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Music Therapy and Psychoneuroimmunological Markers in Children With Chronic Disease: A Systematic Review

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Abstract: *Stress conditions in children with chronic disease affect psychoneuroimmunological markers. One of the mind-body modalities commonly used in pediatric chronic disease is music therapy. This systematic aim was evaluating the effect of music therapy on psychoneuroimmunological markers among children with chronic disease. Articles published between March 31, 2014, and April 1, 2023, were retrieved from five databases: Scopus, PubMed, Web of Science, EBSCOhost, and ProQuest. Rayyan, an AI-powered tool for systematic literature reviews, facilitated paper selection. Studies were screened based on pre-defined inclusion and exclusion criteria. The PRISMA checklist guided selection, and the JBI Critical Appraisal for quality assessment. Data analysis employed a descriptive approach. A total of 15 articles published between 2014 and 2023 were included in this review. 10 (66,7%) of 15 studies assessed the effectiveness of music therapy on psychological and physiological responses. Meanwhile, five (33,3%) studies assessed the effectiveness of music therapy on neuroimmunological markers. Among the five studies, one did not exhibit a statistically significant impact. In contrast, the remaining four studies displayed a significant impact of music therapy on neuroimmunological markers. The most studies assessed the impact of music therapy on psychological and physiological responses, but only a small proportion assessed the effectiveness of music therapy on neuroimmunological markers. Music therapy can be considered a safe and generally well-accepted intervention in pediatric health care to manage psychoneuroimmunological markers.*

Keywords: *child, chronic disease; music therapy, psychoneuroimmunology*

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INTRODUCTION

Chronic diseases have emerged as the leading cause of mortality on a global scale, exhibiting a rising prevalence across diverse age groups, genders, and ethnic backgrounds (Anderson & Durstine, 2019). Chronic disease is a health problems that last for three months or longer, interfere with the child's normal activities, and require repeated hospitalization, and home health care (CDC, 2021; King, 2017). Common types of chronic diseases in children include asthma, cystic fibrosis, epilepsy, congenital heart disease, diabetes mellitus, depression, and developmental disabilities such as Attention Deficit Hyperactivity Disorder (ADHD), cerebral palsy, and autism spectrum disorder (CDC, 2021). Children who are afflicted with chronic disease undergo the process of diagnosis, receive continuous medical intervention, endure a range of distressing and untreatable symptoms associated with the disease, and face physical limitations as a result of their condition (Compas et al., 2012; Ijoma , et al, 2019).

Children who have experienced early life stress as a result of chronic disease are more likely to exhibit symptoms of stress (White et al., 2021). The impact of stress on children can manifest in physiological responses through the intricate interplay between the nervous system, immune system, and endocrine system (Asnidar et al., 2018). Psychoneuroimmunology (PNI) is an interdisciplinary field that investigates the intricate connections between stress regulation, human behavior, and the interplay among the nervous, endocrine, and immune systems (White et al., 2021). PNI serves as the foundational basis for comprehending integrative therapies from a scientific perspective. The potential relationship between psychological stress and relaxation and their effects on immune functions can be observed through the psycho-neuro-endocrine-immune networks. These networks represent complex interactions between psychological processes, neurological activity, hormonal responses, and immune system function. Psychological stress, for example, can trigger physiological responses in the body, including the release of stress hormones like cortisol, which can impact immune function. Conversely, relaxation techniques may counteract stress by promoting a state of calmness, which could positively influence immune responses (Hasanah et al., 2023; Chacin-Fernández et al., 2019; González-Díaz et al., 2017).

Music therapy is a comprehensive form of care that encompasses activities such as listening to, engaging in creative processes, or engaging in physical movements in response to music (Yinger & Gooding, 2014). This therapeutic approach has the potential to enhance various aspects of an individual's well-being, including physical, emotional, cognitive, and social needs. Prior research has examined the efficacy of music therapy in relation to psychoneuroimmunological markers. Finn et al. and Fancourt et al. conducted a comparable study that suggests the existence of a biological pathway connecting music therapy and PNI (Finn & Fancourt, 2018; Fancourt et al., 2014). This systematic review explored the evidence base on the impact of listening to music on biological response in both clinical and nonclinical settings, in healthy and sick populations from neonatal age to the elderly. In a parallel systematic review conducted by Sittler et al. was determined that the impact of music therapy on psychobiological indicators is primarily manifested through the reduction of autonomic nervous system (ANS) activity in individuals with dementia. The evaluation in this study was carried out on a sample of adult participants encompassing a wide range of conditions (Sittler et al., 2021). However, studies that assess the impact of music therapy on psychoneuroimmunological markers, especially in children with chronic diseases, have not yet been found.

