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Research

The Effectiveness of Play Therapy on Anxiety, Pain, and Fatigue in Children With Cancer: A Systematic Review and Meta-Analysis

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Abstract

Background: Childhood cancer and its treatments often lead to significant psychological and physical distress, including anxiety, pain, and fatigue. Play therapy has been proposed as a non-pharmacologic, child-centered intervention that can enhance coping and improve well-being during hospitalization. However, evidence regarding its effectiveness remains limited and varies considerably across studies.

Method: This systematic review and meta-analysis was conducted according to the PRISMA guidelines and registered with the International Prospective Register of Systematic Reviews (PROSPERO). Six electronic databases were systematically searched. Randomized controlled trials published between 2014 and 2024 were included based on predefined inclusion criteria (pediatric oncology population, play-based interventions, randomized controlled trial design, and outcomes related to anxiety, pain, or fatigue). Four eligible trials involving 193 children aged 6–18 years undergoing cancer treatment were analyzed. Intervention characteristics (duration, frequency, and delivery), outcome measures, and effect sizes were extracted. A random-effects model was applied to synthesize results across studies.

Results: Play therapy interventions, which included structured play, medical play, and creative therapeutic activities, produced significant improvements in psychological and physical outcomes. Meta-analysis showed a large effect in reducing anxiety (SMD = −2.28, 95% CI [−4.25, −0.31], $p = .0002$) and a moderate effect in reducing pain (SMD = −1.63, 95% CI [−2.08, −1.19], $p < .00001$). Although reductions in fatigue were observed, the findings did not reach statistical significance. Heterogeneity was high, reflecting variation in intervention type, session duration, and measurement tools.

Discussion: Findings from this meta-analysis indicate that play therapy shows promise in reducing anxiety and pain among pediatric oncology patients, while evidence regarding fatigue remains limited. However, these results should be interpreted cautiously due to the small number of eligible trials, substantial heterogeneity in intervention types and outcome measures, and variability in methodological quality. These limitations highlight the need for further large-scale, theory-driven randomized controlled trials with standardized outcome measures focused specifically on anxiety, pain, and fatigue. Incorporating structured play therapy into clinical care—where appropriate—may offer meaningful support for children experiencing treatment-related anxiety, pain, and fatigue.

Keywords: anxiety, cancer, fatigue, pain, pediatric oncology, play therapy, systematic review and meta-analysis

Introduction

According to data from the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), approximately 275,000–400,000 children aged 0–19 are diagnosed with cancer worldwide each year. However, when accounting for undiagnosed and unregistered cases, the actual incidence of childhood cancer is likely higher than reported, underscoring its status as a significant global health issue (IARC, 2025; WHO, 2025).

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The burden of childhood cancer remains substantial across both high-income countries (e.g., the United States, with an estimated 15,000 new cases annually) and low- and middle-income countries (e.g., Turkey, with approximately 2,800 new cases per year). Collectively, childhood cancer accounts for approximately 1.5% of all cancer diagnoses globally (Bhatia et al., 2023; Turkish Ministry of Health, 2016).

Hospitalization is often experienced as traumatic by children due to separation from familiar family routines, exposure to unfamiliar clinical settings, repeated invasive procedures, and a perceived loss of control (Coughtrey et al., 2018; Koukourikos et al., 2015; Liu et al., 2023). Care and treatment interventions are associated with physical and psychosocial challenges in children (Koukourikos et al., 2015). These effects become especially pronounced in children being treated for chronic illnesses, such as pediatric oncology patients. Pediatric oncology patients endure significant physical and psychological challenges due to the nature of cancer and the intensity of its treatments (Coughtrey et al., 2018). Prolonged hospital stays, invasive procedures, and uncertainty about recovery frequently increase anxiety, pain, and fatigue in these children (Ibrahim & Amal, 2020; Liu et al., 2023). In children with chronic illnesses like leukemia, these psychosocial effects are likely to disrupt treatment processes and diminish overall quality of life (Ramdaniati et al., 2023; Thomas et al., 2022).

The use of play during care and treatment processes for hospitalized children is essential for supporting their physical and psychosocial well-being (Koukourikos et al., 2015). Play serves as a natural medium for children to express their emotions, meet their emotional needs, and cope with stress. In this context, play therapy has emerged as a vital intervention to alleviate the psychosocial and physical symptoms experienced by pediatric oncology patients (Ibrahim & Amal, 2020). As emphasized by pediatric psychologists, child-life specialists, and pediatric nurses, therapeutic play is recommended as a structured, child-centered, non-pharmacologic approach that helps reduce treatment-related distress and supports children's coping capacity in oncology settings. The literature highlights the positive effects of play therapy on reducing anxiety, managing pain, and improving fatigue (Godino-Iáñez et al., 2020; Liu et al., 2023; Scarponi & Pession, 2016; Thomas et al., 2022). It has been shown to be effective in managing pre- and post-surgical anxiety, enhancing emotional recovery, and promoting overall well-being (Godino-Iáñez et al., 2020).

