effect sizes and the groups of each study were performed using the CMA software package (The Comprehensive Meta-analysis software). Hedges' g was used to measure the effect size because of variations in sampling and measuring instruments (15,23). Hedges' g is determined by dividing the product of standardized mean difference between groups by means of a combined standard deviation of the two groups (23). Cohen (24) says that the effect size is small if it is less than 0.20 and large if it is greater than 0.80. According to this classification, an effect size of  $d < 0.20$  is small,  $0.20 < d < 0.80$  is medium, and  $d \geq 0.80$  is large. In meta-analysis studies, a fixed-effect or a random-effect model is used according to heterogeneity (15). If the universe effect sizes of the studies in the meta-analysis do not change, the fixed-effect model is employed, whereas the random-effect model is used if the universe effect sizes vary from study to study. In this study, a random-effect model was employed because of the heterogeneity of the studies, which was determined as a result of homogeneity tests (15). Cochran's Q statistics, p-value, and  $I^2$  tests were employed to test the heterogeneity

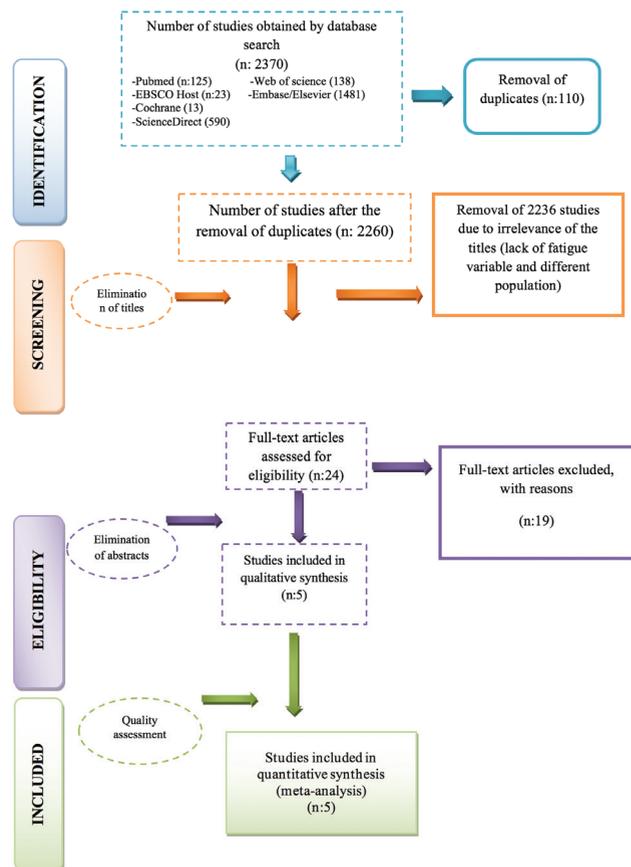


Figure 1. Flow diagram for the selection of studies

of the effect sizes. In determining the significance of the Q test, it is recommended that the limit value for p should be taken as 0.1. In the heterogeneity assessment, if the heterogeneity ratio (I<sup>2</sup>) is below 25%, it does not exist; it is low if the ratio is between 25-50%; it is moderate if the ratio is between 51-75%; and high if the ratio is greater than 75% (25). To test publication bias, Rosenthal and Orwin fail-safe N, Funnel plot chart, Duval and Tweedie's trim and fill test, rank correlation, Egger regression, and Begg and Mazumdar rank correlations tests were employed (15). As the significance levels of the papers included in the study ranged between 0.01 and 0.05, the significance level of the statistical analyzes in this study was taken as 0.05.

### Ethical Consideration

This study was approved by the Institutional Review Board of the University (IRB approval number: 4753-GOA-2019/12-04). Since the literature review model is used in the study, it does not directly affect humans or animals. Therefore, patient consent is not required.

### Results

All of the five studies included in the meta-analysis were research papers. Theses were not included in this study. The research included in the meta-analysis included research dating from 2015 to 2019 (Table I).