Identifying the body's biological responses through psychoneuroimmunological markers can be used as a potential objective tool in assessing the effectiveness of music therapy in pediatric chronic disease (Yan, 2016). Cortisol is one of the most commonly used biomarkers in research related to music therapy (Finn & Fancourt, 2018). Cortisol has many functions in the human body, such as mediating the stress response, regulating metabolism, the inflammatory response, and immune function (Oakley & Cidlowski, 2013). Cortisol measurement can be performed through various methods such as saliva, urine, and sweat, as well as plasma or serum (El-Farhan et al., 2017). Other studies have revealed that cortisol examination using non-invasive methods (such as saliva, urine, and sweat) is considered more feasible than invasive methods (such as plasma or serum) because invasive interventions induce additional stress and thus affect the actual stress value/state (Iqbal et al., 2023).

The formulation of an intervention grounded in the principles of PNI has the potential to offer empirical validation of the interconnectedness among psychological stress, chronic disease, and the therapeutic application of music. This research is important to add empirical evidence about the effectiveness of music therapy through modulation of the psychoneuroimmunological system in pediatric chronic disease.

METHODS

Research design

The systematic review conducted in this study adhered to the guidelines outlined in The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) (Page et al., 2021). The present

systematic review has been duly registered with PROSPERO, bearing the registration number CRD42023413389.

Search Methods

The articles published from March 31, 2014, to April 1, 2023, were searched from five databases (Scopus, PubMed, Web of Science, EBSCOhost, and ProQuest). The main search term was "music therapy", combined using the Boolean "AND/OR" with terms related to "psychoneuroimmunological markers" and "children with chronic disease".

Inclusion and exclusion criteria

The process of selecting and searching involved the utilization of inclusion and exclusion criteria. The PICO model was used to determine the inclusion and exclusion criteria as a framework. Inclusion criteria are: **P (Population):** The review should consist of individuals between the ages of 0 and 18 who are afflicted with a chronic disease. Meanwhile, a child or children are defined as a human being who is below the age of 18 years (Ziba Vaghri et al, 2022). **I (Intervention):** The music therapy interventions utilized encompass various forms, including active, receptive, or a combination of both approaches. Active music therapy involves the direct participation of individuals in musical activities such as playing musical instruments or singing. Meanwhile, receptive music therapy entails listening to or observing musical stimuli without active participation from the participants. The music therapy activities in this study can be conducted with the assistance of certified music therapists or independently by individuals without the accompaniment of a formally certified music therapist. **C (Comparison):** Group refers to the control group or comparison group that does not receive a music therapy intervention. **O (outcome):** The research should examine at least one psychoneuroimmunological marker, specifically focusing on psychological responses (pain levels, stress levels, depression, anxiety, worry, fear, distress, and sleep quality) measured using standardized questionnaires. Physiological indicators (heart rate, pulse, blood pressure, temperature, SpO2, blood glucose, hemoglobin, platelets, bilirubin, creatinine, fever, nausea, vomiting, tension headaches, diarrhea, or constipation) should be included. Neuroimmunological markers consist of neuroendocrinological markers (Serotonin, dopamine, GABA, glutamate, norepinephrine, cortisol, BDNF, acetylcholine, oxytocin) and immunological markers (cytokines, immunoglobulins, T Cells, B Cells, CRP, lymphocyte levels, NK cell cytotoxicity levels, IL-6, eosinophils) (Dantzer, 2018; Shamoon et al., 2021). A neuroimmunological marker refers to a specific biological parameter or substance that is used to assess the interaction and relationship between the nervous system and the immune system (Dantzer, 2018) that can be measured through the saliva, hair, blood, or urine tests.

