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Review Article

Psychoneuroimmunological Markers of Psychological Intervention in Pediatric Cancer: A Systematic Review and New Integrative Model

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SUMMARY

Purpose: Pediatric cancer is a serious problem and still becomes a global challenge today. Various complex stressors due to diagnosis, disease symptoms, and various side-effects from the treatment that children with cancer undergo will cause problems in the child's psychoneuroimmunological aspects. Psychological interventions designed to modulate the stress response include psychoneuroimmunological markers. Unfortunately, there is little evidence to support the effect of psychological interventions on psychoneuroimmunological markers. This systematic review aims to assess the effectiveness of psychological interventions on psychoneuroimmunological markers in children with cancer and to provide a new integrative model for further research.

Methods: This systematic review uses four main databases (Scopus, PubMed, ScienceDirect, and ProQuest). The guideline used Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Selecting articles used the Rayyan application. The quality study was conducted using Joanna Briggs Institute (JBI)'s critical appraisal tools. The data were analyzed using the population, intervention, comparison, outcome, and study design (PICO) Synthesis based on similarities and differences in study characteristics to interpret the results.

Results: The search results in this systematic review found 1653 articles, 21 of which matched the predetermined inclusion and exclusion criteria. Most of the designs used were randomized controlled trials (57.1%). Massage therapy was the most common type of psychological intervention (14.2%). Almost half of the studies measured psychological responses (38.0%), and psycho-physiological responses (42.9%), and only a small proportion assessed the effectiveness of psychological interventions on neuroimmunological markers in pediatric cancer.

Conclusions: We recommend the use of psychological interventions as an additional intervention in managing psychoneuroimmunological markers of pediatric cancer. This study offers a new integrative model demonstrating the interaction between stress and psychological intervention involving neuroendocrine and immune mechanisms. However, future researchers need to test all domains of these new integrative models. This will reveal the complex interactions among these components and understand their relevance to health outcomes.

Introduction

Cancer ranks as the second most prevalent cause of mortality among children aged 1 to 14 years, following accidents. According to available data, it is projected that around 1040 children below the age of 15 in the United States will experience mortality due to cancer in the year 2023 [1]. Multiple empirical studies have

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indicated that the well-being of children and their families can be adversely affected by diseases and adverse effects associated with different forms of cancer treatment, including chemotherapy, radiation therapy, surgery, and bone marrow transplants [1–4]. The administration of the treatment can exacerbate the symptoms of heightened distress that are commonly linked to the adverse effects of the treatment and its toxic properties [5]. In addition to the physical manifestations of the disease and the adverse effects of the treatment regimen, pediatric cancer patients are subjected to an extensive period of hospitalization, which may elicit a range of emotional responses including fear, anger, and sadness [6]. According to previous research, children and adolescents diagnosed with cancer often describe experiencing both physical and psychosocial transformations resulting from their therapeutic interventions. Additionally, they frequently encounter stigmatization from others and express a strong desire to regain a sense of normalcy that they had prior to their illness [4].

The majority of pediatric patients diagnosed with cancer encounter at least one distressing symptom, with a significant proportion experiencing at least one highly distressing symptom [7]. According to prior studies, a significant majority of children undergoing cancer treatment exhibit various symptoms, including reduced appetite (87.0%) and pain (86.0%) [8]. Additionally, these children commonly experience fatigue, nausea, vomiting, and sleep disturbances [5,9,10]. A range of factors can contribute to the occurrence of stressful conditions in children. This finding is consistent with prior scholarly investigations, which elucidate that children diagnosed with cancer exhibit notable indications of anxiety, stress, and depression [11]. The presence of symptoms related to anxiety, stress, and depression during the course of treatment has the potential to adversely impact the overall quality of life experienced by individuals [12].

Numerous scholarly sources elucidate the significant advancements witnessed in the domain of pediatric cancer treatment and supportive care in recent decades. As a result, the current 5-year survival rate for pediatric cancer exceeds 80.0% [13]. This assertion is corroborated by additional research studies which have documented favorable outcomes among a significant number of pediatric cancer survivors subsequent to their treatment. Nevertheless, the majority of subgroups encountered psychological distress and a decline in health-related quality of life [14]. There exists a significant body of evidence within the cancer population that establishes a correlation between psychological stress and a decline in immune function [15]. The impact of psychological distress on the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis has been recognized, leading to disruptions in the integration of neurohormonal and immunological processes [13,16–18]. The occurrence of psychological stress prompts communication between the brain and the immune system, thereby exerting an influence on immune function. The bidirectional communication between the immune system and the brain is facilitated through reciprocal pathways. Both directions are associated with the progression of diseases. This becomes particularly pertinent in cases where the psychological stress persists over an extended period of time, or when there is a chronic activation of the immune system. In both scenarios, there is a decrease in both physical and mental activity, which has the potential to contribute to the development and progression of illness and disease [18,19].

The psychoneuroimmunological perspective is derived from the integration of psychological distress and the body's biological conditions [19]. Psychoneuroimmunology (PNI) is a discipline that investigates the impact of the interplay between psychological, neural, and immunological mechanisms on both human health and behavior [20–22]. Additional scholarly literature elucidates that PNI is a discipline that exhibits a strong interconnection with stress regulation, the intricate interplay between human behavior, and the intricate functioning of the nervous, endocrine, and immune systems [20–23]. This discipline encompasses the comprehension of the impact that thoughts, emotions, and behaviors can exert on the immune response and overall well-being [20–22]. In the field of pediatric oncology, research on psychoneuroimmunology (PNI) aims to elucidate the interplay between psychological factors, the nervous system, and the immune response, as well as their impact on cancer pathology and therapeutic interventions [24,25].

Several interventions have been devised to assist pediatric cancer patients in managing psychoneuroimmunological markers, with psychological interventions being one such approach. Nevertheless, there exists a lack of consensus regarding the precise delineation of the terminology associated with psychological intervention. According to a meta-review conducted by Hodges et al. [26] states that the description of the terms of intervention that are often used in research are ‘psychosocial’, psychological, psychotherapy, nonpharmacological, behavioral, supportive, psychoeducational, psychosomatic, psychiatric, and noninvasive. Hoffman et al. [27] define psychological interventions as a method or strategy used to manage a person's physical, psychological, and neurocognitive response interventions. These interventions can be categorized into various approaches, including relaxation techniques, distraction techniques, cognitive behavioral therapy (CBT) strategies, mindfulness-based stress reduction, acceptance and commitment therapy, cognitive therapy functional, health coaching, biofeedback, education, and counseling.

There is a growing body of research focused on cancer survivors, which indicates that a range of psychological interventions have the potential to mitigate psychological distress, enhance coping mechanisms, and positively impact immune function by influencing the neuro-endocrine and immune systems [24]. The existing body of literature has extensively documented the correlation between psychological stress and cancer across different age groups. Nevertheless, the existing body of literature indicates a scarcity of empirical support regarding the impact of psychological interventions on psychoneuroimmunological markers, specifically within the context of pediatric cancer. The utilization of psychoneuroimmunological markers to identify the physiological reactions of the body can serve as a prospective objective measure in evaluating the efficacy of psychological interventions in the context of pediatric cancer [28].

This review aims to provide empirical evidence regarding the efficacy of psychological interventions in modulating the psychoneuroimmunological system in pediatric cancer patients. Furthermore, this review presents an integrative framework that offers a comprehensive understanding of the interplay between pediatric cancer, psychological intervention, and the intricate processes involved in nervous system development. This framework allows for the evaluation of the impact on children's psychoneuroimmunological markers as a means of assessing these novel pathways. This systematic review aims to contribute to the advancement of interventions by providing a comprehensive overview of the integration of biopsychosocial factors, psychological interventions, and PNI in the context of pediatric cancer. The objective of this systematic review is to evaluate the efficacy of psychological interventions in modulating psychoneuroimmunological markers among pediatric cancer patients.

Methods

The guideline used to conduct this systematic review is The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) [29]. This systematic review has been registered with PROSPERO with registration number CRD42023392169.

Inclusion and exclusion criteria

The selection and search criteria used inclusion and exclusion criteria. The inclusion criteria include: (1) using PICOS (population, intervention, comparison, outcome, and study design). P (Population), means the study must involve children aged 0 to 18 years who suffer from cancer, I (intervention), is the use of all types of psychological interventions (we replicate the definition provided by Hoffman et al. [27] by defining psychological intervention as one of the following approaches: all kinds of relaxation techniques, all kinds of distraction technique, cognitive behavioral therapeutic strategies, mindfulness based stress reduction, acceptance and commitment therapy, cognitive functional therapy, health coaching, biofeedback, education, and counseling), C (comparison), is the control group or comparison group that is not psychological intervention, O (outcome), means studies include an analysis of at least one psychoneuroimmunological response in the form of a psychological responses (there is a feeling that someone feels like stress level, depression level, anxiety level, fear, fatigue level, quality of sleep, and quality of life that is measured by using a questionnaire); physiological responses (an individual response physically characterized by an increase heart rate, pulse, blood pressure, pain level, appearance nausea, vomiting, and fever); and neuroimmunological response (the body's response to stimuli involving the central nervous system (CNS) and the immune system that is measured by one of the saliva, hair, blood, or urine tests such as cortisol, leukocytes, cytokines, immunoglobulins and other immune responses). Study design (S) is all types of quantitative research; (2) the year of publication is the last ten years, between 2013 and 2022; (3) the articles taken are published in English. The exclusion criteria are (1) protocol studies, conference presentations, editorials, review articles, case reports, and case series, qualitative research, applied or development designs; (2) Studies involving molecular indicators or DNA; and (3) studies combining psychological intervention therapy with pharmacological intervention (use of drugs).

Search strategy

Reviewers scanned academic databases from the study commencement date from December 2022 to February 09, 2023. Searches were performed on four databases (Scopus, PubMed, ScienceDirect, and ProQuest). The minimum standard for searching the literature in a systematic review is minimally using a combination of 4 main databases [30]. The consequence of using these four main databases is that researchers will produce fewer search results, and there is a possibility of missing relevant references. However, in this systematic review, we also use Google Scholar to minimize the possibility of missing relevant references. In general, researchers consider combining four main databases equipped with Google Scholar to provide efficient results in this systematic review.