Article information	Aim	Methods	Statistical Analysis	Conclusion
Kudubes AA, Bektas M, Mutafoğlu K. (12). The effect of fatigue-related education on pediatric oncology patients' fatigue and quality of life. <i>Journal of Cancer Education</i> , 1-12.	This study aims to analyze the effect of fatigue-related education for pediatric oncology patients aged 7-12 and their parents on their fatigue and quality of life.	This study was conducted with 80 children with cancer and their parents who were assigned to either the control group (n=40) or the experimental group (n=40). The experimental group received a fatigue-related educational program. The data were collected three times: prior to the program, 3 months later, and 6 months afterwards.	Multidimensional variance analysis, the Bonferroni adjusted t-test and regression analysis were used to analyze the data.	A significant difference was found among the experimental and the control group for total mean scores and the mean scores of subdimensions of the scale for the Assessment of Fatigue-child form in terms of the interactions of group, time, and group*time (p<0.05). Significant differences were found among the experimental and control groups' mean scores on the scale for the Quality of Life-child and Parents form in terms of the interactions of group, time, and group*time (p<0.05). Fatigue-related education is an effective education model as a way to reduce fatigue and increase the quality of life of children with cancer. The use of fatigue-related education by nurses in pediatric oncology clinics will have positive effects on children and their parents.
Lam KK, Li WH, Chung OK, Ho KY, Chiu SY, Lam HS, Chan GC (28). An integrated experiential training programme with coaching to promote physical activity, and reduce fatigue among children with cancer: A randomised controlled trial. <i>Patient education and counseling</i> , 101 (11), 1947-1956.	This study examined the effectiveness of an integrated programme in promoting physical activity, reducing fatigue, enhancing physical activity self-efficacy, muscle strength and quality of life among Chinese children with cancer.	A randomised controlled trial was conducted in a Hong Kong public hospital. Seventy eligible children were randomly assigned to an experimental group (n=37) or a control group (n=33). The experimental group received an integrated programme with 28 home visits from coaches over a 6-month period. The control group received a placebo intervention. The primary outcome was fatigue at 9 months (3 months after intervention completion). Secondary outcomes were physical activity levels, physical activity self efficacy, muscle strength and quality of life at 9 months, assessed at baseline, and 6 and 9 months after starting the intervention.	To minimise attrition bias, the intention-to-treat principle was applied, and participants were analysed according to their initial group assignment. Inferential statistics (e.g. independent sample t-tests, chi-square and Fisher's exact tests) were performed to compare age, gender, parents' educational attainment, diagnosis and treatment received between those who were willing to participate and those who were not.	The experimental group reported significantly lower levels of cancer-related fatigue, higher levels of physical activity and physical activity self-efficacy, greater right- and left-hand grip strength and better quality of life than the control group at 9 months. The programme is effective and feasible to implement among children with cancer and offers an alternative means of ameliorating the healthcare burden.