In addition, the articles under consideration are limited to those published in the English language. Furthermore, the selected articles must have been published within the past decade, specifically between the years 2014 to 2023. Exclusion criteria is: The criteria for exclusion cover various study types, such as protocol studies, conference presentations, editorials, review articles, case reports, case series, qualitative research, and studies utilizing applied or development designs. Furthermore, studies concentrating on cognitive changes or molecular indicators and those integrating music therapy with other interventions are also not included.

Screening of articles

Three reviewers (YSA, NQ, ZH) searched academic databases. Subsequently, two reviewers (IH and IK) carried out the paper selection process. It is strongly advised that two independent reviewers screen all studies. Independent reviewers are tasked with the responsibility of screening to exclude studies that do not meet the inclusion criteria. In the screening process, all voting must be blinded, ensuring that colleagues cannot see each other's votes until they have cast their own and vice versa (Furlan JC, Singh J, Hsieh J, 2011). Rayyan, an AI-powered tool for systematic literature review, was employed to select the papers. This web and mobile app has proven effective in systematic review processes, demonstrating its potential to ease the workload of reviewers (Ouzzani et al., 2016). The authors

conducted a two-stage assessment and screening of remaining papers: first, a title and abstract screening, followed by a full-text screening. During the initial stage, titles and abstracts were evaluated, and papers were selected if they mentioned music and included terms related to psychoneuroimmunological markers. Abstracts were further assessed based on pre-established inclusion and exclusion criteria. In the second stage, the authors independently reviewed the complete texts. Subsequently, a comprehensive review was conducted, and the authors engaged in collaborative discussions regarding the collected data.

Conflicts or disagreements among reviewers were resolved either by involving a third reviewer or through consensus-based discussions. The third reviewer played a crucial role in assisting the review process by addressing differences of opinion between the initial two reviewers. When disagreements arose, the third reviewer helped decide whether a particular study should be included in the review analysis. Consensus, in this context, involved discussions and negotiations among reviewers to agree on the inclusion or exclusion of a study in the review analysis. Various methods, such as direct discussions, voting, or the Delphi methodology for anonymous voting, were employed to achieve consensus. A five-point Likert rating scale was used to gauge the level of agreement, with a strong consensus defined as agreement reaching ≥ 80%, a weak agreement between 68% - 79.9%, and disagreement as agreement <68% (Furlan JC, Singh J, Hsieh J, 2011).

Data extraction

The inclusion criteria specified in each paper were extracted using Microsoft Excel spreadsheets. Data extraction was carried out independently by three independent reviewers, namely IH, NN and IK. The execution of the extraction process should be carried out by a panel of 2-3 impartial reviewers (Tawfik et al., 2019).

Quality appraisal

In terms of the quality of the studies, a significant proportion of them can be categorised as "Good," as indicated by a JBI score exceeding 75%. Hence, it is possible to approach all studies through the utilization of synthetic analysis.

Question	Studies included Randomised Control Trial (RCT) (13 item Question)						Studies included NonRandomised Control Trial (NonRCT) (9 item Question)			
Q1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q3	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q4	N	N	N	Y	Y	N	N	Y	Y	Y
Q5	N	N	Y	Y	N	N	N	N	N	Y
Q6	N	Y	Y	Y	N	N	Y	Y	Y	N
Q7	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Q8	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q10	Y	Y	Y	Y	Y	Y	77.8%	88.8%	88.8%	88.8%
Q11	Y	Y	Y	Y	Y	Y				
Q12	Y	Y	Y	Y	Y	Y				
Q13	Y	Y	Y	Y	Y	Y				
Total Score	76.9%	84.6%	92.3%	92.3%	76.9%	84.6%				
Category	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good

Data analysis

A meta-analysis was deemed unsuitable for this study due to substantial variability in research design, study population, interventions, duration, instruments, and outcomes across the included studies. Given the diverse nature of these studies, a narrative synthesis was chosen as the most effective

method to integrate their findings. The synthesis involved a preliminary thematic analysis, including the search, listing, and presentation of results in tabular form. Subsequently, the results were further discussed and structured into themes. The synthesis process began with the identification of study characteristics (Population, Intervention, Comparison, and Outcome) in each article, followed by grouping according to the Cochrane Handbook for Systematic Reviews (Cumpston et al., 2021).