There is a notable lack of comprehensive meta-analyses that systematically address the effects of play therapy on anxiety, pain, and fatigue in pediatric oncology patients. This meta-analysis aims to synthesize existing literature to better understand the impact of play therapy on this patient population and to contribute to clinical practice guidelines. Evaluating whether play therapy is an effective intervention to meet both the physical and psychological needs of pediatric oncology patients is of critical importance because anxiety, pain, and fatigue are highly prevalent and distressing treatment-related symptoms in this population, and identifying effective supportive interventions is essential for improving children's well-being.

This study addresses the following fundamental questions.

1. How does play therapy affect anxiety levels in children undergoing cancer treatment?
2. How does play therapy affect pain intensity in children undergoing cancer treatment?
3. How does play therapy affect fatigue levels in children undergoing cancer treatment?

Method

This meta-analysis was conducted in accordance with the PRISMA statement guidelines (Page et al., 2021). The meta-analysis protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD420250650867).

Search Strategy

The literature search was conducted across six major electronic databases—Cochrane Library (including the Cochrane Central Register of Controlled Trials), Medline (EBSCO), ProQuest, PubMed, Scopus, and Web of Science spanning the period from January 1, 2010 to December 31, 2024. The search strategy incorporated a combination of keywords and MeSH terms relevant to the target population ("cancer," "chemotherapy," "child, "hematology," "osteosarcoma," "leukemia"), intervention type ("art therapy," "drawing," "filial therapy," "occupational therapy," "play-based," "play therapy"), outcomes ("anxiety," "depression," "fatigue," "pain," "stress," "symptoms") and study type ("controlled clinical trial," "randomized controlled trial") (see Supplementary Files —Table S1).

To refine the search, logical operators were used to combine relevant terms, and the search strategies were adjusted for each database. Additionally, reference lists of the included studies were manually reviewed to find any further relevant studies. The search criteria and eligibility filters were clearly defined using the PICOS (Population, Intervention, Comparison, Outcomes, Study design) framework to ensure accuracy and consistency.

Eligibility Criteria

Studies were eligible for inclusion if they met the following criteria:

1. Study Design: Randomized controlled trials (RCTs) published in English in peer-reviewed journals between January 1, 2014 and December 31, 2024.
2. Population: Children aged 3–18 years diagnosed with cancer and undergoing treatment.
3. Intervention: Therapeutic play interventions specifically designed to reduce anxiety in this population.
4. Delivery Mode: At least six face-to-face play therapy interventions that included feedback.
5. Comparison Group: Control groups receiving passive conditions, such as standard care or routine interventions.
6. Outcome Measures: Use of standardized anxiety, fatigue, and pain assessment tools.

Studies were excluded if they met any of the following conditions:

1. Published as conference proceedings or abstracts without full-text availability.
2. Duplicate publications of the same study.
3. Provided incomplete data or lacked sufficient statistical analysis (e.g., protocol papers, feasibility studies).
4. Examined play therapy modalities of animal-assisted therapy or music therapy.
5. Investigated massage therapy or muscle relaxation techniques without a play-based component.
6. Focused on mindfulness, cognitive-behavioral, or imagination-based interventions.
7. Utilized technology-based interventions (e.g., virtual reality, mobile apps, tablets, websites).
8. Assessed therapeutic play activities used solely for procedural distraction (e.g., intravenous catheter insertion, lumbar puncture).

Study Selection and Data Extraction

Articles identified through searches across six databases were imported into EndNote Software (Version 21.5) for reference management. The EndNote platform was also utilized to systematically verify records across databases, merge results, and eliminate duplicates.

Following this process, three independent researchers screened the titles and abstracts of the remaining studies. Studies that did not meet the inclusion and exclusion criteria were removed. In cases of disagreement, the authors resolved discrepancies through discussion.

Next, full-text articles were retrieved and assessed in detail based on the predefined eligibility criteria. Any disagreements at this stage were resolved through discussion among the researchers. Data extracted from the included trials were recorded by independent authors using the data extraction form, including study information (authors, year, and place of publication), study design, sample characteristics (age, diagnosis, and sample size), description of intervention (duration of intervention, number of sessions and session durations, and control group), outcome measures (tools and scales used to assess anxiety), assessment time (assessment and follow-up times), and results (p values). The complete list of excluded studies along with the reasons for exclusion is provided in the supplementary file (see Supplementary Files—Table S2).

