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MANAGEMENT OF SYMPTOM CLUSTERS IN PEDIATRIC ONCOLOGY: A NARRATIVE REVIEW

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Abstract

Background: Symptom clusters, particularly fatigue–pain–sleep disturbance, are highly prevalent in pediatric oncology and significantly impair quality of life, emotional well-being, and treatment adherence. Despite increasing recognition of these symptom interactions, management approaches remain predominantly symptom-specific.

Objective: To critically synthesize recent evidence published between 2018 and 2025 regarding the mechanisms and management strategies of symptom clusters in children with cancer.

Methods: A narrative review was conducted using PubMed, Scopus, CINAHL, and Google Scholar databases. A total of 412 records were identified, of which 61 full-text articles were screened and 28 studies met the inclusion criteria and were included in the review.

Results: The findings suggest that symptom clusters share common inflammatory and neuropsychological pathways. Non-pharmacological interventions including cognitive behavioral therapy (CBT), progressive muscle relaxation (PMRT), guided imagery (GI), and digital health interventions demonstrated moderate effectiveness across multiple symptoms. Multimodal and nurse-led interventions showed improved outcomes compared with single-symptom management approaches.

Conclusion: Symptom cluster–based care appears to be more effective than isolated symptom management in pediatric oncology. However, heterogeneity in study design and outcome measures limits generalizability. Further pediatric-specific randomized controlled trials are required to strengthen the evidence base.

Keywords: Pediatric Oncology; Symptom Clusters; Cancer-related Fatigue; Pain Management; Sleep Disturbance; Cognitive Behavioral Therapy; Nurse-led Interventions; Quality of Life.

INTRODUCTION

Children undergoing cancer treatment frequently experience multiple concurrent symptoms that interact synergistically, resulting in symptom clusters rather than isolated symptoms. Symptom clusters have become an important area of concern in pediatric oncology because of their significant impact on physical functioning, emotional well-being, quality of life, and treatment adherence. Among these, the fatigue–pain–sleep disturbance cluster is the most commonly reported and has been recognized as one of the major contributors to symptom burden in children with cancer [1,8].

Recent advances in pediatric oncology research have shifted attention toward cluster-based symptom management approaches, recognizing that multiple symptoms may share common underlying biological and psychological mechanisms. Emerging evidence suggests the involvement of pro-inflammatory cytokine activation, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α),

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hypothalamic–pituitary–adrenal (HPA) axis dysregulation, neuroendocrine alterations, and treatment-related toxicity in the development and persistence of symptom clusters [2,3].

Despite increasing recognition of symptom clusters and their underlying mechanisms, current clinical management remains largely symptom-specific and often fails to address the interconnected nature of symptom experiences in pediatric patients. Consequently, integrated and multidimensional approaches are increasingly being explored to improve patient outcomes.

Therefore, this narrative review aims to evaluate and critically synthesize current evidence regarding symptom cluster mechanisms and management strategies in pediatric oncology, with particular emphasis on non-pharmacological and nurse-led interventions.

METHODS

Ethical approval and informed consent were not required because this study was a narrative review based exclusively on previously published literature. No external funding or financial support was received for this study.

Search Strategy

A structured narrative review was conducted to evaluate recent evidence regarding symptom cluster mechanisms and management strategies in pediatric oncology. Literature searches were performed using PubMed, Scopus, CINAHL, and Google Scholar databases.

The search strategy included the following terms: (pediatric OR child*) AND (cancer OR oncology) AND (symptom cluster OR fatigue pain sleep) AND (intervention OR management)

Eligibility Criteria

Inclusion criteria:

• Studies published between 2018 and 2025
• Pediatric population (≤18 years)
• Studies focusing on symptom clusters or multi-symptom interventions

Exclusion criteria:

• Adult-only studies
• Non-interventional studies
• Studies not focused on symptom cluster–based management

Study Selection

Titles and abstracts identified through database searching were screened for relevance. Eligible articles were selected for full-text assessment and final inclusion. The study selection process followed a PRISMA-based approach to improve transparency and consistency in article selection.

A total of 412 records were identified during the initial search process. After screening and eligibility assessment, 28 studies were included in the final narrative review.

Data Synthesis

Data from included studies were narratively synthesized with emphasis on symptom cluster mechanisms, intervention strategies, and reported clinical outcomes. Due to variability in study design and outcome reporting, statistical meta-analysis was not performed.