RESULTS

The total number of studies from this initial database search found 1,727 articles (1,160 articles from the main database and 567 articles from additional databases). Articles that have been filtered from the database are entered into the Rayyan tools. These articles were examined, and we found 148 duplicate articles. After we screened titles and abstracts and reviewed the full text independently, we found 15 studies that met the inclusion and exclusion criteria in this study. These 15 articles consist of 14 articles sourced from the main database and 1 article obtained from additional databases (Figure 1).

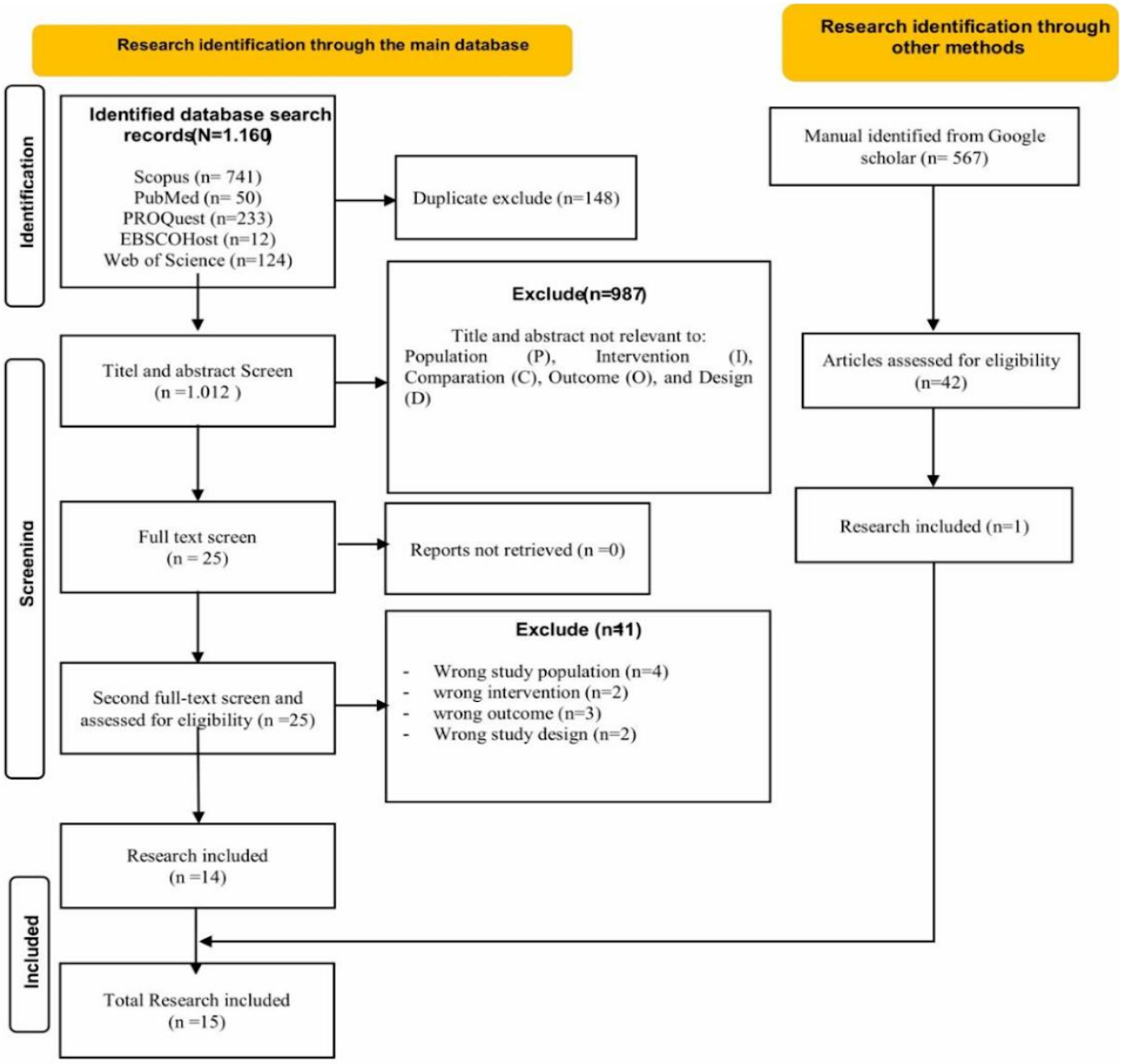

Figure 1.
Flowchart used in selecting studies using PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses)

The author acquired a total of 1,346 articles from the designated databases. A total of 15 studies were found to meet the inclusion criteria in the present systematic review. Table 1 presents the depiction of the proportion of study characteristics acquired.