Assessment of Bias in Included Studies

The risk of bias in the randomized controlled trials included in the meta-analysis was assessed using the Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). This tool evaluates bias across five key domains, as outlined in the Cochrane Handbook: (a) bias arising from the randomization process, (b) bias due to deviations from intended interventions, (c) bias resulting from missing outcome data, (d) bias in outcome measurement, and (e) bias in the selection of the reported result.

Three independent authors, all of whom are trained in systematic review methodology, have previous publications in meta-analysis, and are experienced in the appraisal of randomized controlled trials (RCTs), systematically categorized each study into one of three risk levels: low risk of bias, high risk of bias, or some concerns. Across four out of five domains, four studies were deemed to have a low risk of bias. However, in domain two (bias due to the effect of assignment to the intervention), concerns arose due to the inherent challenge of blinding intervention providers. Following thorough evaluation among researchers, this was recognized as an intrinsic limitation of the intervention rather than a methodological weakness. Consequently, the studies were ultimately assessed as having a low risk of bias and high methodological quality (Figure 1).

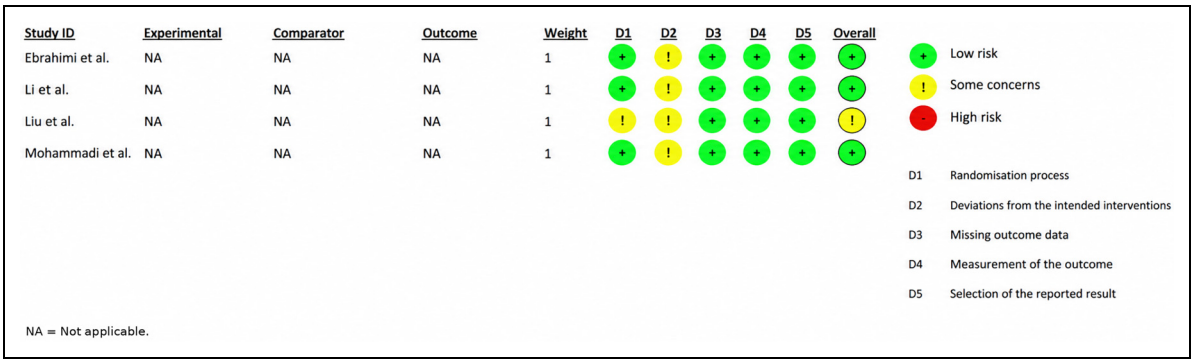
Data Analysis

Meta-analysis was performed using RevMan software (Version 5.4). Continuous outcome measures were analyzed using standardized mean difference (SMD) to account for differences in measurement scales between studies. A random-effects model was applied due to the methodological and clinical diversity observed among the included studies (e.g., differences in intervention type, duration, and population characteristics).

Heterogeneity between studies was assessed using the chi-squared (χ^2) test and the I^2 statistic. An I^2 value of 25% was considered low, 50% moderate, and 75% or higher indicated substantial heterogeneity. To explore potential sources of heterogeneity, subgroup analyses were performed based on intervention duration (short-term vs. long-term interventions).

Figure 1

Risk of bias assessment of included studies using the RoB 2 tool.



Note. RoB 2 = Version 2 of the Cochrane risk-of-bias tool for randomized trials.

In addition, a sensitivity analysis was performed to assess the effect of individual studies on the overall results. Funnel plots and Egger's test were also planned to assess potential publication bias, although the small number of included studies limited the interpretability of these methods.

Ethics Statement

This study did not require Institutional Review Board approval because it is a meta-analysis of previously published studies. All data used in this review were obtained from publicly available sources, and no individual patient-level data were accessed.

Findings

Study Selection

A total of 3,544 studies were identified through the systematic review process from the databases PubMed, Cochrane Library, ProQuest, Scopus, Web of Science, and MEDLINE. In addition, 156 trials were identified manually from other sources such as Google Scholar. A total of 3,700 records were included in the review.

After removing duplicate records ($n = 139$), 3,561 studies were included in the review. As a result of the title and abstract screening, 3,152 studies were eliminated based on their titles, and 364 studies were eliminated based on their abstracts. At the end of this screening process, 45 full-text articles were selected for a detailed review.

During the full-text review, 41 studies were excluded due to sample mismatch ($n = 16$), inappropriate study design ($n = 8$), type of intervention ($n = 15$), and inappropriate outcome measures ($n = 2$). Finally, four randomized controlled trials that met all inclusion criteria were selected for qualitative and quantitative synthesis (meta-analysis). The study selection process is visualized in Figure 2 using the PRISMA 2020 flowchart.