The main search term is “psychological intervention” combined using the Boolean “AND/OR” with terms related to “psychological and physiological responses” and “neuroimmunological markers”. Then the related term “children with cancer” was added. The author defines synonyms with the keyword as follows: (“Paediatrics” OR “Child” OR “childhood” OR “Children” OR “Adolescent” OR “teen” OR “teenagers”) AND (“cancer” OR “pediatric cancer” OR “childhood cancer” OR “neoplasm”) AND (“psychology” OR “psychological” OR “Psychological programs” OR “Psychological intervention” OR “psychotherapeutic” OR “psychotherapy”) AND (“Psychoneuroimmunology” OR “Psychoneuroimmunology responses” OR “psychology” OR “Physiology” OR “neurology” OR “endocrinology” OR “immunology” OR “Biological Markers” OR “Biomarkers” OR “cortisol” OR “leukocyte” OR “Cytokines” OR “lymphocytes” OR “immunoglobulins” OR “interleukins” OR “anxiety” OR “distress” OR “stress” OR “pain” OR “Fatigue” OR “Heart rate” OR “blood pressure” OR “respiratory rate” OR “body temperature” OR “blood oxygen”). Full search strategies for all resources can be seen in supplementary Appendix 1.

Selection of study

All authors (IH, NN, IL, WFR, ZH, and TR) scanned academic databases. Then we conduct the process of selecting articles. Four reviewers (IH, WFR, ZH, and TR) used Rayyan's intelligent systematic review to select articles. Rayyan is a web and mobile app for systematic reviews. Rayyan proved effective in conducting a systematic review and has significant potential to lighten the load of reviewers [31]. Articles filtered from the four main databases were entered into the Rayyan application. The total number of studies from this initial database search found 1,652 articles (898 from the main database and 754 from the auxiliary database). These articles were then checked, and the duplicates were removed.

IH, WFR, ZH, and TR independently reviewed the titles and abstracts yielded by this comprehensive search and subsequently selected articles based on the predetermined inclusion and inclusion criteria. Titles and abstracts were screened to include articles that first referred to psychological interventions and then had any terms related to PNI responses (as listed in the search terms above). We found 34 relevant studies from the main database and independently read them in full text. Then, disagreements between reviewers were resolved by consensus or by the decision of a third independent reviewer. A level of consensus of 80.0% or higher was considered to represent strong agreement [32]. Finally, 21 studies were included in this systematic review (13 articles from the main database and eight articles from the supplementary database (Figure 1).

Data extraction, analysis, and synthesis

Data were taken from each article that met the inclusion criteria. The data extraction process uses a Microsoft Excel sheet. All articles were read, and all authors extracted the data independently. Then, any discrepancies were discussed and resolved consensually. When differences could not be resolved, a third opinion would be sought, which might prove unnecessary. Given the apparent heterogeneity among studies in the type of psychological intervention, length of intervention, and study design, a meta-analysis was impossible. Thus, we only conducted a narrative review of the findings. Analysis using PICO Synthesis. The stages of the synthesis process begin with identifying the characteristics of the study (Population, Intervention, Comparison, Outcome, and study design) in each article obtained, then grouping them based on the Cochrane Handbook for Systematic Reviews [33].

Risk of bias and study quality

The authors identified study quality by considering the risk of bias. This assessment aims to assess a study's methodological quality and determine the extent to which a study has overcome possible biases in its design, implementation, and analysis. To identify the risk of bias, this systematic review uses The Joanna Briggs Institute (JBI) Critical Appraisal tools following the research design [34]. Each research design has different questions. Researchers must assess the articles that have been selected. The scoring results come from the scoring results from the percentage, which is $\geq$ 75% = Good, 50–75% = Fair, and <50% = Poor [35].

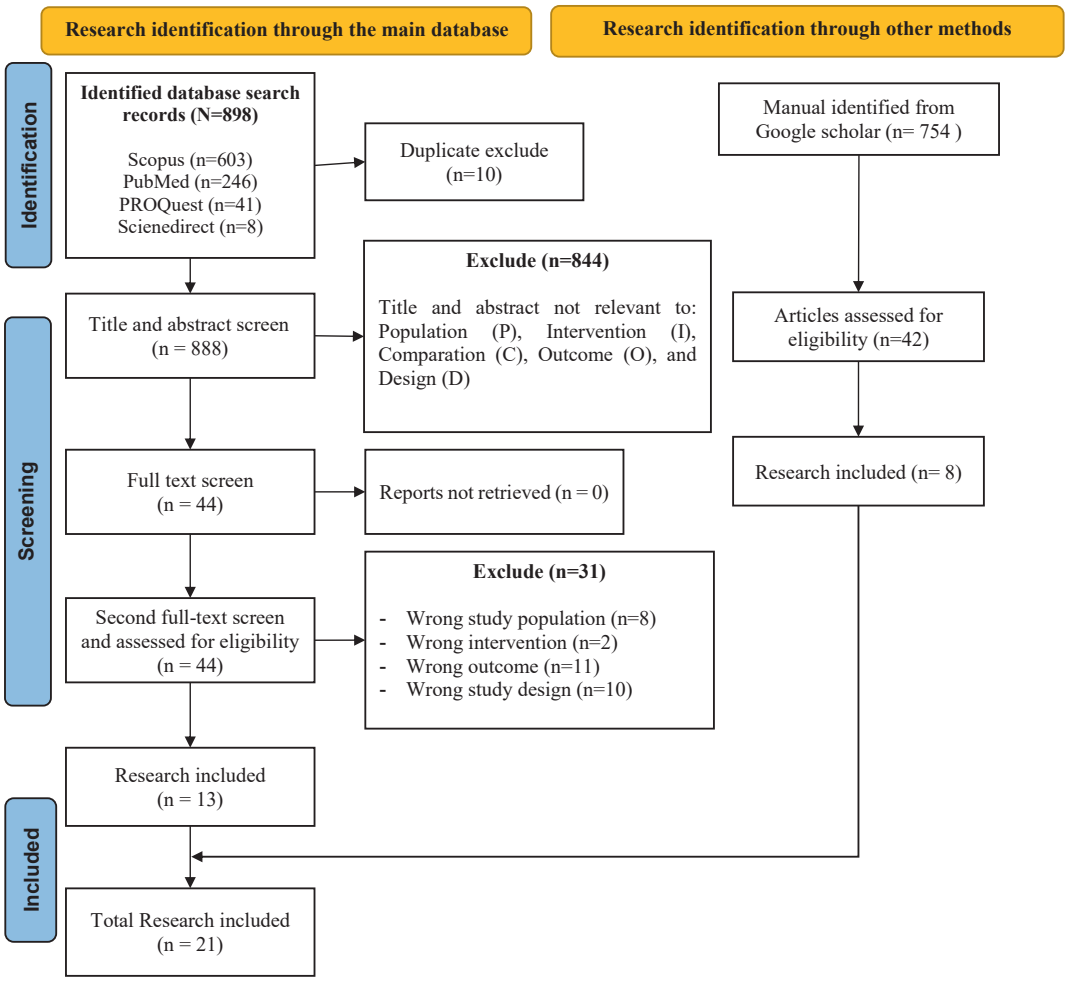

Figure 1. Flowchart Used in Selecting Studies Using PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) [32].

Model development

This study offers a new integrative model that shows the interaction between several factors affecting stress levels, which can be observed through neuroendocrine and immune mechanisms. Meanwhile, this integrative model also demonstrates how psychological interventions can modulate the effects of these various factors on neuroendocrine and immune mechanisms, ultimately influencing health outcomes. The conceptual framework of this new integrative model was created based on the conceptual framework of the biopsychosocial model [36] integrated with the field of PNI [19] and the results of this systematic review (Figure 2).

The biopsychosocial model is structured by several domains, including psychosocial, biological, and health behaviors, stress, psychological interventions, neuroendocrine and immune system mechanisms, and health outcomes. The biopsychosocial model describes the interaction among the factors that influence the stress of a person's life. Those factors encompass psychosocial, biological, and health behaviors that lead to susceptibility (or resistance) to disease, onset, disease symptoms, disease development, exacerbation, recovery, and quality of life through the process of involving neuroendocrine and immune mechanisms. Meanwhile, health psychological interventions are regarded to modulate the effects of these various factors on neuroendocrine and immune mechanisms, which in turn will influence health outcomes. The indicators for each domain refer to the results of a literature search and this systematic review's results.

The new integrative model shows the integration between the biopsychosocial model in the domain of neuroendocrine mechanisms and the immune system and psychoneuroimmunology (PNI). PNI is a field of medical science that examines the relationship between psychological stress and physiological processes in the body. The mind, nervous, endocrine and immune systems have a reciprocal relationship anatomically and biochemically [19]. PNI in the new integrative model is organized into four domains: psychology, physiology, neuroendocrinology, and immune systems. The indicators for these four domains are compiled based on our results in this systematic review.

In the psychological intervention domain, the authors arrange the types of psychological interventions in the new integrative model according to the results of the author's synthesis in this systematic review. Based on the biopsychosocial model, the domain of psychological intervention consists of cognitive behavioral stress management (CBSM), relaxation, hypnosis, meditation, emotional disclosure, adherence-based interventions, sleep hygiene, exercise, social support groups, psychotherapy, imagery, distraction, behavioral pain management, yoga, massage, biofeedback, drug/alcohol prevention/rehabilitation, psychotherapy, and behavioral conditioning. All of these interventions can be used in any type of disease or condition. However, the types of psychological interventions set in the integrative model framework are the psychological interventions that can be used in children with cancer, considering that this systematic review was carried out on the population of children with cancer.