Table 1. Description of the percentage of study characteristics (n=15)

Component	Characteristic	(n=15)	Percentage (%)
Year Publication	2014-2018	4	26.7
	2019-2023	11	73.3
Country	China	3	20.0
	Turkey	2	13.3
	Indonesia	2	13.3
	Germany	2	13.3
	Korea	1	6.7
	Italy	1	6.7
	Iran	1	6.7
	Sweden	1	6.7
	Egypt	1	6.7
	Netherlands	1	6.7
Design study	Randomized controlled Trial	6	40.0
	Non-Randomized Controlled Trial	9	60.0
Type of chronic disease	Congenital Heart Disease	5	33.3
	ADHD	1	6.7
	HSCT	1	6.7
	Thalassemia	1	6.7
	Cancer	1	6.7
	Leukaemia	3	20.0
	Asthma	1	6.7
	All type of chronic disease	1	6.7
	Depression	1	6.7
Type of music therapy	Active music therapy	1	6.7
	Receptive music therapy	9	60.0
	Both active music therapy and receptive music therapy	4	26.7
	Unclear	1	6.7
Duration of intervention/session	Preferred by the child	1	6.7
	During catheterization	1	6.7
	30-60 minutes	7	46.7
	15-29 minute	4	26.7
	Not clear	1	6.7
Parameters evaluated	Psycho and physiological markers	10	66.7
	Neuroimmunological markers	5	33.3

The review shows a significant increase in publications, with 73.3% of the studies spanning from 2014 to 2023. The majority (20.0%) of the research originates from China. Non-randomized controlled trials were the predominant study design (60.0%), and congenital heart disease was the most commonly studied chronic disease (33.3%). Receptive music therapy was the primary approach (60.0%), lasting more than 30-60 minutes in 46.7% of the interventions. Most studies (66.7%) focused on evaluating psychological and physiological markers, while only 33.3% assessed neuroimmunological markers.

Impact of music therapy on psychoneuroimmunological markers

The effect of music therapy on psychoneuroimmunological markers is divided into several themes, briefly presented in Table 2.

Table 2. Impact of music therapy on Psychoneuroimmunological markers

Study	Psychological responses					Physiological markers												Neuroimmunological markers			
	Anxiety	Stress/ distress	Fear	Emotion	Depression	Pain	HR	RR	Temp	BP	MAP	SaO2	BG	PLT	Br	Cr	Hb	Cort	5-HT	CRP	Lymph
(Y. L. Huang et al., 2021)						↓* p<0.05	↓* p<0.05	↓* p<0.05			↓* p<0.05	↑ p>0.05)									
(Y.-L. Huang et al., 2021)	↓* p<0.01						↓* p<0.05				↓* p<0.05										
(Karakul et al., 2022)	↓* p=0.025		↓* p=0.001			↓ 0.977	↓* 0.021	↓ p=0.090		↓* 0.002		↑ 0.219									
(Hasanah et al., 2020)																		↓ p=0.99			
(Park & Lee, 2022)		↓* p<0.01			↓* p<0.001		↓* p<0.001			↓* p<0.001								↓* p<0.001	↑* p<0.001		
(Sheikhi, et al., 2020)	↓* p<0.001																				
Giordano et al., 2020	↓*																				
(Kuhlmann, et al., 2020)		↓ p=0.085				↓* p=0.027	↓* p=0.003														
(Geipel, et al., 2022)				↓*	↓*													↓*			
(Kobus et al., 2022)							↓*			↓*		↑*									
(Polat et al, 2015)	↓* p<0.05																				
(Roslita et al, 2017)							↓* p<0.05	↓* p<0.05				↑* p<0.05									
(Zhang et al, 2022)				↓* p<0.001		↓* p<0.001	↓* p<0.001					↓* p<0.001									
(Uggla et al,2016)							↓* p<0.001					↓* p=0.03		NA	NA	NA	NA			NA	NA
(Abd-Elshafy et al., 2015)		↓*				↓*	↓		↓	↓		↓	↑*					↓*	↓*		