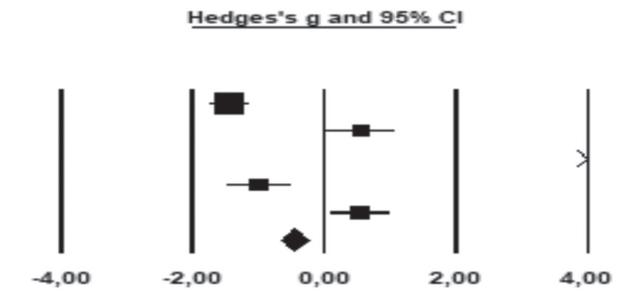
<p>Vieira MLDS, Fonseca FLA, Costa LG, Beltrame RL, Chaves CMDS, Cartum J, Rocha KC. (29). Supplementation with selenium can influence nausea, fatigue, physical, renal, and liver function of children and adolescents with cancer. <i>Journal of medicinal food</i>, 18 (1), 109-117.</p>	<p>The present study evaluated the health-related quality of life of patients undergoing chemotherapy for the treatment of leukemias and lymphomas (LL) and solid tumors (ST) while receiving Selenium (Se) supplementation.</p>	<p>This is a randomized, double-blind, crossover study that evaluated the quality of life (EORTC-QLQC30 questionnaire), renal and liver functions of patients supplemented with Se.</p>	<p>The results analyses were performed by adopting a significance level of 5% in compliance with the following models: Descriptive statistics; measure of central tendency; equality of means test (Student's t-test); equality of medians test (Mann-Whitney U).</p>	<p>There was no statistically significant alteration in LL patients. However, the fatigue and nausea scores after 30 days did decrease in this group as well as in the ST group. After 1 year supplementation with Selenium, a more noticeable decrease in the scores concerning fatigue and nausea could be observed in the ST group, when compared with the beginning of the study. The LL patients also presented a decrease in the fatigue scores and physical functions. The kidney function as well as liver function has improved after Se supplementation when compared with the placebo intake in LL and ST patients, more remarkably in the LL group. Supplementation with Selenium promotes the reduction of chemotherapy side effects in cancer patients, especially by improving the conditions of patients with fatigue, nausea, and impaired physical function. Renal and liver functions have also improved.</p>
<p>Li WH, Ho KY, Lam KKW, Lam HS, Chui SY, Chan GC, Chung OK. (26). Adventure-based training to promote physical activity and reduce fatigue among childhood cancer survivors: A randomized controlled trial. <i>International journal of nursing studies</i>, 83, 65-74.</p>	<p>This study examined the effectiveness of an adventure-based training programme in promoting physical activity, reducing fatigue, and enhancing self-efficacy and quality of life among Hong Kong Chinese childhood cancer survivors.</p>	<p>A prospective randomised controlled trial. Hong Kong Chinese childhood cancer survivors aged 9-16 years who reported symptoms of fatigue and had not engaged in regular physical exercise in the past 6 months. The experimental group underwent a 4-day adventure-based training programme. The control group received a placebo intervention. The primary outcome was fatigue at 12 months. Secondary outcomes were physical activity levels, self-efficacy and quality of life at 12 months.</p>	<p>We performed intention-to-treat analyses. Descriptive statistics, independent sample t-tests, chi-square, ANOVA test</p>	<p>From 6 January, 2014 to 8 June, 2015, we randomly assigned 222 eligible childhood cancer survivors to either an experimental (n=117) or a control group (n=105). The experimental group showed statistically significantly lower levels of cancer-related fatigue (p&lt;0.001), higher levels of self-efficacy (p&lt;0.001) and physical activity (p&lt;0.001), and better quality of life (p&lt;0.01) than the control group at 12 months.</p>
<p>Ramezani N, Moafi A, Nadjarzadeh A, Yousefian S, Reisi N, Salehi-Abargouei A. (27). The Effect of Soy Nut Compared to Cowpea Nut on Body Weight, Blood Cells, Inflammatory Markers and Chemotherapy Complications in Children with Acute Lymphoblastic Leukemia: A Randomized Controlled Clinical Trial. <i>Nutrition and cancer</i>, 70 (7), 1017-1025.</p>	<p>The present randomized controlled clinical trial studied the effect of soy nut on children with B-cell acute lymphoblastic leukemia (ALL) who were in the maintenance phase of chemotherapy.</p>	<p>The eligible patients were randomized to receive 30 g/day soy or cowpea nut powder for 12 weeks.</p>	<p>Wilcoxon Mann-Whitney U Anova Kolmogrov-Smirnov test T-test</p>	<p>Dietary intake, physical activity, anthropometric measurements, complete blood count, serum albumin, serum highly sensitive C-reactive protein (hs-CRP), and Tumor necrosis factor alpha (TNF-α) as well as chemotherapy side effects were assessed at the start and the end of the study. In total 29 and 27 children completed the study (aged 6.34±2.44 and 5.85±2.35 years) in soy and cowpea nut groups, respectively. The total energy and protein intake, and physical activity as well as body weight, body mass index, number of red blood cells, hemoglobin and hematocrit levels, and fatigue were significantly improved in the soy nut group compared to patients who consumed cowpea nut (p&lt;0.05). Soy nut intake might improve the nutritional status, anemia, and fatigue in children with ALL.</p>

Table II displays the check results for the homogeneity of the studies included in the meta-analysis. Q and I<sup>2</sup> values were calculated as 237,165 and 98,313 for fatigue, respectively.