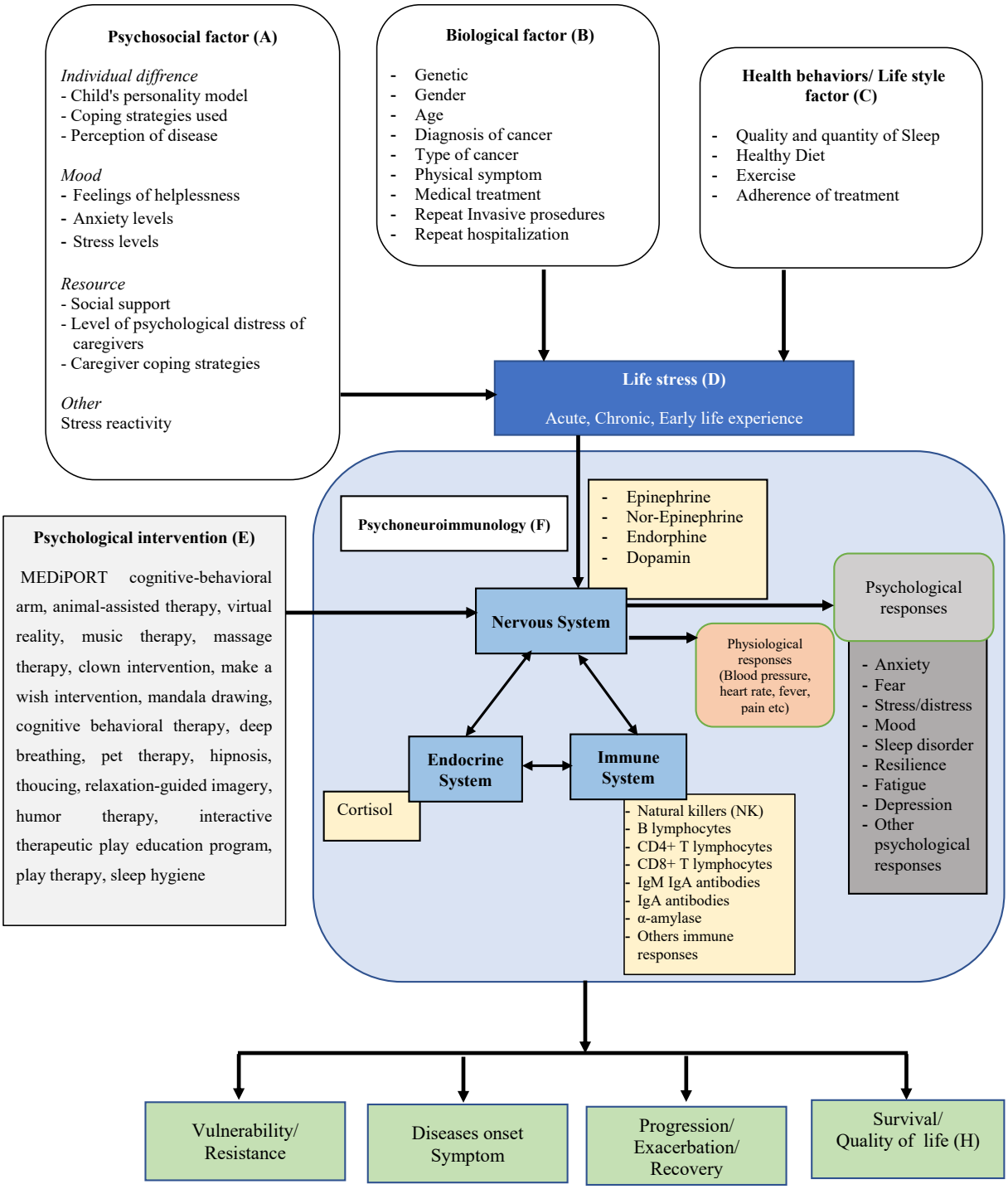

Figure 2. Illustration of the New Integrative Model [19,36].

Results

Study characteristic

The author obtained 1653 articles through all the specified databases. Studies that met the inclusion criteria in this systematic review were 21 articles. A description of the percentage of study characteristics obtained is shown in Table 1.

Based on the table above shows that most of the designs used were randomized controlled trials 12 (57.1%). At the same time, the types of psychological interventions used vary widely. The most common type of psychological intervention was massage therapy 3 (14.2%). Almost half of the studies measured psychological responses 8 (38.0%), and psycho-physiological responses 9 (42.9%), and only a small proportion assessed the effectiveness of psychological interventions on neuroimmunological markers in pediatric cancer.

Table 1 *Description of Study Characteristics (n = 21).*

Component	Characteristic	(n = 21)	Percentage (%)
Study design	Randomized controlled trial	12	57.1
	Nonrandomized controlled trial	9	42.9
Intervention type	Psychosocial intervention	1	4.8
	Mediport cognitive-behavioural arm	1	4.8
	Animal-assisted interventions	2	9.5
	Virtual reality	1	4.8
	Music therapy	1	4.8
	Massage therapy	3	14.2
	Clown intervention	1	4.8
	Make a wish intervention	1	4.8
	Mandala drawing	1	4.8
	The home-based multimodal symptom-management program	1	4.8
	Integrated experiential training program with coaching	1	4.8
	Adventure-based training	1	4.8
	Cognitive behavioral therapy	1	4.8
	Psychological intervention base psychoneuroimmunology	1	4.8
	Therapeutic play	1	4.8
	Mindfulness-based stress reduction	1	4.8
	Art therapy (drawing, painting and ceramic art)	1	4.8
	Drawing and writing technique	1	4.8
Outcome	Psychological responses	8	38.0
	Neuroimmunological markers	1	4.8
	Psychological and physiological responses	9	42.9
	Psychological responses and neuroimmunological markers	1	4.8
	Physiological responses and neuroimmunological markers	1	4,8
	Psycho-physio-neuroimmunological marker	1	4.8

Risk of bias and study quality

Almost all studies included in this systematic review (n = 18) have a study quality category as “Good” with a score above 75.0% using the Joanna Briggs Institute (JBI) critical appraisal so that all studies can be carried out synthesis analysis (see Table 2).

Impact of psychological intervention

From searching several scientific-based data, 21 studies illustrated that psychological interventions positively impacted psychoneuroimmunological responses in children with cancer. Based on this review, the author divides the impact of psychological intervention into two themes, including: (1) psychological responses (e.g., pain, anxiety, stress/distress, mood, fear, fatigue, depression, sleep quality, quality of life, and other psychological responses) and physiological responses (e.g., fever, pain, nausea, vomiting, blood pressure, heart rate, and other physiological responses); (2) psycho-physio and neuroimmunological marker (e.g., cortisol, NK cell, B lymphocytes, CD4+ T lymphocytes, CD8+ T lymphocytes, IgM antibodies, IgA antibodies, α-amylase, and another neuroimmunological marker).

1. Impact of psychological interventions on psychological and physiological responses.

Almost all of the research in this systematic review assesses the effectiveness of psychological interventions on psychological responses (stress/distress, fear, anxiety, fatigue, depression, decreased sleep quality, and quality of life) and physiological responses (blood pressure, heart rate, pain, nausea, vomiting, and fever). Nine studies assessed the effectiveness of interventions on psycho-physiological responses [37–45] and eight studies only assessed psychological responses but did not assess children's physiological responses [46–52].

Based on these studies, some studies show insignificant results. The psychological intervention in the form of MEDiPORT was reported to have no significant effect on the level of pain felt by children with cancer who underwent needle insertion. MEDiPORT is a 3-foot-tall humanoid robot (NAO hardware produced by Softbank Robotics and MEDi software produced by RxRobots. The robot is self-standing, able to walk, has hands that can self-adapt and grip, has eyes with light emission diodes, and has two speakers and four microphones to detect and project sounds. The robot can be programmed using a proprietary software development kit [37]. In addition, other studies have reported that massage therapy in adolescents with cancer undergoing hospitalization shows no significant changes in anxiety, mood, or fatigue from before to after the intervention [49]. This review shows that all studies that measure psychological responses use questionnaires. The questionnaires used varied, but most of the psychological problems assessed were the child's level of anxiety, mood, fear, and distress/stress level. At the same time, the physiological response is assessed through symptoms such as pain, nausea, vomiting, fever, and changes in vital signs such as blood pressure and heart rate. Measurement of pain level and assessment of symptoms such as nausea and vomiting in all studies used a questionnaire. Meanwhile, measuring vital signs such as blood pressure and heart rate uses standard tools. Diastolic and systolic blood pressure and heart rate in this study were used to measure children's physiological stress. Research has found that measuring physiological responses is always accompanied by assessing psychological responses using a questionnaire.

2. Impact of psychological intervention on the psycho-physio-neuroimmunological marker.

Based on this review, we found that there was one article that only assessed the effectiveness of psychological interventions on neuroimmunological markers [53], one article assessing psycho-neuroimmunological markers [54], one article assessing physio-neuroimmunological markers [24], and one article assessing psycho-physio-neuroimmunological markers [55].

Based on this review, music therapy is one of the psychological interventions used to manage neuroimmunological responses. Music therapy does not statistically affect cortisol levels but

Table 2 *Checklist For Randomized Control Trial (RCT) And Non Randomized Control Trial (Non RCT) From The Joanna Briggs Institute (JBI).*

Studies Included Randomised Control Trial (RCT) (13 Item Question)																
No	Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total score	Category
1	(Jibb et al., 2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13	100.0% (Good)
2	(McCullough et al., 2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13	100.0% (Good)
3	(Gerçeker et al., 2021)	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N	Y	11/13	84.6% (Good)
4	(Shoshani et al., 2016)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	N	Y	10/13	76.9% (Good)
5	(Gürcan and Atay Turan, 2021)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	N	10/13	76.9% (Good)
6	(Lam et al., 2018)	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	11/13	84.6% (Good)
7	(Jacobs et al., 2016)	N	N	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	9/13	69.0% (Fair)
8	(Li et al., 2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13	100.0% (Good)
9	(Zhang et al., 2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13/13	100.0% (Good)
10	(Hsiao et al., 2019)	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	Y	Y	9/13	69.0% (Fair)
11	(Cheng and Tan, 2021)	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	N	N	7/13	53.8% (Fair)
12	(Liu et al., 2019)	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	10/13	76.9% (Good)
Studies Included Non-Randomized Control Trial (Non RCT) (9 Item Question)																
No	Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9					Total score	Category
13	(Hasanah et al., 2020)	Y	Y	Y	N	Y	N	Y	Y	Y	-	-	-	-	7/9	77.0% (Good)
14	(Genik et al., 2020)	Y	Y	Y	Y	Y	N	Y	Y	Y	-	-	-	-	8/9	88.8% (Good)
15	(Lopes-Junior et al., 2020)	Y	Y	Y	N	Y	N	Y	Y	Y	-	-	-	-	7/9	77.0% (Good)
16	(Cheng and Tan, 2021)	Y	Y	Y	Y	Y	Y	Y	Y	Y	-	-	-	-	9/9	100.0% (Good)
17	(Çelebioğlu et al., 2015)	Y	Y	Y	Y	Y	N	Y	Y	Y	-	-	-	-	8/9	88.8% (Good)
18	(Altay et al., 2017)	Y	Y	Y	N	Y	N	Y	Y	Y	-	-	-	-	7/9	77.0% (Good)
19	(Patil et al., 2021)	Y	Y	Y	Y	Y	N	Y	Y	Y	-	-	-	-	8/9	88.8% (Good)
20	(Silva and Osó Rio, 2018)	Y	Y	Y	N	Y	N	Y	Y	Y	-	-	-	-	7/9	77.0% (Good)
21	(Chacin-Fernández et al., 2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	-	-	-	-	9/9	100.0% (Good)