Note: HR: Heart rate; RR: Respiratory rate; Temp: Body temperature; BP: blood pressure; MAP: Mean Arterial Pressure; SaO2: Oxygen saturation; Cort: Cortisol; 5-HT: 5-hydroxytryptamine (Serotonin); BG: Blood glucose; CRP: C-Reactive Protein; Lymph: Lymphocyte; Hb: Hemoglobin; PLT: Platelet/thrombocyte; BR: Bilirubin; Cr: Creatinine; ↓: Increase; ↑: Decrease: *: significant statistically, NA: Not available

DISCUSSION

This review identified psychological responses, including pain, stress/distress, depression, and anxiety. Physiological indicators measured vital signs, blood glucose, hemoglobins, platelets, bilirubin, and creatinine. Some studies assessed neuroendocrinological markers (serotonin, cortisol), and one studied immunological biomarker (C-reactive protein, lymphocytes), though results were unavailable. Variability exists in study design, sample size, population characteristics, music therapy type, frequency, duration, and indicators assessed. These differences can impact study outcomes, influencing the understanding of music therapy's effectiveness across diverse populations and conditions.

This study shows inconsistency in the study design aspect. Most of the research uses experimental design and a small number of studies use observational design. Differences in research designs, such as experimental vs observational, can affect the validity of internal and external studies (Majid, 2018). The design of the study, the primary outcome, sampling method used, dropout rate, effect size, power, level of significance, and standard deviation are some of the multiple factors which affect the sample size. An optimum sample size needs to be employed to identify statistically significant differences if they exist and obtain scientifically valid results. The larger the sample size, the more insightful information, identification of rare side effects, lesser margin of error, higher confidence level, and models with more accuracy (Gumpili & Das, 2022).

Differences in population characteristics such as age, sex, and type of chronic disease may affect response to music therapy. The effects of music therapy may differ between these different groups. This is supported by previous literature which explains that population characteristics such as age, gender, type of chronic disease, cultural background, and general health level can influence an individual's response to music therapy (Gold et al., 2009). In addition, different types of music therapy in these studies can also affect the effectiveness of music therapy interventions. Several studies provide music therapy in the form of active music, receptive and a combination of both. Active music interventions are useful for improving symptoms, cognition, behavior, and dependence. In Instead, the receptive music intervention only had a stabilizing effect on behavior (Gómez-Gallego et al., 2021). The receptive group may reach a peak therapeutic effect faster, but the active group may have a higher peak effect (Atiwannapat et al., 2016). Different study revealed by Millet et al. stated that both active and passive music therapy interventions may be equally effective in reducing anxiety in pediatric patient (Millett & Gooding, 2017).

This review highlights challenges in the variability of music therapy session duration and frequency, hindering conclusive findings. The existing scholarly literature, including prior systematic reviews and original research, lacks sufficient information on optimal timing and musical styles (Li et al., 2020). Zhang et al.'s comprehensive meta-analysis of 322 studies on cancer patients indicates a lack of understanding regarding the optimal timing and duration for positive physical and psychosocial effects (Zhang et al., 2012). Studies, such as those by J. M. Zhang et al. (2012) and Chlan et al. (2013), employ diverse methodologies, initiation points, and durations of music therapy (Zhang et al., 2012); (Chlan et al., 2013). Chlan et al. suggest granting patients autonomy in deciding the frequency, duration, and timing of music interventions (Linda L. Chlan et al., 2013). Considering music therapy type, genre, and intervention duration is imperative imperative (Finn & Fancourt, 2018).

Music therapy, supported by various studies, effectively manages physiological and psychological responses. A previous study suggests it serves as a beneficial supplementary treatment for cancer patients, addressing anxiety, depression, pain, and overall quality of life, with an optimal intervention duration of 1-2 months (Li et al., 2020). Foroushani et al. found favorable impacts on physiological indicators in neonates in the ICU, including heart rate, oxygen saturation, respiratory rate, and resting energy expenditure (Sophia et al, 2020). Lieber et al.'s assessment during cerebral, coronary, and peripheral angiography demonstrated the positive impact of music therapy on psychological factors (anxiety levels) and physiological responses (heart rate, blood pressure) in individuals undergoing the procedure (Lieber et al., 2019). The research results from Chahal, et al stated that music therapy is effective in reducing anxiety and stabilizes *physiological parameters* (temperature, pulse rate, respiration rate, systolic blood pressure, diastolic blood pressure and oxygen saturation) in ICU patient (Chahal et

al., 2021). Music therapy is effective in reducing levels of depression and *physiological parameters* (sistole blood pressure) in elderly people who were in a living nursing home (Gök Ugur et al., 2017).