Table III presents the effect sizes of the studies investigating the effect of fatigue-reducing interventions on the fatigue levels of children with cancer. The mean effect sizes at 95% significance level were determined as follows: -1.452 for Li et al. (26); 0.560 for Ramezani et al. (27); 7.606 for Kudubeş et al. (12); -0.995 for Lam et al. (28); and 0.544 for Vieira et al. (29) (Table II, Figure 2). As a result, it was determined that the effect of Li et al. (26) on fatigue had a negative large effect size, the effect of Ramezani et al. (27) on fatigue had a positive medium effect size, the effect of Kudubeş et al. (12) on fatigue had a positive large effect size, the effect of Lam et al. (28) on fatigue had a negative large effect size, and the effect of Vieira et al. (29) on fatigue had a positive medium effect size (12,26-29).

To check the publishing bias, Rosenthal and Orwin fail-safe N, Funnel plot map, Duval and Tweedie's trim and fill check, rank correlation, Egger regression, and Begg

and Mazumdar rank correlation test were used. It was determined that for an effect size of 0, five studies were needed when the Rosenthal fail-safe N according to the fatigue level of children with cancer was examined, one study was needed when the Orwin fail-safe N was examined, and two studies were needed when the Duval and Tweedie's trim and fill test was considered. No publication bias was found



**Figure 2.** The effect sizes of the studies investigating the effect of fatigue-reducing interventions on the fatigue levels of children with cancer according to hedges' g test  
CI: Confidence interval

	Q	df	Table X <sup>2</sup> value	p	I <sup>2</sup>
<b>Fatigue</b>	237.165	4	9.488	0.000	98.313

Fatigue	n	Mean Effect Size	SE	Variance	95% CI		Z	p
Li et al. (26)	222	-1.452	0.151	0.023	-1.748	-1.156	-9.614	0.000
Ramezani et al. (27)	56	0.560	0.273	0.074	0.026	1.094	2.054	0.040
Kudubes et al. (12)	80	7.606	0.642	0.412	6.349	8.863	11.856	0.000
Lam et al. (28)	70	-0.995	0.254	0.064	-1.493	-0.498	-3.921	0.000
Vieira et al. (29)	72	0.544	0.240	0.058	0.074	1.015	2.267	0.023
		-0.471	0.104	0.011	-0.675	-0.268	-4.534	0.000

SE: Side effect, CI: Confidence interval, n: Number

	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	Allocation concealment					
Li et al. (26)	-	-	+	+	-	-	-
Ramezani et al. (27)	-	-	-	+	-	-	-
Kudubes et al. (12)	+	+	+	+	-	-	-
Lam et al. (28)	-	-	+	-	-	-	-
Vieira et al. (29)	-	-	-	-	-	-	-

according to Begg and Mazumdar rank correlations tests, Funnel plot graph, or Egger regression analysis ( $p > 0.05$ ).

Four studies describe the sequence of allocations, and two studies describe a blinded study design for participants and personnel. Two studies describe a blinded study design for outcome assessment. All of the studies describe attrition bias, reporting bias and other bias (Table IV).

## Discussion

Due to the rising occurrence of cancer cases and survival rates in children, management of symptoms has become more important. The definition of fatigue, which is one of the most important symptoms impacting the QoL of pediatric oncology patients, has been on the agenda in recent years. Especially, the high rates of fatigue in pediatric oncology patients have attracted attention to this issue and revealed the need for determining fatigue-reducing interventions (8). Therefore, the aim of this meta-analysis study was to determine the effect of fatigue-reducing interventions on the fatigue levels of pediatric oncology patients.

In this meta-analysis study, the total sampling size in the five studies included in the study was 500. The detailed sampling sizes in the five studies analyzed in this study were determined as follows: 222 in Li et al. (26); 56 in Ramezani et al. (27); 80 in Kudubes et al. (12); 70 in Lam et al. (28); and 72 in Vieira et al. (29) (12,26-29).

$Q$ ,  $p$  and  $I^2$  values were used in the Heterogeneity test regarding the studies included in the meta-analysis.  $Q$  values were found to range between 26.916 and 1,033.459, while  $I^2$  values ranged between 81.424% and 99.419%. In the literature, while the statistical significance limit value for  $p$  is accepted as 0.10 for the significance of  $Q$  test in heterogeneity evaluation, if the heterogeneity ratio ( $I^2$ ) is below 25%, heterogeneity is considered non-existent; heterogeneity is low if the ratio is between 25-50%; heterogeneity is moderate if the ratio is between 51-75%; and high if the ratio is greater than 75% (25). According to the heterogeneity test in this study, the effect of fatigue-reducing interventions on the fatigue level of children with cancer yielded a heterogeneous distribution ( $Q=237.165$ ,  $I^2=98.313\%$ ,  $p < 0.001$ ). In line with this finding, the studies included showed a heterogeneous characteristic and the average effect sizes were calculated according to the random effects model.