Study Characteristics

This meta-analysis includes four randomized controlled trials that investigated the effects of play therapy applications on anxiety levels in children undergoing cancer treatment (Ebrahimi et al., 2019; Li et al., 2023; Liu et al., 2023; Mohammadi et al., 2021). A total of 193 children were included across four randomized controlled trials (96 in intervention groups and 97 in control groups), as detailed in Table 1. The included studies were published between 2019, 2021, and 2023; two studies were conducted in Iran, and two studies were conducted in China. The participants were aged between 6 and 18 years, and they were all children with cancer who were receiving chemotherapy. The diagnoses included acute leukemia, osteosarcoma, and other solid tumors.

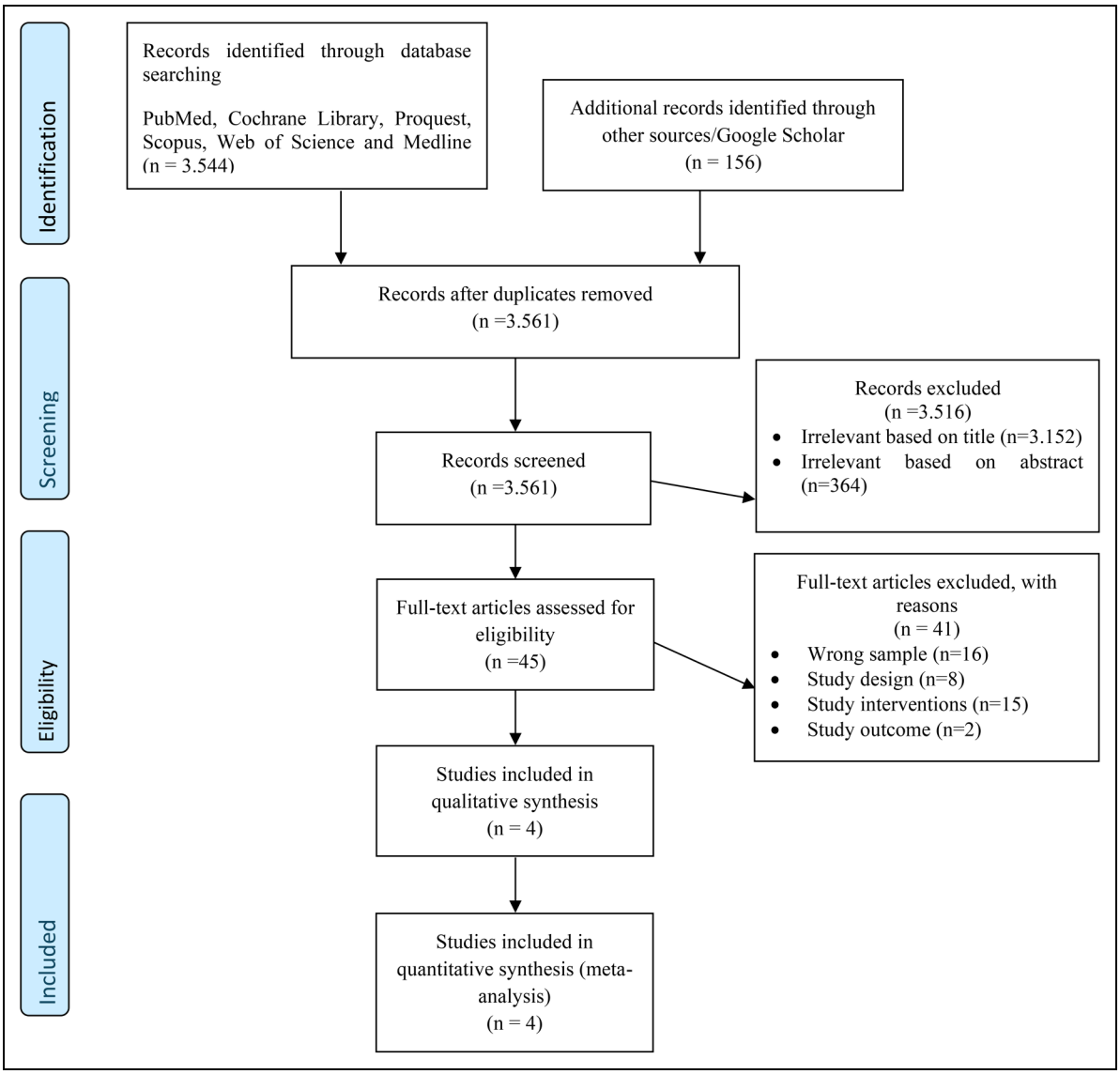
Pre-intervention (baseline) measurements were carried out in all the trials, and no significant differences were found between the experimental and control groups. Post-intervention measurements were usually taken immediately after application or within a few days at the latest. Three trials also included follow-up measurements, which ranged from 1 hr to 4 weeks. However, only the measurements after the first intervention were included in the meta-analysis. The control groups only received standard medical care. None of the four trials was structured according to a theoretical model. The detailed characteristics of the trials are shown in Table 1.