Out of the total of 15 studies examined, one study indicated a statistically significant impact of music therapy on only neuroendocrinological markers among children diagnosed with chronic disease and four studies on both psychophysiological responses and neuroimmunological markers. The impact of music therapy especially on neuroimmunological markers varies widely. In neuroendocrinological markers, we found two biomarkers were assessed, namely serotonin and cortisol. Serotonin is a neurotransmitter that plays an important role in the human nervous system. Functionally, serotonin is included in the neurobiological or neurological aspect, because it plays a role in regulating mood, emotion, sleep, appetite, and various cognitive functions. Meanwhile, cortisol is one of the most common stress biomarkers within pediatric research. Cortisol is produced by the hypothalamic-pituitary-adrenal (HPA) axis, a physiologic system that governs neuroendocrine responses to stress (Slopen et al., 2014).

The most widely evaluated neuroendocrinological marker indicator is cortisol. The cortisol examination method is carried out through blood plasma, hair and also saliva. The cortisol hormone is widely recognised as the primary hormone for assessing hormonal levels within the body, serving as a prominent biochemical indicator for both acute and chronic stress (Lee et al., 2015). Furthermore, it has been reported in other studies that the stress hormone cortisol is frequently employed as a biomarker for assessing the effectiveness of music therapy interventions (Finn & Fancourt, 2018); (Taets et al., 2019).

Implication and limitations

This systematic review has limitations, including the lack of consistency in chronic disease diagnoses, age groups of children, study designs, and assessed outcomes, preventing the possibility of conducting a meta-analysis. The inclusion of various music interventions, such as listening or watching music, adds complexity due to the different sensory stimulations involved. Future studies should aim for greater homogeneity in these aspects to enhance internal validity, facilitate meta-analysis, and yield clearer results. Assessing study quality is crucial, and while the JBI framework used for bias evaluation is widely applicable, individual assessments by authors remain subjective. The diverse terminology and types of chronic diseases in children pose challenges in identifying relevant studies. It is important to carefully select specific keywords in future research to avoid overlooking pertinent studies.

This review is among the first evidence-based efforts to assess the effectiveness of music therapy in influencing psychoneuroimmunological markers in pediatric patients with chronic diseases. It can be a foundational resource for future researchers exploring the impact of music therapy on various biomarkers that have yet to be studied. The review highlights that many hormones, neurotransmitters, and immune cells involved in music therapy-activated pathways have not been thoroughly examined. Administered by healthcare professionals, it includes education, counseling, or training to improve the overall well-being of children with chronic illnesses. The study emphasizes the importance of psychological intervention as a crucial element in comprehensive nursing care for pediatric patients with chronic diseases. Consequently, these findings can guide stakeholders considering the integration of music therapy as a consistent supplementary intervention for children with chronic diseases during their hospital treatment.

CONCLUSION

Music therapy is an essential component of the holistic care. This review found that most studies assessed the impact of music therapy on psychological and physiological responses, but only a small proportion assessed the effectiveness of music therapy on neuroimmunological markers in children with chronic disease. In general, this review concluded that music therapy can improve psychoneuroimmunological markers in children with chronic diseases. Music therapy can be

considered a safe and generally well-accepted intervention in pediatric health care to manage psychoneuroimmunological markers.

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AUTHOR CONTRIBUTIONS
Idyatul Hasanah, Chui Ping Lei, Zikrul Haikal, Apriani Susmita Sari, Domingos Soares, & Kurniati Prihatin: Conceptualization, Methodology, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Supervision, Investigation, Validation, & project administration.

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CONFLICT OF INTEREST STATEMENT
The authors declare no conflict of interest.

REGISTRATION NUMBER
The present systematic review has been duly registered with PROSPERO, bearing the registration number CRD42023413389.

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