The effect sizes of studies investigating the effect of fatigue-reducing interventions on the fatigue levels of pediatric oncology patients were found as follows: the effect determined by Li et al. (26) on fatigue was a negative large

effect size (-1.452), the effect determined by Ramezani et al. (27) on fatigue was a positive medium effect size (0.560), the effect determined by Kudubeş et al. (12) on fatigue was a positive large effect size (7.606), the effect determined by Lam et al. (28) on fatigue was a negative large effect size (-0.995), and the effect determined by Vieira et al. (29) on fatigue was a positive medium effect size (0.544) (12,26-29). In the literature, a significant negative correlation was found between fatigue-reducing interventions and fatigue (9-12). It was observed that as the interventions both in this meta-analysis study and in the above discussed studies from the literature increased, the levels of fatigue decreased. Fatigue symptoms are very common in children with cancer because of both the cancer itself and the method of treatment (2,5). Although the symptoms of fatigue are often ignored by health professionals, studies emphasize that diagnosing fatigue and administering fatigue-reducing interventions are important in managing fatigue (8). Activity and exercise regulation, providing appropriate nutritional support, stress management, and regulation of sleep in children with cancer significantly reduce fatigue levels. It is also emphasized that regular training activities on these issues are also effective (12). This is why fatigue-reducing interventions are thought to be effective in reducing fatigue experienced by pediatric oncology patients.

To test the existence of publication bias in this meta-analysis, Rosenthal and Orwin fail-safe  $N$ , Funnel plot chart, Duval and Tweedie's trim and fill test, rank correlation, Egger regression, and Begg and Mazumdar rank correlations tests were employed. These analyses calculate the number of studies that may be missing in a meta-analysis (15,25). It is recommended that using a single method should be avoided and other methods should also be used to determine publication bias. When the Rosenthal error protection coefficient, one of the technical methods, was considered, the number of studies required to bring the effect size to zero was large, which indicated that no publication bias existed in this study. However, when other methods were examined in this study, it was found that this study might include publication bias in the majority of the methods. When analyzing the results of this meta-analysis study, it is recommended that this fact be considered.

## Conclusion

It was determined that fatigue-reducing interventions administered to children with cancer affected the status of fatigue in these children. Due to the small number of studies included in this meta-analysis review and the

likelihood of publishing bias based on this small number, new studies with a high level of evidence concerning the delivery of fatigue-reducing treatments in children with cancer are required to explain the findings. In particular, it is recommended that randomized-controlled experimental studies should be planned and effect sizes and power analysis should be carried out in these studies.

### Implications for Nursing Practice

Fatigue management is very important in children with cancer. Reducing their tiredness helps to boost the child's QoL. Therefore, studies in this area are valuable. Studies investigating efforts to reduce fatigue should be increased. This meta-analysis examines studies that reduce fatigue and shows the power effects of interventions applied to children with cancer.

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### Ethics

**Ethics Committee Approval:** This study was approved by the Institutional Review Board of the University (IRB approval number: 4753-GOA-2019/12-04).

**Informed Consent:** Patient consent is not required.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Concept: A.A.K., Design: A.A.K., Data Collection or Processing: A.A.K., Analysis or Interpretation: M.B., A.A.K., Literature Search: M.B., Writing: A.A.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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### References