Characteristics of Interventions

Different types of play therapy approaches were used in the included studies. Ebrahimi et al. (2019) applied filial therapy training to mothers once a week for a total of 10 weeks. These trainings taught emotional reflection, limit setting, and child-directed play skills based on the Child–Parent Relationship Therapy model, which focuses on the child–parent relationship. Mohammadi et al. (2021)

Figure 2

Flowchart of the study selection based on PRISMA guidelines.



used a total of eight sessions of play-based occupational therapy over 2 weeks. In this intervention, the children chose the games they preferred, and the therapists were actively involved in the games. Li et al. (2023) used child life-based play therapy, delivered twice a week for 8 weeks. These therapies included medical games, role play, relaxation techniques, and social-emotional support activities. In the study conducted by Liu et al. (2023), group drawing art therapy was used twice a week for 8 weeks. The therapies consisted of warm-up activities, free-theme drawing, and sharing sessions (Table 1).

The studies used different measures to assess anxiety levels: Depression Anxiety Stress Scale–21 (DASS-21), Children's Depression Inventory (CDI), Screen for Child Anxiety Related Emotional Disorders (SCARED), Pediatric Patient-Reported Outcomes Measurement Information System–Anxiety Short Form (Pediatric PROMIS-Anxiety), Faces Anxiety Scale (FAS), and Therapy-Related Symptom Checklist (TRSC). The interventions lasted from 2 weeks to 8 weeks, and the sessions lasted from 30 to 100 min. The number of sessions was usually 8. Some studies also assessed secondary variables such as pain, fatigue, participation in daily life, and self-acceptance. In all four trials, there was a significant reduction in anxiety in the play therapy groups (Table 1).

Table 1.