Results

TOPIC AREAS AND DISCUSSION

Common Symptom Clusters in Pediatric Oncology

The reviewed evidence consistently identified symptom clustering as a major concern in pediatric oncology. Among the reported clusters, fatigue–pain–sleep disturbance emerged as the most frequently observed combination and was associated with reduced physical functioning, impaired emotional well-being, and decreased treatment adherence [2]; [3]. In addition to physical symptom groupings, psychological symptom clusters involving anxiety, depression, and emotional distress were frequently described and often overlapped with physical symptom burden.

Pathophysiological Mechanisms of Symptom Clusters

Current evidence suggests that symptom clusters may develop through interconnected biological and psychological pathways. Several studies identified inflammatory processes as an important contributing mechanism, particularly elevated cytokine activity involving interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which were associated with fatigue and sleep disturbances [4]. Additional mechanisms including neuroendocrine dysregulation, hypothalamic–pituitary–adrenal axis alteration, circadian rhythm disruption, and treatment-related toxicity were also reported. Psychological stress appeared to further intensify symptom

perception, particularly among adolescent patients.

Management Approaches for Symptom Clusters

Non-Pharmacological Interventions

Across the reviewed literature, non-pharmacological approaches demonstrated broad applicability for symptom cluster management. Cognitive behavioral therapy (CBT) was associated with improvement in fatigue, sleep disturbance, and emotional distress outcomes [5]. Progressive muscle relaxation (PMRT) and guided imagery (GI) demonstrated beneficial effects on fatigue and anxiety outcomes [1]. Music therapy interventions were associated with reduced pain intensity and emotional distress [6]. Digital health interventions improved symptom monitoring and facilitated patient engagement during treatment [7].

Pharmacological Management

Pharmacological approaches remained essential for management of severe pain and individual symptom control. However, available evidence suggested limited effectiveness of pharmacological strategies when addressing multiple co-occurring symptoms simultaneously, emphasizing the need for integrated treatment approaches [4].

Nurse-Led Symptom Management

Several studies highlighted the importance of nurse-led interventions in improving symptom cluster recognition and management. Structured symptom assessment tools, patient education, and early supportive care approaches demonstrated improved symptom monitoring and timely intervention among pediatric oncology populations [8].

Comparative Evidence Across Intervention Strategies

Comparative findings across included studies suggested that multimodal approaches combining behavioral and pharmacological strategies may provide broader symptom improvement than single-intervention approaches. CBT-based interventions appeared to demonstrate the most comprehensive effects across symptom domains, whereas PMRT and guided imagery appeared useful as adjunctive supportive interventions.

Overall Interpretation of Current Evidence

Collectively, the reviewed evidence supports a transition from isolated symptom management toward symptom cluster–based care models in pediatric oncology. Nevertheless, heterogeneity in intervention design, outcome measures, and study populations limits direct comparison across studies and highlights the need for further pediatric-specific evidence.

PRISMA Flow Summary

Records identified through database searching (n=412) → Full-text articles assessed for eligibility (n=61) → Studies included in narrative review (n=28)

Table 1: Summary of Included Studies

Author	Year	Sample	Intervention	Outcomes
Yeh CH et al. [2]	2020	Pediatric oncology patients	Symptom assessment	Fatigue–sleep–pain correlation
Baggott C et al. [3]	2019	Children with cancer	Symptom cluster analysis	Cluster identification
van Dijk-Lokkart EM et al. [5]	2019	Pediatric cancer	CBT	Reduced fatigue, improved sleep
Uggla L et al. [6]	2018	Hospitalized children	Music therapy	Reduced pain, distress
Wu HS et al. [7]	2021	Cancer patients	Digital intervention	Symptom monitoring improvement
Hooke MC et al. [8]	2021	Pediatric oncology	Nurse-led care	Improved symptom outcomes