Note: Y: Present; NA: Not Applicable; N: Not Present; RCT: Randomized Control Trial; Non RCT: Non Randomized Control Trial; JBI: The Joanna Briggs Institute.

clinically shows a positive effect in reducing cortisol levels. The study suggested that the results that were not statistically significant could be caused by several things, including the small sample size, the range of results for measuring cortisol levels that were too far apart, the homogeneity of clinical conditions and levels of stress exposure, environmental factors, and the time and duration of therapy music that is too long [53]. Meanwhile, a study by Lopes Junior et al. (2020) reported that the clown intervention positively impacted cortisol levels but did not impact α-amylase levels in children with cancer. Future research should focus on a specific tumor type, have homogeneous samples, and use a more detailed investigation with robust statistical analyses. Future studies could also identify pediatric cancer inpatient profiles most likely to benefit from this type of intervention regarding age, gender, frequency of clown visits, and follow-up period [54]. In addition, a related study was also conducted in the UK and found that pediatric patients with leukemia who underwent PNI-based psychological interventions had a strong correlation between improvements in several key immune markers and a more satisfactory evolution of various clinical aspects of the disease, symptomatic treatment, and quality of life [24]. Quasi-experimental research conducted in Taiwan also identified the effectiveness of therapeutic play on changes in psychological, physiological, and neuroendocrine aspects. This study reports that therapeutic play interventions can reduce anxiety, heart rate (HR), and cortisol scores before External beam radiotherapy (EBRT) in children with brain tumors [55]. A summary of the studies can be seen in Table 3.

Development of a new integrative model

The following illustrates a new integrative model that explains the relationship between the biopsychosocial model, PNI, and psychological intervention in children with cancer. Based on the results of a systematic review and the incorporation of several theoretical concepts, the development of this new integrative model is divided into four domains, including.

1. Factors that affect stress (Box A-C)

Based on the biopsychosocial model, the factors influencing a person's stress condition include psychosocial, biological, and health behavior. Psychosocial processes (Box A) are factors that influence a person's interpretation and response to stressors which include individual differences (e.g., the child's personality model, coping strategies used, and perceptions of illness); mood (e.g., feeling of helplessness, anxiety levels, and stress levels); resources (e.g., social support, care-giver's coping strategies, care-giver's degree of psychological distress); other (stress reactivity). Biological factors (Box B) are factors that influence a person's response to a stressor, including genetics, gender, age, diagnosis of cancer, type of cancer, physical symptoms, medical treatment, repeat invasive procedures, and repeat hospitalization. Health behaviors/lifestyle factors (Box C) are factors that influence a person's response to a stressor, e.g., quality and quantity of sleep, healthy diet, exercise, and treatment adherence. The indicators for each psychosocial, biological, and health behavior domain refer to previous literature, which discusses the factors that influence stress regulation in children with cancer [23].

2. Stress

Stress is a person's inability to cope with perceived threats to one's mental, physical, emotional, and spiritual well-being, resulting in physiological responses and adaptations [56]. All cancer patients experience distress due to the diagnosis, effects of the disease, or treatment being undertaken [57]. Life stress (Box D) can be acute or chronic. Acute stress lasts minutes to hours, and chronic stress lasts months to years [19]. Acute and chronic stress will affect

Table 3 *Summary of Study Description (n = 21).*

No	Author, year	Country	Design	Sample Size (N) Age Mean ± SD/Median (Mean-Max)		Participant and setting	Type of intervention		Instrument	Outcome		Result
				Intervention group age	Control group age		Intervention group	Control group		Psychological and physiological responses	Psychoneuro immunological markers	
1	(Hsiao et al., 2019)	Taiwan	Quasi-Experimental	n = 7 Age: 0–18 years mean ± SD 0.65 ± 0.27	n = 6 Age: 0–18 years mean ± SD 4.81 ± 2.75	Patients with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) aged <18 years who underwent BMP and lumbar puncture (n = 13)	Psycho-social interventions consisting of preparation and cognitive behavioral interventions	Without psychosocial interventions	Observational Scale of Behavioral Distress (OSBD-R)	Distress level	–	The mean age at diagnosis of leukemic was 6.6 years (range: 3–11 years). Fifteen patients were diagnosed with acute lymphoblastic leukemic, and 3 were diagnosed with acute myeloid leukemic. The mean OSBD-R total score in the 7 patients with psychosocial intervention was significantly lower than the mean score in the 6 patients without intervention (0.65 vs 4.81, pZ0.002). Pre- and post-psychosocial interventions for BMA and LP behavioral disorders were evaluated for the remaining 5 patients. Consistently, there was a significant decrease in the OSBD-R score after the intervention (3.04 vs. 7.81, pZ0.025)
2	(Jibb et al., 2018)	Canada	Randomized controlled trial	n = 19 Age: 4–9 years mean ± SD 2.6 ± 3.5	n = 21 Age: 4–9 years mean ± SD 3.5 ± 3.9	Pediatric patients aged 4 to 9 years with cancer who underwent needle insertion (n = 40)	MEDiPORT cognitive-behavioral arm (robot using evidence-based cognitive-behavioural interventions) or active distraction arm (robot dancing and singing)	No control group	1. Face Pain Scale— Revised (FPS-R) 2. The Children's Fear Scale (CFS) 3. Behavioral Approach-Avoidance Scale (BAADS)	1. Pain level 2. Degree of fear 3. Distress level	–	Overall, MEDiPORT and this study were acceptable to the participants. There was no significant difference in pain intensity between arms (P = .68), but there was less pressure during the procedure on the distracted arm. No differences between groups were observed for the fear and distress subscale (P = .012).
3	(McCullough et al., 2018)	USA	Randomized controlled trial	n = 60 Age: 3–17 years mean ± SD 8.9 ± 4.5	n = 46 Age: 3–17 years mean ± SD 8.1 ± 4.6	Newly diagnosed cancer patients, aged 3 to 17 years (n = 106)	Animal-assisted interventions	standard care	1. The State-Trait Anxiety Inventory™ 2. Pediatrica Quality of Life Inventory 3. Child blood pressure and heart rate	1. Anxiety level 2. Blood pressure and heart rate	–	Children in both groups experienced a significant decrease in anxiety (P < .001). However, there were no significant differences between groups over time at any of the observed measures.
4	(Gerçeker et al., 2021)	Turkey	Randomized controlled trial	n = 21 Age: 6–17 years mean ± SD 2.4 ± 1.8	n = 21 Age: 6–17 years mean ± SD 5.3 ± 1.8	Hematology-oncology pediatric patients undergoing port with Huber needle aged >6 to <17 years (n = 42)	Virtual reality	standard care (without VR)	1. Wong-Baker Faces Pain Rating Scale 2. Children's Anxiety Meter 3. Child Fear Scale	1. Pain level 2. Level of anxiety 3. Degree of fear	–	Patient self-reported pain scores in the VR and control groups were 2.4 ± 1.8 and 5.3 ± 1.8, respectively. This study found statistically significant differences between groups in pain scores

												(p < .001). Statistically significant differences were found between groups according to self-reported and parental fear and anxiety scores after the procedure. Self-reported fear scores in VR and control groups were 0.8 ± 0.9, 2.0 ± 1.0, self-reported anxiety scores were 2.9 ± 2.0, 5.4 ± 2, respectively 0 (p < .001).
5	(Hasanah et al., 2020)	Indonesia	Pre-experimental study	n = 30 Age: 6–18 years median (min-max) Children: 0.00 (9.35 −3.18) Adolescent: 0.54 (2.47 −3.95)	None	Pediatric patients with leukemia aged 6–18 years who undergoing IV line insertion (n = 30)	Music therapy	no control group	ELISA	–	Cortisol levels	Cortisol levels before and after music therapy each had a median (min–max) of 4.14 (0.25–9.89) and 3.47 (0.16 −15.31). The median difference in cortisol levels was 0.67 ng/ml. This ≥0.05 ng/ml change indicates the clinical effect of music therapy on cortisol levels. Although music therapy did not significantly affect salivary cortisol levels (p = .99), this study revealed a clinical effect of music therapy in reducing cortisol levels.
6	(Genik et al., 2020)	Canada	Pre-post single group pilot study	n = 8 Age: 8–18 years mean ± SD 14.57 ± 2.51	None	Pediatric patients aged 8–18 years with cancer (n = 8)	Massage therapy	no control group	1. PainSquad App 2. Faces Pain Scale-Revised (FPS-R) 3. Children's Fear Scale (CFS).	1. Pain level 2. Degree of fear 3. Quality of life	–	All participants rated the MT intervention as acceptable and agreed that the intervention helped muscle pain (Mean = 4.80; Median = 5.00/5; range: 4–5; SD = 0.45), reduced anxiety/stress (Mean = 4.40; Median = 4, 00/5; range: 4–5; SD = 0.55), helped relax (Mean = 5.00; Median = 5.00/5; range: 5; SD = 0.00), and significantly increased their QOL overall (Mean = 4.60; Median = 5.00/5; range: 4–5; SD = 0.55).
7	(Lopes-Junior et al., 2020)	Brazil	Quasi Experimental	n = 16 Age: 6–14 years mean ± SD 11.4 ± 3.44	none	Pediatric patients with cancer undergoing chemotherapy aged 6–14 years (n = 16)	Clown intervention	no control group	1. High sensitivity enzyme-linked immunosorbent assay kit 2. Child Stress Scale-ESI 3. PedsQL Multidi mensional Fatigue Scale.	1. Stress level 2. Quality of life	Levels of salivary cortisol and α-amylase	Compared to baseline measurements, total psychological stress and fatigue levels improved after the clown intervention at the +4 h collection time point (P = .003 and P = .04, respectively). Salivary cortisol showed a significant decrease after the clown intervention at +1, +9, and +13 h collection time points (P < .05); however, α-amylase levels remained unchanged