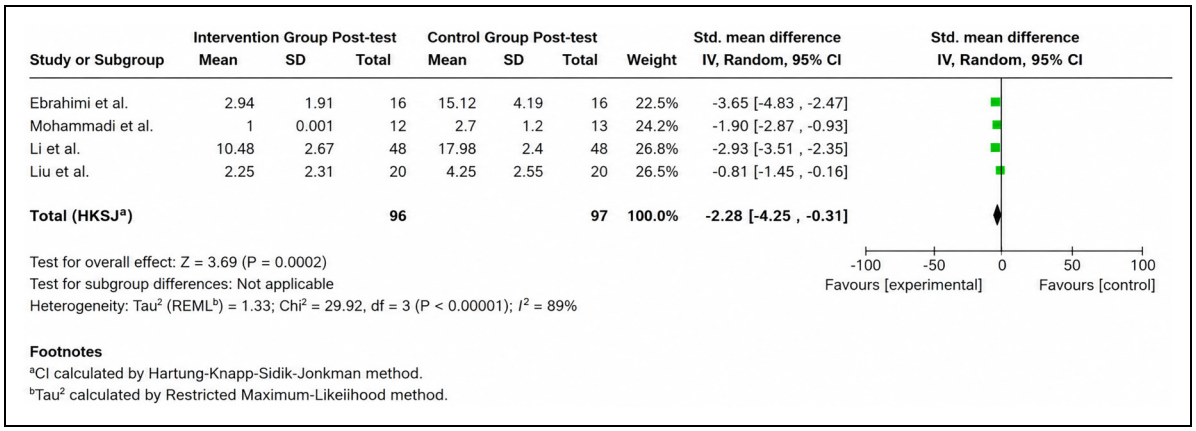
Characteristics of Included Studies

Author (year), country	Study design	Characteristics of participants	Interventions	Outcome measures	Assessment time	Results
Ebrahimi et al. (2019), Iran	RCT parallel	Children aged 6–12 diagnosed with cancer; $n = 32$ (16 per group)	*Intervention group:* filial therapy, 10 weekly sessions; mothers applied play therapy at home with supervision. *Control group:* routine care + individual counseling sessions	- CDI - DASS-21 - WBFPRS	Baseline and immediately after 10-week intervention	Significant reduction in depression, anxiety, and stress in mothers ($p < .001$); significant decrease in children's depression ($p < .001$).
Mohammadi et al. (2021), Iran	RCT parallel	Children aged 7–12 undergoing chemotherapy; $n = 25$ (12 intervention, 13 control)	*Intervention group:* play-based occupational therapy, eight sessions over 2 weeks. *Control group:* traditional OT services on demand	- TRSC - FAS - VAS-F - WBFPRS - CPAS-P	Baseline and immediately after the intervention	Significant improvement in symptom management and daily activity participation ($p < .001$); reduced pain, fatigue, and anxiety scores.
Li et al. (2023), China	RCT parallel	Children aged 8–14 with acute leukemia undergoing chemotherapy; $n = 96$ (48 per group)	*Intervention group:* child life intervention, 8 weeks, twice weekly, 30–40 min sessions; medical play, role-play, relaxation, and support activities. *Control group:* routine chemotherapy-related care	- Pediatric PROMIS - SDSC	Baseline and 3 days post-intervention	Significant improvement in pain, anxiety, fatigue, and sleep disturbance ($p < .001$); no significant change in excessive somnolence.
Liu et al. (2023), China	RCT parallel	Children and adolescents aged 7–18 diagnosed with osteosarcoma; $n = 40$ (20 per group)	*Intervention group:* group drawing art therapy, eight sessions over 8 weeks, 90–100 min each. *Control group:* routine osteosarcoma care	- SCARED - SAQ	Baseline and after the final session	Significant reduction in anxiety ($p < .05$); significant increase in self-acceptance and self-evaluation scores ($p < .001$).

Note. RCT = randomized controlled trial; CDI = Children's Depression Inventory; DASS-21 = Depression Anxiety Stress Scale–21; WBFPRS = Wong-Baker Faces Pain Rating Scale; OT = occupational therapy; TRSC = Therapy-Related Symptom Checklist; FAS = Faces Anxiety Scale; VAS-F = Visual Analog Scale–Fatigue; CPAS-P = Children Participation Assessment Scale; PROMIS = Patient-Reported Outcomes Measurement Information System; SDSC = Sleep Disturbance Scale for Children; SCARED = Screen for Child Anxiety Related Emotional Disorders; SAQ = Self-Acceptance Questionnaire.

Figure 3.

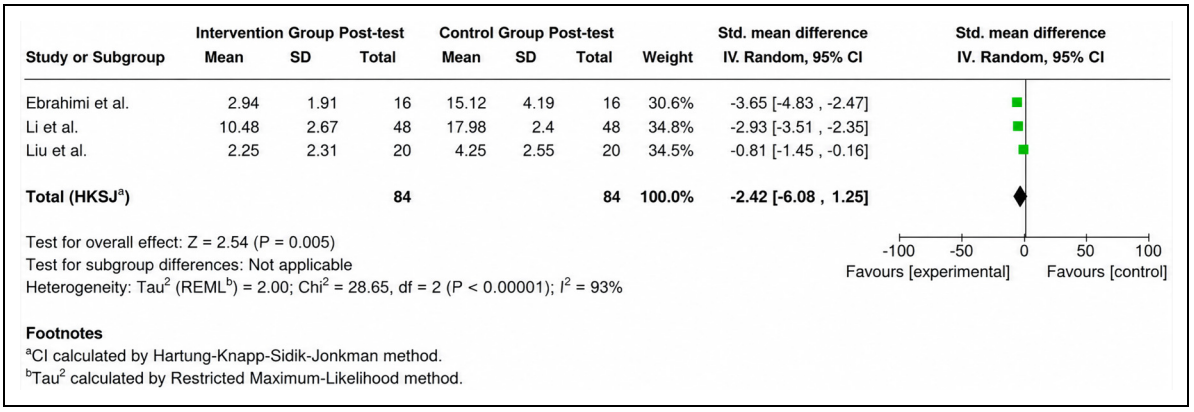
Meta-analysis of the effect of play therapy on anxiety levels in children diagnosed with cancer.



Note. CI = confidence interval; IV = inverse variance.

Figure 4.

Meta-analysis of the effect of long-term play therapy on anxiety levels in children diagnosed with cancer.



Note. CI = confidence interval; IV = inverse variance.

The Effect of Play Therapy on Anxiety in Children Diagnosed With Cancer

In the overall analysis, which included four studies, it was observed that the use of play therapy significantly reduced anxiety levels in children undergoing cancer treatment. The results showed a significant reduction in anxiety immediately after the play therapy intervention (SMD: −2.28, 95% CI [−4.25, −0.31], $p = .0002$). In addition, a high degree of overall heterogeneity was observed ($I^2 = 89\%$) (Figure 3).