1. Di Battista A, Dupuis LL, Cassidy M, et al. Parent attributions about child symptoms related to cancer therapy. *J Pediatr Oncol Nurs* 2017; 34:44-50.
2. Ye ZJ, Zhang Z, Liang MZ, et al. Symptoms and management of children with incurable cancer in mainland China. *Eur J Oncol Nurs* 2019; 38:42-9.
3. Van Cleve L, Muñoz CE, Savedra M, et al. Symptoms in children with advanced cancer: Child and nurse reports. *Cancer Nurs* 2012; 35:115-25.
4. Williams PD, Williams AR, Kelly KP, et al. Symptom checklist for children with cancer. *Cancer Nurs* 2012;35:89-98.
5. Berger AM, Abernethy AP, Atkinson A, et al. NCCN Clinical Practice Guidelines Cancer-related fatigue. *J Natl Compr Canc Netw* 2010; 8:904-31.
6. Hockenberry M, Hinds PS. Fatigue in children and adolescents with cancer: Evolution of a program study. *Semin Oncol Nurs* 2000; 16:261-72.
7. Mock V. Fatigue management: Evidence and guidelines for practice. *Cancer* 2001; 92:1699-707.
8. Piper BF, Cella D. Cancer-related fatigue: definitions and clinical subtypes. *J Natl Compr Canc Netw* 2010; 8:958-66.
9. de Nijs EJ, Ros W, Grijpdonck MH. Nursing intervention for fatigue during the treatment for cancer. *Cancer Nurs* 2008; 31:191-206.
10. Genc RE, Conk Z. Impact of effective nursing interventions to the fatigue syndrome in children who receive chemotherapy. *Cancer Nurs* 2008; 31:312-7.
11. Scruggs B. Fatigue assessment and management. *Home Health Care Management Practice* 2009; 22:16-25.
12. Kudubes AA, Bektaş M, Mutafoğlu K. The effect of fatigue-related education on pediatric oncology patients' fatigue and quality of life. *J Cancer Educ* 2019; 1-12.
13. Chang CW, Mu PF, Jou ST, Wong TT, Chen YC. Systematic review and meta-analysis of nonpharmacological interventions for fatigue in children and adolescents with cancer. *Worldviews Evid Based Nurs* 2013; 10:208-17.
14. Tomlinson D, Diorio C, Beyene J, Sung L. Effect of exercise on cancer-related fatigue: A meta-analysis. *Am J Phys Med* 2014; 93:675-86.
15. Bakioğlu A, Özcan Ş. Meta-Analiz. Nobel Akademi Yayıncılık, Ankara, 2016.
16. Jain V, Sharma R, Singh S. Doing meta-analysis in research: A systematic approach. *Indian J Dermatol Venereol Leprol* 2012; 78:242-50.
17. Dinçer S. Eğitim Bilimlerinde Uygulamalı Meta-Analiz. Pegem Akademi Yayıncılık, Ankara, 2014.
18. Ellis PD. The Essential Guide to Effect Sizes (5th edition). Cambridge University Press, Cambridge-UK, 2012.
19. Cumming G. Understanding the New Statistics. Routledge, Taylor and Francis Group, New York, 2012.
20. Moher D, Liberati A, Tetzlaff J, Altman D. The PRISMA group preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *PLoS Med* 2009; 6:1000097.
21. DeCoster J. Meta-analysis Notes. Institute for Social Science Research University of Alabama, 2009.
22. Zangaro GA, Soeken KL. A meta-analysis of studies of nurses' job satisfaction. *Res Nurs Health* 2007; 30:445-58.
23. Cooper H. Research Synthesis and Meta-Analysis: A Step-By-Step Approach. Sage publications, Thousand Oaks, Kaliforniya, ABD, 2016.
24. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Routledge, UK, 1988.
25. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta analyses. *BMJ* 2003; 327:557-60.
26. Li WH, Ho KY, Lam KKW, et al. Adventure-based training to promote physical activity and reduce fatigue among childhood cancer survivors: A randomized controlled trial. *Int J Nurs Stud* 2018; 83:65-74.

27. Ramezani N, Moafi A, Nadjarzadeh A, Yousefian S, Reisi N, Salehi-Abargouei A. The effect of soy nut compared to cowpea nut on body weight, blood cells, inflammatory markers and chemotherapy complications in children with acute lymphoblastic leukemia: A randomized controlled clinical trial. *Nutr Cancer* Sep 2018; 10:1-9.
28. Lam KKW, Li WHC, Chung OK, et al. An integrated experiential training programme with coaching to promote physical activity, and reduce fatigue among children with cancer: A randomised controlled trial. *Patient Educ Couns* 2018; 101:1947-56.
29. Vieira ML, Fonseca FL, Costa LG, et al. Supplementation with selenium can influence nausea, fatigue, physical, renal, and liver function of children and adolescents with cancer. *J Med Food* 2015; 18:109-17.