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Table 3 (*continued*)

No	Author, year	Country	Design	Sample Size (N) Age Mean ± SD/Median (Mean-Max)		Participant and setting	Type of intervention		Instrument	Outcome		Result
				Intervention group age	Control group age		Intervention group	Control group		Psychological and physiological responses	Psychoneuro immunological markers	
8	(Shoshani et al., 2016)	Israel	Randomized controlled trial	n = 32 Age: 5–12 years mean ± SD 10.13 ± 3.51	n = 31 Age: 5-12 years mean ± SD 10.67 ± 4.71	Pediatric patients aged 5–12 with early diagnosis of cancer (n = 63)	Make a wish intervention	waiting list control group without make a wish intervention	1. The Brief Symptom Inventory-18 (BSI) 2. The Global Severity Index (GSI) 3. PedsQL 4. The Positive and Negative Affect Schedule for Children (PANAS-C) 5. Herth Hope Index (HHI) 6. The Life Orientation Test-Revised (LOT-R)	1. Level of distress 2. Depression 3. Level of anxiety 4. Quality of life	–	Children in the intervention group showed significant reductions in general distress (d = 0.54), depression (d = 0.70), and anxiety symptoms (d = 0.41), improvement in health-related quality of life (d = 0 .59), expectation (d = 0.71), and positive affect (d = 0.80) and there was no significant change in other measures in the control group.
9	(Gürcan and Atay Turan, 2021)	Turkey	Randomized controlled trial	n = 30 Age: 12–17 years mean ± SD 14.26 ± 1.79	n = 30 Age: 12–17 years mean ± SD 13.56 ± 1.67	Adolescent patients with cancer aged 12 –17 years who are hospitalized (n = 60)	Mandala drawing	routine care only	Anxiety and Depression Scale dan Memorial Symptom Assessment Scale	1. Levels of anxiety and depression 2. Psychological symptoms	–	Anxiety and depression scores decreased significantly in the intervention group, compared to the control group, after 5 days of intervention, $F(1.57) = 28.9$, $p < .01$, $\eta 2 = 0.337$. Similarly, psychological symptom scores decreased significantly in the intervention group, compared to the control group, $F(1.57) = 69.7$, $p < .001$, $\eta 2 = 0.550$).
10	(Cheng and Tan, 2021)	Singapore	Randomized controlled trial	n = 25 Age: 10–18 years mean ± SD 13.9 ± 2.4	n = 25 Age: 10–18 years mean ± SD 13.4 ± 2.6	Pediatric patients with cancer aged 10–18 who are undergoing chemotherapy (n = 50).	The home-based multimodal symptom-management program	usual care	Memorial Symptom Assessment Scale 10 –18 and the State Anxiety Scale for Children.	1. Symptoms 2. Anxiety	–	Between-group comparisons showed that the intervention group had significantly reduced fatigue over time ($P < .05$). However, no differences were found with respect to nausea and vomiting, pain, mucositis, and anxiety between groups. Both children and parents reported positive experiences with symptom management programs.
11	(Çelebioğlu et al., 2015)	Turkey	Quasy experimental	n = 12 Age: 4–15 years mean ± SD 7.66 ± 3.86	n = 13 mean ± SD 8.00 ± 3.31	Pediatric patients aged 4–15 years in children with cancer (n = 25)	massage therapy	standard treatment (without massage therapy)	Analog visual scale	Pain and anxiety levels	–	When the pain and anxiety levels of the pre-test and post-test groups were compared, no statistically significant difference was found ($P > .05$). It was determined that the pain and anxiety levels in the

											experimental group decreased significantly. This study provides preliminary evidence for the effectiveness of massage in children in reducing pain and anxiety arising from intrathecal therapy or bone marrow aspiration.
12	(Lam et al., 2018)	China	Randomized controlled trial	n = 37 Age: 9–18 years mean ± SD 12.8 ± 2.5	n = 33 Age: 9–18 years mean ± SD 12.5 ± 2.5	Pediatric patients with cancer aged 9–18 years (n = 70)	Integrated experiential training program with coaching	placebo interventions	1. The Chinese version of the Fatigue Scale (Cancer-related fatigue) 2. The Chinese University of Hong Kong Physical Activity Rating for Children and Youth 3. Paediatric Quality of Life Inventory cancer module v. 3.0 (Quality of life)	1. Fatigue level 2. Physical activity 3. Quality of life	–	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 grip strength, and better quality of life than the control group at 9 months.
13	(Jacobs et al., 2016)	Washington DC	Randomized controlled trial	n = 18 Age: 12–21 years mean ± SD 15.5 ± 2.6	n = 16 Age: 12–21 years mean ± SD 16.0 ± 2.5	Adolescent patients aged 12–21 with cancer who are hospitalized for at least 4 consecutive days.	Massage therapy	waitlist control (without massage)	1. Sleep was measured with actigraphy 2. Fatigue Scale Adolescent 3. The State Trait Anxiety Scale, State Portion 4. Behavioral, Affective and Somatic Experiences Scale Revised, Parent-Report and Child-Report (BASES)	1. Sleep quality 2. Fatigue level 3. Level of anxiety 4. Moods	–	The results showed that there was no significant change in anxiety, mood or fatigue from pre to post intervention. However, there was a trend toward increased night time and overall sleep in the intervention group compared to standard care, but no between-group differences on patient-reported outcome measures (2.3, P = .049).
14	(Li et al., 2018)	Hongkong	Randomized controlled trial	n = 117 Age: 9–16 years mean ± SD 12.8 ± 1.9	n = 105 Age: 9–16 years mean ± SD 12.5 ± 2.6	Pediatric patients with cancer aged 9–16 years (n = 222)	Adventure-based training	placebo interventions	Fatigue Scale–Child (FS–C)	fatigue level	–	The experimental group showed statistically significantly lower levels of cancer–related fatigue (P < .001), higher levels of self-efficacy (P < .001) and physical activity (P < .001), and better quality of life (P < .01) than the control group at 12 months.
15	(Zhang et al., 2019)	China	Randomized controlled trial	53 cases were from the children aged from 8 to 12 years old and 46 cases from 13 to 18 years old. mean ± SD Not mentioned	53 cases were from the children aged from 8 to 12 years old and 46 cases from 13 to 18 years old. mean ± SD Not mentioned	Pediatric cancer patients receiving chemotherapy aged 8–18 years (n = 106)	Cognitive behavioral therapy	routine psychological care	The Conner–Davidson Resilience Scale (CD-RISC) and depression anxiety stress scale (DASS)	Resilience, stress and anxiety levels	–	Before the intervention, there was no significant difference in the psychological adjustment abilities between the 2 groups (P > 0.05 for all). After the intervention, the total CD-RISC score was significantly higher (56.09 ± 7.29 vs 44.75 ± 5.40),

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Table 3 (*continued*)

No	Author, year	Country	Design	Sample Size (N) Age Mean ± SD/Median (Mean-Max)		Participant and setting	Type of intervention		Instrument	Outcome		Result
				Intervention group age	Control group age		Intervention group	Control group		Psychological and physiological responses	Psychoneuro immunological markers	
												while the depression score (4.57 ± 2.94 vs 7.25 ± 4.25), anxiety (5.83 ± 3.07 vs 8.66 ± 4.92), stress (7.51 ± 4.33 vs 11.17 ± 4.25) were clearly lower in the CBT group than in the control group ($P < 0.05$ for all). Additionally, the reduction in negative mood scores in children with a yolk sac tumor was most pronounced in the CBT group.
16	(Chacin-Fernández et al., 2019)	UK	Non-randomized, open-label clinical trial	n = 16 Age: 5–15 years mean ± SD 10.1 ± 0.9	n = 10 Age: 5–15 years mean ± SD 9.8 ± 1.2	Pediatric patients with leukemia undergoing chemotherapy (n = 26)	Psychoneuro immunology-based psychological interventions.	psychoeducation in relation to their treatment and disease,	1. Immunological evaluation using flow cytometry and immunotur bidimetry 2. Quality of Life was assessed using the QoL Questionnaire in Pediatric Oncology.	1. Duration of signs and symptoms (Fever and Pain) 2. Duration of administration of pain therapy, antibiotics and antipyretics	Immune markers - Natural killers (NK) - B lymphocytes - CD4+ T lymphocytes - CD8+ T lymphocytes - IgM IgA antibodies - IgA antibodies	Psychoneuro immunology-based interventions improve immune markers (CD8+ T, B, and natural killer cells, serum immuno globulin A, and immuno globulin M) and quality of life, while shortening the duration of fever and the use of antipyretics, antibiotics, analgesics, and respiratory therapy. Immunity markers correlate with clinical conditions. Thus, psychoneuroimmunology-based interventions can reduce hospital costs and improve patient well-being
17	(Altay et al., 2017)	Turkey	Quasi-experimental design	n = 30 Age: 9–16 years mean ± SD 2.56 ± 267	Without control group	Pediatric patients with cancer who are undergoing treatment aged 9 –16 years (n = 30)	Drawing and writing technique	no control group	The State Anxiety Inventory	anxiety level	–	A lower State Anxiety Inventory score indicates lower anxiety after the intervention (36.86 ± 4.12 compared to before (40.46 ± 4.51) ($p < .05$).
18	(Patil et al., 2021)		Quasi-experimental design	n = 15 Age: 7–12 years Not mentioned mean ± SD	n = 15 Age: 7–12 years Not mentioned mean ± SD	Pediatric patients with cancer aged 7 –12 years (n = 30)	art therapy (drawing, painting and ceramic art)	routine therapy	Perceived stress scale dan Hamilton anxiety rating scale (HAM-A)	Stress and anxiety	–	The effect of art therapy in the experimental group showed a significant difference in mean post-test stress and anxiety scores ($p = .00069$ and $p = 0.000642$) compared to controls. Comparison of anxiety scores with all types of cancer showed a significance of $p = .010$ in the experimental group compared to the controls in the post-test