The Effect of Long-Term Play Therapy on Anxiety in Children Diagnosed With Cancer

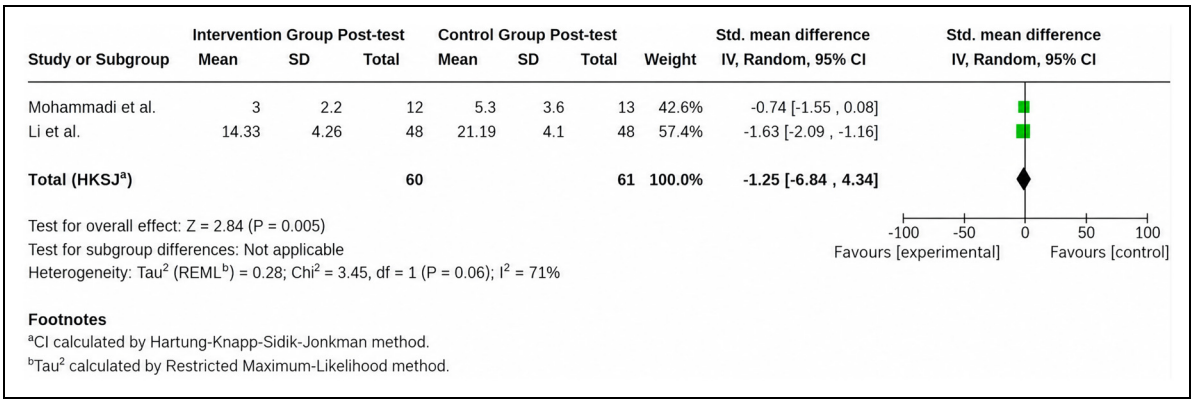
This subgroup analysis included three studies that implemented long-term intervention programs. The analysis re-evaluated the effect of play therapy on anxiety levels. The findings showed a reduction in anxiety following long-term play therapy interventions; however, this effect was not statistically significant (SMD: −2.42, 95% CI [−6.08, 1.25], $p = .005$). Substantial heterogeneity was present across studies ($I^2 = 93\%$) (Figure 4).

The Effect of Play Therapy on Fatigue in Children Diagnosed With Cancer

This analysis included two studies that examined the effect of play therapy on fatigue levels in children undergoing cancer treatment. The results indicated a non-significant reduction in fatigue levels among children receiving play therapy (SMD: −1.25, 95% CI [−6.84, 4.34], $p = .20$). A moderate level of heterogeneity was detected ($I^2 = 71\%$) (Figure 5).

Figure 5.

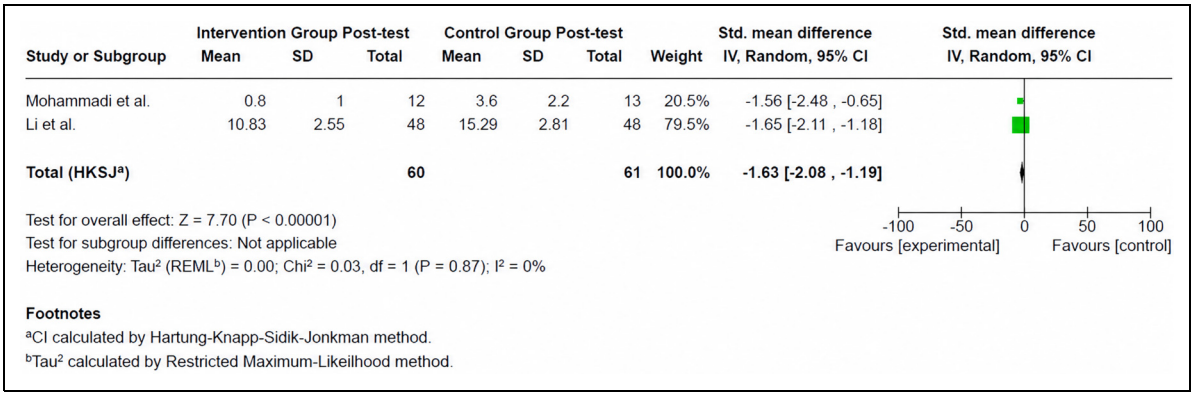
Meta-analysis of the effect of play therapy on fatigue levels in children diagnosed with cancer.



Note. CI = confidence interval; IV = inverse variance.

Figure 6.

Meta-analysis of the effect of play therapy on pain levels in children diagnosed with cancer.



Note. CI = confidence interval; IV = inverse variance.

The Effect of Play Therapy on Pain in Children Diagnosed With Cancer

In this analysis evaluating pain levels, data from two studies were used. The results showed a statistically significant reduction in pain among children who received play therapy interventions (SMD: −1.63, 95% CI [−2.08, −1.19], $p < .00001$). The heterogeneity in this analysis was negligible ($I^2 = 0\%$), indicating methodological consistency across studies (Figure 6).