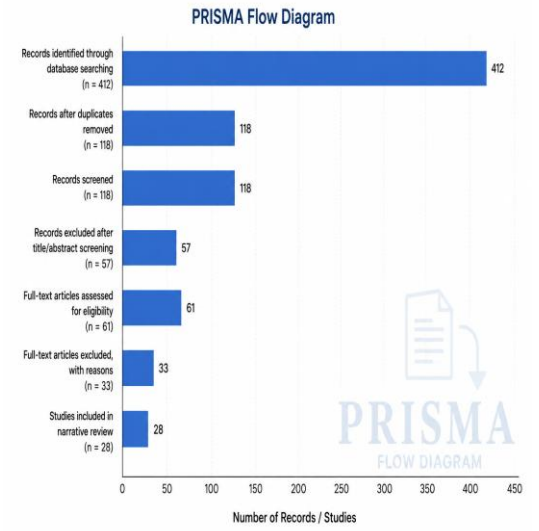

Figure 1: Graph of Included Studies

Table 2: Detailed Search Strategy Table

Database	Search Terms	Filters	Records Retrieved	Records Included
PubMed	(pediatric OR child*) AND cancer AND symptom cluster	2018–2025, English	145	10
Scopus	pediatric oncology AND symptom management	2018–2025	112	7
CINAHL	children with cancer AND symptom clusters	2018–2025	78	5
Google Scholar	pediatric oncology symptom cluster intervention	2018–2025	77	6

Quality Appraisal: The methodological quality of included studies was assessed using appropriate critical appraisal tools. Randomized controlled trials were evaluated using the Cochrane Risk of Bias framework, observational studies using the JBI Critical Appraisal Checklists, and mixed-method studies using MMAT criteria. Most studies demonstrated moderate methodological quality; common limitations included small sample sizes, single-center recruitment, and heterogeneity of outcome measures.

DISCUSSION

This narrative review highlights the growing importance of symptom cluster–based management in pediatric oncology. The reviewed evidence suggests that symptom clusters are influenced by interconnected biological, psychological, and treatment-related mechanisms, upporting the need for integrated approaches rather than isolated symptom management.

Among the available interventions, non-pharmacological approaches demonstrated broad applicability across multiple symptom domains. Cognitive behavioral therapy (CBT), progressive muscle relaxation (PMRT), guided imagery (GI), music therapy, and nurse-led supportive strategies were repeatedly associated with improvements in symptom burden and patient well-being. However, considerable variability in intervention protocols, outcome measures, and study designs limited direct comparison across studies.

Recent literature increasingly supports personalized symptom management based on developmental stage, treatment characteristics, and individual symptom profiles. Digital health–based monitoring and supportive care interventions represent emerging strategies with potential to improve symptom recognition and continuity of care; however, further validation in pediatric populations remains necessary.

The evidence indicates that symptom clusters are not merely co-occurring symptoms but represent interconnected biological and psychosocial phenomena. Inflammatory cytokines, neuroendocrine dysregulation, treatment toxicity, and psychological stress collectively contribute to symptom burden. Compared with single-symptom interventions, multimodal approaches such as CBT combined with supportive nursing care appear to produce broader and more sustained improvements. However, substantial heterogeneity across studies limits direct comparison. Few studies employed standardized symptom-cluster outcome measures, reducing the strength of conclusions. The current evidence, therefore, supports cluster-based assessment and management while highlighting the need for stronger pediatric-specific evidence.

Implications for Practice

- Implement routine symptom cluster–based assessment in pediatric oncology settings
- Integrate CBT, PMRT, and guided imagery into supportive care plans
- Utilize digital health tools to support symptom monitoring and communication
- Strengthen nurse-led assessment, education, and symptom management programs

Future Research Directions

Future studies should focus on large multicenter randomized controlled trials, development of standardized symptom-cluster assessment tools, longitudinal evaluation of symptom trajectories, integration of biomarker-based research, and validation of digital-health and nurse-led interventions across diverse pediatric oncology populations.

Limitations

This review has several limitations. First, the narrative review design limits quantitative comparison across studies. Second, the available

evidence included a limited number of pediatric randomized controlled trials. Third, heterogeneity in intervention protocols, study populations, and outcome measures restricted direct comparison and generalizability of findings.

CONCLUSION

This narrative review highlights the importance of symptom cluster–based management in pediatric oncology. The reviewed evidence suggests that multimodal approaches integrating non-pharmacological and supportive care strategies may improve symptom outcomes more effectively than isolated symptom-focused interventions. Nurse-led approaches and structured symptom assessment appear to support early recognition and comprehensive management of symptom burden. However, variability across available studies limits direct comparison and broad generalization of findings. Overall, adopting integrated and patient-centered symptom management approaches may strengthen supportive care practices and improve the quality of pediatric oncology care.

Conflict of Interest

The authors declare no conflict of interest.

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