19	(Liu et al., 2019)	China	Randomized controlled trial	n = 46 Age: 10–21 years mean ± SD 15.9 ± 5.2	n = 45 Age: 10–21 years mean ± SD 16.2 ± 4.9	Pediatric patients with osteosarcoma aged 10–21 years (n = 91)	Mindfulness-based stress reduction	routine therapy (no psychological intervention)	1. Wong-Baker Faces Pain Rating Scale (WBRS) 2. The Hamilton Anxiety Rating Scale (HAM-A) 3. The Pittsburgh Sleep Quality Index (PSQI)	1. Pain level 2. Anxiety level 3. Sleep quality	–	There were no significant differences in sociodemographic and clinical parameters between the intervention and control groups. The intervention program significantly alleviated the psychological and physiological complications in patients with osteosarcoma. Specifically, this study revealed that 8 weeks of the combined MBSR/MT intervention effectively reduced pain and anxiety scores and improved sleep quality in patients.
20	(Tsai et al., 2013)	Taiwan	Quasi-experimental design	9 patients aged 3 −12 years (median = 8.12 years)	10 patients aged 3 −14 years (median = 8.9 years)	Brain tumor patients, aged 3 −15 years (n = 19)	Therapeutic play	general medical procedures	The Beck Youth Anxiety Inventory dan Faces Anxiety Scale	1. Anxiety level 2. Heart rate	Salivary cortisol concentration	The study group had significantly lower anxiety, HR and cortisol scores and expressed fewer negative emotions than the control group before External beam radiotherapy (EBRT).
21	(Silva and Osó Rio, 2018)	Italy	Quasi-experimental design	n = 24 Age: 6–12 years mean ± SD 8.58 ± 1.98	none	Pediatric patients with a diagnosis of solid tumor aged 6 to 12 years (n = 24)	Animal assisted therapy	no control group	1. Child Stress Symptoms Inventory 2. Quality of Life Evaluation Scale 3. Child Depression Inventory 4. Adapted Brunel Mood Scale: Faces Pain Scale 5. AAT Assessment Questionnaire	1. Stress 2. Pain 3. Mood 4. Anxiety, depression 5. Quality of life 6. Heart rate, and blood pressure.	-	This study reported reductions in pain (p = .046, d = −0.894), irritation (p = 0.041, d = −0.917), stress (p = .005; d = −1.404) and a trend toward improvement in depressive symptoms (p = .069; d = −0.801).

Note: AAT: Animal Assisted Therapy; ALL: Acute Lymphoblastic Leukemia; AML: Acute Myeloid Leukemia; BAADS: behavioral Approach-Avoidance Scale; BASES: behavioral, Affective And Somatic Experiences Scale; BMP: Bone Marrow Puncture; BMA: Bone Marrow Aspiration; CD4+: Cluster Of Differentiation 4; CFS: Children's Fear Scale; CBT: Cognitive behavioral Therapy; EBRT: External Beam Radiotherapy; DASS: Depression Anxiety Stress Scale; FPS-R: Faces Pain Scale-Revised; FS-C: Fatigue Scale–Child; HR: Heart Rate; HHI: Herth Hope Index; IgM: Immunoglobulin M; IgA: Immunoglobulin A; LP: Lumbar Puncture; MBSR/MT: Mindfulness-Based Stress Reduction; MT: Massage Therapy; NK: Natural Killers; OSBD-R: Observational Scale Of behavioral Distress; PedsQL: Pediatrics Quality Of Life; QoL: Quality Of Life; SD: Standard Deviation; BSI: The Brief Symptom Inventory-18; GSI: Global Severity Index; PANAS-C: The Positive And Negative Affect Schedule For Children; LOT-R: The Life Orientation Test-Revised; HAM-A: The Hamilton Anxiety Rating Scale; PSQI: The Pittsburgh Sleep Quality Index; CD-RISC: The Conner-Davidson Resilience Scale; VR: Virtual Reality; WBRS: Wong-Baker Faces Pain Rating Scale.

the stress response through psychoneuroimmunological markers (psychological responses, neuroendocrine and immune markers) (Box E).

3. Psychological interventions

Psychological interventions (Box F) are designed to modulate the stress response and promote health behaviors by teaching individuals more adaptive methods of dealing with perceived stress. Psychosocial interventions are useful for treating stress-related disorders and can influence the course of chronic disease [58]. Based on the results of this review, we identified 18 types of psychological interventions used to manage psychoneuroimmunological markers in children with chronic illness, including MEDiPORT cognitive-behavioral arm, animal-assisted therapy, virtual reality, music therapy, massage therapy, clown intervention, make-a-wish intervention, mandala drawing, cognitive behavioral therapy, deep breathing, pet therapy, hypnosis, touching, relaxation-guided imagery, humor therapy, interactive therapeutic play education program, play therapy, and sleep hygiene.

4. Neuroendocrine and immune mechanisms

Neuroendocrine and immune system mechanisms in the biopsychosocial model suggest integration from the field of psychoneuroimmunology (PNI). Box F shows the bidirectional communication of PNI, which is the mechanism that occurs in a two-way interaction between the neuroendocrine and immune axes that mediates the relationship between biobehavioral factors (Box A–D). PNI is divided into four domains: psychology, physiology, neuroendocrinology, and immunology. The indicators for all domains are compiled based on the results of this systematic review. Based on the results of our systematic review, the psychological system domain is assessed through several indicators such as anxiety, fear, stress/distress, mood, sleep disorder, resilience, fatigue, and depression. The physiology domain is evaluated through indicators such as blood pressure, heart rate, fever, and pain. The authors found no studies in this systematic review that assessed the neurological system through neurological markers such as dopamine, epinephrine, norepinephrine, β-endorphins, or other markers. Meanwhile, in the endocrine system domain, the indicators assessed were cortisol, and the immune system indicators assessed included: Natural killers (NK), B lymphocytes, CD4+ T lymphocytes, CD8+ T lymphocytes, IgM IgA antibodies, IgA antibodies, and α-amylase).

Table 3 provides a brief description of the new integrative model.

Discussion

Effectiveness of psychological interventions on the psychological and physiological responses in children with cancer

The utilization of psychological interventions in the management of mental health among pediatric oncology patients holds promise for enhancing both psychological and physical health outcomes. A total of nine studies were conducted to evaluate the efficacy of various interventions, including animal-assisted intervention, cognitive behavioral therapy, virtual reality, massage therapy, mandala drawing, the home-based multimodal symptom-management program, and mindfulness-based stress reduction, in terms of their impact on psychological and physical responses [37–45]. Three out of nine studies indicated that psychological interventions did not yield statistically significant outcomes in terms of the psychological and physiological responses observed in children diagnosed with cancer. The statistical analysis conducted in a study indicates that there is no significant evidence to support the effectiveness of massage therapy in managing the physiological and psychological responses of children diagnosed with cancer [43]. Moreover, the utilization of the MEDiPORT humanoid robot for the purpose of mitigating procedural pain and distress in pediatric cancer patients yielded comparable outcomes in both the control and intervention groups [37]. The study found that the home-based multimodal symptom-management program was effective in reducing fatigue among participants. However, there was no significant difference observed between groups in terms of reducing nausea and vomiting, pain, mucositis, and anxiety [42].

Out of the nine studies examined, six of them indicated that various psychological interventions, including animal-assisted intervention, cognitive behavioral therapy (CBT), virtual reality, mandala drawing, and mindfulness-based stress reduction (MBSR), have been found to be effective in managing the psychological and physiological responses experienced by children diagnosed with cancer. This aligns with a prior systematic review conducted in the United Kingdom in 2017. The review indicated that a total of nine studies demonstrated statistically significant enhancements in psychological outcomes. The aforementioned findings suggest that psychological interventions have demonstrated efficacy in diminishing anxiety, physical symptoms, depressive symptoms, and enhancing overall quality of life [59].

Several other studies have documented the efficacy of psychological interventions, particularly those that employ more targeted and specific approaches. Animal-assisted therapy has been successfully utilized across different age groups and for various disease diagnoses. For instance, it has been employed in the context of pediatric surgery for children [60]; as well as for children diagnosed with Post-Traumatic Stress Disorder (PTSD) [61]; and those receiving treatment in acute care pediatric settings [62]. Contrary to the aforementioned viewpoint, Feng et al. [63] conducted a systematic review that found no significant impact of animal-assisted therapy on anxiety, depression, stress, and heart rate among hosptialized children and adolescents. In the field of psychology, CBT has emerged as a prevalent intervention technique. This approach has been modified to cater to various age groups, including children, adolescents, adults, couples, and families. The cognitive aspect of CBT focuses on mitigating exaggerated and negative thoughts related to pain, while the behavioral component involves implementing relaxation techniques and activating coping behaviors [64,65] Psychological intervention has been found to have an impact on brain mechanisms, leading to a decrease in both pain and anxiety experienced by individuals. According to existing scholarly works, various aspects of successful psychological intervention may be corroborated by alterations in neural circuitry. These alterations are typically characterized by decreased activation and/or diminished hyperconnectivity in brain regions associated with pain processing, emotion, and cognitive control [64].

According to the review, a total of eight studies exclusively evaluate the efficacy of psychological interventions in managing the psychological reactions exhibited by children diagnosed with cancer [46–52,66]. Seven out of the eight studies presented in this analysis have indicated that psychological interventions possess considerable potential in effectively managing psychological responses among children. Additional empirical evidence has also documented the positive impact of psychological interventions on the psychological responses of children with various conditions. For instance, studies have shown the effectiveness of music therapy in children undergoing surgery and those with asthma [67,68]; virtual reality (VR) therapy in children with sickle cell disease and those undergoing surgery [69,70]; pet therapy for children undergoing hospitalization [71]; hypnosis in children with cancer, in children

with burns, and children with Crohn's disease [72–76]; parental touch followed by music therapy in critically ill children [77]; relaxation-guided imagery in children undergoing surgery [78]; humor therapy in children with atopic dermatitis [79]; interactive therapeutic play education program for children undergoing surgery [80]; and play therapy in children undergoing elective surgery and in children undergoing liver transplantation [81–84]. Certain studies have the potential to be grounded in empirical evidence, as they demonstrate that psychological interventions have a notable impact on the management of psychological reactions, thereby enhancing the overall quality of child healthcare [46]. The implementation of psychological interventions presents cancer patients with a comprehensive approach to healthcare, potentially safeguarding the overall physical and psychological welfare of individuals diagnosed with cancer [85].