Discussion

This systematic review and meta-analysis identified that play therapy interventions resulted in a significant reduction in children's anxiety levels while being treated for cancer. These finding are consistent with previous systematic reviews in other populations. Godino-Iáñez et al. (2020) reported that play therapy supported the psychological well-being of hospitalized children. Similarly, a recent meta-analysis by Zhang et al. (2024) demonstrated that play-based distraction interventions significantly reduced anxiety levels in children undergoing medical procedures (Zhang et al., 2024). Play therapy is not just an activity where children play games, but a structured therapeutic technique to understand the emotional difficulties the child is experiencing, help them express them, and guide this process toward recovery. In this respect, play therapy provides a safe space that allows the child to overcome their psychological defenses and helps them to cope with traumatic experiences (Lin & Bratton, 2015). The effectiveness of the interventions in our study could be attributed to the fact that the applications were structured according to this process.

In subgroup analyses, a more significant reduction in anxiety was observed in studies using subjective measures. However, the heterogeneity in this subgroup is quite high ($I^2 > 85\%$). This may be due to differences in intervention content, session duration, practitioner profiles, and age group differences (Higgins et al., 2022). For example, in some studies that were not included but were assessed within the scope of the systematic review, the duration of application was limited to only one or two sessions (Gürcan & Atay Turan, 2021; Piasai et al., 2018). It is likely that these short applications make it difficult for the therapeutic effect to become statistically significant.

In the analyses of fatigue levels, although a positive change was observed in the experimental groups, this difference was not found to be statistically significant. This finding may be related to the fact that fatigue is a multidimensional symptom (physical, psychological, and emotional) and is difficult to define, especially in children (Coughtrey et al., 2018). In addition, the variety of tools used to measure fatigue makes it difficult to combine results.

In the analysis conducted on pain levels, it was found that play therapy applications statistically significantly reduced children's pain perception. This result shows that non-pharmacological approaches could also be effective in the management of physical symptoms (Deshpande & Shah, 2019; Paes et al., 2021). Mechanisms such as emotional relaxation of the child, reduction of stress hormones, and changes in attentional focus through play therapy could reduce physical complaints. These findings indicate that play therapy is an effective intervention tool at both psychological and psychosomatic levels (Lin & Bratton, 2015; Thomas et al., 2022).

Clinical Implications for Pediatric Oncology Nursing

The findings of this meta-analysis provide important clinical implications for pediatric oncology nursing practice. Anxiety, pain, and fatigue are among the most prevalent and distressing symptoms experienced by children undergoing cancer treatment. Pediatric oncology nurses, who maintain continuous and close contact with patients throughout hospitalization, play a critical role in the assessment and management of these symptoms. Based on these findings, pediatric oncology nurses should consider incorporating structured therapeutic play into routine symptom management practices. Integrating developmentally appropriate therapeutic play interventions into nursing care plans may contribute to reducing treatment-related distress, supporting emotional regulation, and improving the overall hospital experience for children with cancer. In this context, supporting pediatric oncology nurses to promote and facilitate therapeutic play techniques is essential for strengthening holistic, child-centered oncology care.

Strengths, Limitations, and Future Directions

This systematic review and meta-analysis fills an important gap by synthesizing the limited number of randomized controlled trials that have investigated the effects of play therapy on reducing anxiety in children with cancer. The main strengths of the review include the inclusion of only randomized controlled trials, the inclusion of both subjective and objective measures of anxiety, and the overall high methodological quality.

However, the limited number of trials and sample sizes limit the generalizability of the results. In addition, there was high heterogeneity due to differences in intervention duration, content and measurement tools, and other psychological outcomes such as depression, anxiety, and sleep disturbance were not adequately addressed.

It is recommended that future studies develop structured play therapy protocols, that these protocols be based on theoretical foundations, and that randomized controlled trials with larger samples and long-term follow-up be included. In particular, training and certification of health professionals (e.g., pediatric nurses, child development specialists) in play therapy is essential to improve the quality of practice. Incorporating the perspectives and clinical experience of play therapists and child life specialists may further enhance the feasibility and child-centeredness of these structured protocols. Ensuring diversity of interventions and standardizing measurement tools will also facilitate comparability of different practices.

Summary

This meta-analysis and systematic review shows that play therapy applications are particularly effective in reducing anxiety and pain levels in children undergoing cancer treatment. Although the positive change observed in fatigue levels did not reach statistical significance, it shows that the therapeutic process could contribute to children's overall well-being.

The use of structured play therapy processes to reduce anxiety allows children to gain space for emotional expression, develop coping skills, and have a more positive hospital experience. In this context, play therapy as a non-pharmacological, child-centered, and cost-effective intervention should be considered and supported in pediatric oncology clinics.

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Ethical Considerations

As this study is a systematic review and meta-analysis of previously published data, ethical approval was not required.

Informed Consent

As this study is a systematic review and meta-analysis of previously published data, informed consent was not required.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data Availability Statement

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Supplemental Material

Supplemental material for this article is available online.

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