According to a study conducted on children with cancer, approximately one out of every eight studies revealed no statistically significant alterations in anxiety, mood, or fatigue levels following the implementation of psychological intervention through massage therapy [49]. Nevertheless, this finding contradicts the conclusions drawn from previous systematic reviews, which demonstrated the efficacy of massage therapy in effectively mitigating stress levels among children receiving palliative care in hospital settings [86,87]. Massage therapy has been found to have beneficial effects on various pediatric conditions. The aforementioned factors encompass a range of issues affecting preterm infant growth, psychological well-being, gastrointestinal functioning, painful conditions such as burns and sickle cell disease, muscle tone disorders like cerebral palsy and Down syndrome, as well as chronic illnesses including diabetes, asthma, cancer, and HIV [88].

Effectiveness of psychological interventions on the psycho-physio-neuroimmunological markers in children with cancer

The current body of research examining the efficacy of psychological interventions on psycho-physio-neuroimmunological markers in pediatric populations, particularly those diagnosed with cancer, remains relatively scarce. Based on the findings of this comprehensive systematic review, it was determined that a mere four out of the total of 21 studies examined in this analysis focused on the evaluation of psycho-physio-neuroimmunological markers. In this investigation, the efficacy of psychological interventions on neuroimmunological markers was examined in one study [53]. Additionally, another study focused on psychoneuroimmunological markers [54], while a separate study explored physio-neuroimmunological markers [24]. Furthermore, a study was conducted to investigate the impact of psychological, physiological, and neuroimmunological factors on markers [55].

A single study was identified that exclusively evaluated the neuroimmunological response. According to the study, music therapy has a statistically significant impact on neuroimmunological markers, specifically salivary cortisol levels. This study elucidated the clinical impact of music therapy on the reduction of cortisol levels [53]. This finding aligns with the findings of Finn & Fancourt [89] who conducted a review and observed that 13 out of the 33 biomarkers tested exhibited changes following exposure to music. One of the biomarkers that has been extensively examined is cortisol, a stress hormone. Approximately half of the clinical studies conducted have indicated that listening to music has a stress-reducing impact. Several other biomarkers that have been examined are also components of biological stress pathways, suggesting that the primary mechanism by which music impacts us biologically is through the modulation of the stress response.

The previous literature has provided a description of the mechanism by which music therapy regulates cortisol levels. The auditory perception of music elicits neural responses in the hypothalamus, subsequently triggering the release of endorphins through the activation of the pituitary gland [56,90]. Endorphins, which are endogenous opiates similar to morphine, serve as the body's innate analgesics and possess the ability to mitigate the impact of stressful conditions by modulating cortisol levels [56,90]. According to previous studies, psychological interventions, including animal-assisted activities, have not shown statistically significant effects on salivary cortisol levels and C-reactive protein (CRP) in children who are hosptialized [91]. An additional discovery pertains to the impact of psychological interventions on the levels of noradrenaline and cortisol, while the levels of adrenaline remain unaffected. The intervention had a discernible impact on adrenaline levels exclusively within a time frame of 6-8 days following surgery in patients undergoing Coronary Artery Bypass Graft (CABG) procedures [92].

Three studies were identified that aimed to evaluate the neuroimmunological markers as well as the physical and psychological responses in pediatric patients diagnosed with cancer. The aforementioned studies have documented that various psychological interventions, such as clown intervention, therapeutic play, and psychoeducational intervention, yielded favorable outcomes in terms of physical, psychological, and neuroimmunological indicators in pediatric cancer patients. These indicators include cortisol levels, α-amylase levels, CD8+ T cells, B cells, natural killer (NK) cells, serum immunoglobulin A (IgA), and immunoglobulin M (IgM) [24,54,55]. The implementation of clown intervention has demonstrated efficacy in the management of psycho-physio-neuroimmunological markers among pediatric cancer patients. Nevertheless, the findings of this review exhibit notable disparities when compared to previous research. According to a previous conducted by Ding et al., it was found that clown intervention has a positive impact on distress levels, duration of crying following a medical procedure, and length of hospital stay. Nevertheless, the study findings did not reveal any statistically significant disparity in cortisol levels [93,94]. In contrast, there has been limited research conducted on the efficacy of therapeutic play. No comparable studies evaluating the efficacy of therapeutic play on psycho-physio-neuroimmunological markers were identified by researchers. Nevertheless, according to William et al. [95] it was found that children who underwent therapeutic play intervention exhibited reduced levels of state anxiety scores during both the pre-operative and post-operative periods. In addition, psychoeducation interventions have been implemented in patients undergoing multidrug therapy (MDT) treatment. The research findings indicated that psychoeducation was successful in enhancing spiritual response, perception, stigma, and anxiety, while also reducing cortisol levels [95].

Various psychological interventions have been documented for the management of psycho-physio-neuroimmunological markers. The study conducted by Chang et al. examines the efficacy of psychological interventions, specifically the Laughing Qigong program (LQP), in adolescent patients who are undergoing hospitalization. LQP is an integrative approach that combines the practices of qigong and laughter techniques, emphasizing the interplay between the mind and body. This study examined both neuroimmunological responses, specifically cortisol levels, as well as their impact on physical responses, including heart rate and heart rate variability, and psychological responses, such as mood states, self-esteem, self-efficacy, and depression [96]. In 2021, a study conducted in Peru yielded similar findings, indicating the positive impact of providing augmented reality books on the management of psychological and neuroimmunological responses. The evaluation of emotional stress and neuroimmunological markers in hosptialized children involved the utilization of the Weisz visual

analogue scale to assess psychological responses, alongside the measurement of cortisol levels. This study was unable to provide evidence supporting the hypothesis that reading augmented reality books resulted in a greater reduction of salivary cortisol levels compared to reading a standard book among children who were hosptialized. In addition, it has been found that augmented reality (AR) books have a positive impact on reducing emotional stress, as measured by the Weisz visual analogue scale [97].

Additional psychological interventions encompass the utilization of storytelling, which has been observed to exert an influence on both physiological responses and neuroimmunological markers. Specifically, this intervention has been found to elevate oxytocin levels while concurrently reducing cortisol and pain levels in children undergoing treatment in intensive care units (ICU) [98]. In the realm of psychological interventions, it has been observed that mindfulness-based stress reduction (MBSR) techniques have proven to be advantageous, resulting in notable enhancements in both psychological and biological aspects, including endocrine and immunological markers [99,100]. The existing body of literature pertaining to the neural underpinnings of psychological interventions in cancer patients is currently insufficient, necessitating additional investigation. A study conducted in the Netherlands in 2022 elucidates the mechanisms underlying psychological intervention in the regulation of psychoneuroimmunological responses. According to the study, psychological interventions administered to individuals with cancer have the potential to influence cortical and subcortical brain activity. These changes align with the brain regions associated with distress responses [85].

A new integrative model

Within the specific context of individuals diagnosed with cancer, the prevalence rate of psychological distress is observed to be four times greater compared to the general population. This heightened prevalence of psychological distress is frequently associated with inferior outcomes. Furthermore, a number of cellular and molecular studies have provided evidence supporting the intricate signaling networks influenced by chronic stress-induced psychological distress in the context of cancer development [101]. The experience of receiving a diagnosis, the effects of the disease, and the treatment process can elicit distress among individuals diagnosed with cancer [57]. The correlation between the specific cancer diagnosis of patients and the levels of physical distress, emotional distress, and depressive symptoms has been found to be statistically significant [102]. Furthermore, it should be noted that the administration of the treatment may lead to an exacerbation of the symptoms associated with heightened distress, as indicated by previous research [5]. Cancer survivors are at the greatest risk of developing endocrine disorders over time when they undergo cancer treatments involving radiation in major endocrine organs, including the hypothalamus, pituitary, thyroid, and gonads [13]. The immune system of an individual can be impacted by disorders within the endocrine system [18,56].

In addition to the diagnostic process, the presence of illness, or the administration of treatment, which are known stressors for pediatric cancer patients, a study conducted in Ohio, United States, elucidates that children with cancer experience stress in various domains. These domains include (a) disruptions in daily functioning and roles, such as missing school or falling behind in academic work, being unable to engage in previously enjoyed activities, frequent visits to hospitals or clinics, and concerns about the well-being of family and friends; (b) physical manifestations resulting from treatment, such as feelings of sickness or nausea, anxieties regarding changes in appearance, and discomfort or pain arising from medical procedures; and (c) uncertainties surrounding the nature of cancer, including difficulties comprehending medical explanations, confusion regarding the concept of cancer, and apprehensions about future outcomes [103].

The regulation of the neuroendocrine and immune systems can be influenced by a range of stressors, leading to potential impacts on the health outcomes of children. The impact of stress on immune function is exacerbated, while on the other hand, psychological interventions have the potential to regulate neuroendocrine activity and improve immune system functioning. However, there is limited knowledge regarding the extent to which children with cancer can achieve immunological recovery. The intricate nature of stress-induced factors in pediatric cancer patients and the limited amount of scholarly research examining potential mediating mechanisms, such as the impact of stress and psychological interventions on the immune system. Therefore, future research can employ this novel integrative model framework to manipulate the variables of psychological interventions, thereby facilitating the examination of direct effects on the immune response. The investigation of interventions that are most well-received by pediatric cancer patients is a fundamental aspect of immune effect preservation, thus necessitating additional scholarly inquiry in this domain.

There exist certain limitations to this review. Due to the diversity observed in the psychological interventions employed, the age range of the children included, the study design implemented, and the instruments utilized for outcome assessment, the feasibility of conducting a meta-analysis was precluded. Moreover, while the utilization of the JBI for evaluating bias in this review is comprehensive and adheres to explicit criteria, the individual assessment of studies by each author remains subjective. In order to enhance the comprehensiveness and validity of future research, it is recommended that subsequent investigations incorporate post-intervention evaluations to elucidate the enduring ramifications of the intervention. Additionally, it is crucial to account for the homogeneity of various indicators, including but not limited to gender, type of psychological intervention, type of cancer treatment, stage of cancer, type of instrument employed, methodologically appropriate sample size, and objective tools to assess bias. By considering these factors, researchers can obtain results that are more robust and reliable. Further research is required to comprehensively evaluate the effectiveness of psychological interventions in terms of their impact on neurobiological processes and clinical outcomes. The examination of the associations between observed neurobiological alterations and clinical outcomes is crucial in order to comprehend the potential neural activity changes that may be responsible for the clinical impact of an intervention [85]. The lack of clarity surrounding the terminology used in psychological interventions poses a potential limitation in this review, as it may hinder the identification of additional pertinent studies. When conducting further research, it is imperative to carefully select keywords that are more specific in order to avoid overlooking relevant studies.

Despite the presence of certain limitations, this review possesses several notable strengths. First, it stands as one of the pioneering evidence-based interventions that evaluates the efficacy of psychological interventions on psychoneuroimmunological markers in pediatric cancer patients. Second, it introduces a novel integrative model that can aid healthcare professionals in making informed clinical decisions. This model offers a comprehensive and holistic depiction of the various factors that impact stressful conditions in children with cancer. Furthermore, it provides insights into the mechanisms through which psychological interventions influence physical, psychological, and neuroimmunological markers in this population. It is imperative for future researchers to

thoroughly investigate the various integrative models, encompassing psychosocial factors, biological factors, health behaviors, neuroendocrine and immune system mechanisms, and disease outcomes. This examination should be conducted using a longitudinal design to comprehensively address the intricate interplay among these components and to gain a comprehensive understanding of their significance in relation to health outcomes. Psychological intervention is a viable evidence-based treatment option that can be employed by healthcare professionals in the field of nursing, particularly in the context of pediatric patients diagnosed with cancer. This intervention encompasses educational initiatives, counseling sessions, and training programs, all aimed at enhancing the overall well-being of children grappling with cancer. The findings of the study also emphasize the importance of nurses being aware that psychological intervention is a crucial aspect of providing comprehensive and high-quality nursing care for children with cancer. Consequently, the outcomes of this review may serve as valuable input for relevant stakeholders to incorporate psychological interventions into the nursing curriculum, thereby facilitating the enhancement of nursing students' skills during their collegiate education.

Conclusion

This review shows that many studies have identified the effectiveness of psychological interventions on psychological and physiological responses. However, research assessing the impact of psychological interventions on neuroimmunological markers is still very limited. This systematic review shows that psychological interventions positively impact psychoneuroimmunological markers in children with cancer. So, we recommend the use of psychological interventions as an additional intervention in pediatric cancer. This study offers a new integrative model demonstrating the interaction between several factors that influence stress in children with cancer through neuroendocrine and immune mechanisms. Meanwhile, this integrative model also shows how psychological interventions can modulate the effects of these various factors on neuroendocrine and immune mechanisms, ultimately affecting health outcomes. In addition, little literature evaluates possible mediation pathways, such as the effect of psychological interventions on the neuroendocrine system and the immune system, so this new integrative model framework can be utilized. Future researchers need to test all of these new integrative models, including factors that influence stress in children with cancer, modify psychological interventions, and evaluate their mechanisms on the neuroendocrine and immune systems. This will reveal the complex interactions among these components and understand their relevance to health outcomes.

Authors Contribution

IH: Do Conceptualization, Methodology, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing. NN: Supervision, Methodology, Investigation, Validation; IK: Do Supervision, Validation, Investigation, Data Curation; WFR: Validation, Formal analysis, Investigation, Data Curation, Writing - Original Draft; ZH: Project administration, Supervision; TR: Project administration, Data Curation.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article and/or its supplementary materials.

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Conflict of interest

The authors declare no conflicts of interest concerning the publication of this paper.

Ethical approval

This research is not research involving humans or animals, so the authors do not require ethical approval.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.07.001.

References

1. American Cancer Society. Cancer facts & figures 2023. 2023. Atlanta, Ga.
2. Bhakta N, Liu Q, Ness KK, Baassiri M, Eissa H, Yeo F, et al. The cumulative burden of surviving childhood cancer: an initial report from the St Jude Lifetime Cohort Study (SJLIFE). Lancet. 2017;390:2569–82. https://doi.org/10.1016/S0140-6736(17)31610-0
3. Nurgali K, Jagoe RT, Abalo R. Editorial: adverse effects of cancer chemotherapy: anything new to improve tolerance and reduce sequelae? Front Pharmacol. 2018;9. https://doi.org/10.3389/fphar.2018.00245
4. Jibb LA, Croal L, Wang J, Yuan C, Foster J, Cheung V, et al. Children's experiences of cancer care: a systematic review and thematic synthesis of qualitative studies. Oncol Nurs Forum. 2018;45:527–44.
5. Hooke MC, Linder LA. Symptoms in children receiving treatment for cancer—Part I: fatigue, sleep disturbance, and nausea/vomiting. J Pediatr Oncol Nurs. 2019;36:244–61. https://doi.org/10.1177/1043454219849576
6. Carrion-Plaza A, Jaen J, Montoya-Castilla I. HabitApp: new play technologies in pediatric cancer to improve the psychosocial state of patients and caregivers. Front Psychol. 2020;11. https://doi.org/10.3389/fpsyg.2020.00157
7. Dupuis LL, Cook S, Robinson PD, Tomlinson D, Vettese E, Sung L. Optimizing symptom control in children and adolescents with cancer. Pediatr Res. 2019;86:573–8. https://doi.org/10.1038/s41390-019-0516-3
8. Madden K, Magno Charone M, Mills S, Dibaj S, Williams JL, Liu D, et al. Systematic symptom reporting by pediatric palliative care patients with cancer: a preliminary report. J Palliat Med. 2019;22:894–901. https://doi.org/10.1089/jpm.2018.0545
9. Brinksma A, Sulkers E, Ijpma I, Burgerhof JGM, Tissing WJE. Eating and feeding problems in children with cancer: prevalence, related factors, and consequences. Clin Nutr. 2020;39:3072–9. https://doi.org/10.1016/j.clnu.2020.01.012
10. Steur LMH, Grootenhuis MA, van Someren EJW, van Eijkelenburg NKA, van der Sluis IM, Dors N, et al. High prevalence of parent-reported sleep problems in pediatric patients with acute lymphoblastic leukemia after induction therapy. Pediatr Blood Cancer. 2020;67. https://doi.org/10.1002/pbc.28165
11. Brinkman TM, Recklitis CJ, Michel G, Grootenhuis MA, Klosky JL. Psychological symptoms, social outcomes, socioeconomic attainment, and health behaviors among survivors of childhood cancer: current state of the literature. J Clin Oncol. 2018;36:2190–7. https://doi.org/10.1200/JCO.2017
12. Lopes-Júnior LC, Pereira-da-Silva G, Silveira DSC, Veronez LC, Santos JC, Alonso JB, et al. The effect of clown intervention on self-report and biomarker measures of stress and fatigue in pediatric osteosarcoma inpatients: a pilot study. Integr Cancer Ther. 2018;17:928–40. https://doi.org/10.1177/1534735418781725
13. Sklar CA, Antal Z, Chemaitilly W, Cohen LE, Follin C, Meacham LR, et al. Hypothalamic–pituitary and growth disorders in survivors of childhood cancer: an endocrine society* clinical practice guideline. J Clin Endocrinol Metab. 2018;103:2761–84. https://doi.org/10.1210/jc.2018-01175
14. Michel G, Brinkman TM, Wakefield CE, Grootenhuis M. Psychological outcomes, health-related quality of life, and neurocognitive functioning in survivors of childhood cancer and their parents. Pediatr Clin North Am. 2020;67:1103–34. https://doi.org/10.1016/j.pcl.2020.07.005
15. Kiecolt-Glaser JK, Glaser R. Psychoneuroimmunology and cancer: fact or fiction? Eur J Cancer. 1999;35:1603–7. https://doi.org/10.1016/S0959-8049(99)00197-5
16. Rensen N, Gemke RJBJ, van Dalen EC, Rotteveel J, Kaspers GJL. Hypothalamic-pituitary-adrenal (HPA) axis suppression after treatment with glucocorticoid therapy for childhood acute lymphoblastic leukaemia. Cochrane Database Syst Rev. 2017;2017. https://doi.org/10.1002/14651858.CD008727.pub4

17. Hinds JA, Sanchez ER. The role of the hypothalamus–pituitary–adrenal (HPA) Axis in test-induced anxiety: assessments, physiological responses, and molecular details. Stresses. 2022;2:146–55. https://doi.org/10.3390/stresses2010011
18. Straub RH, Cutolo M. Psychoneuroimmunology—developments in stress research. Wien Med Wochenschr. 2018;168:76–84. https://doi.org/10.1007/s10354-017-0574-2
19. Ader R. Psychoneuroimmunology. 4th ed. vol. 1. Elsevier; 2007.
20. Zacharie R. Psychoneuroimmunology: a bio-psycho-social approach to health and disease. Scand J Psychol. 2009;50:645–51. https://doi.org/10.1111/j.1467-9450.2009.00779.x
21. Tagge EP, Natali EL, Lima E, Leek D, Neece CL, Randall KF. Psychoneuroimmunology and the pediatric surgeon. Semin Pediatr Surg. 2013;22:144–8. https://doi.org/10.1053/j.sempedsurg.2013.05.002
22. Mihić LL, Mihatović D, Šitum M. Psychoneuroimmunology and skin diseases. Rad Hrvat Akad Znan i Umjet Med Znan. 2019;537:25–36. https://doi.org/10.21857/y6zolb8l7m
23. White GE, Caterini JE, McCann V, Rendall K, Nathan PC, Rhind SG, et al. The psychoneuroimmunology of stress regulation in pediatric cancer patients. Cancers (Basel). 2021;13:4684. https://doi.org/10.3390/cancers13184684
24. Chacin-Fernández J, Chacin Fuenmayor M, Piñerua-Shuhaibar L, Suarez-Roca H. Psychological intervention based on psychoneuroimmunology improves clinical evolution, quality of life, and immunity of children with leukemia: a preliminary study. Health Psychol Open. 2019;6. https://doi.org/10.1177/2055102919838902
25. Marusak HA, Harper FW, Taub JW, Rabinak CA. Pediatric cancer, posttraumatic stress and fear-related neural circuitry. Int J Hematol Oncol. 2019;8: IJH17. https://doi.org/10.2217/ijh-2019-0002
26. Hodges LJ, Walker J, Kleiboer AM, Ramirez AJ, Richardson A, Velikova G, et al. What is a psychological intervention? A metareview and practical proposal. Psycho Oncol. 2011;20:470–8. https://doi.org/10.1002/pon.1780
27. Hoffman BM, Papas RK, Chatkoff DK, Kerns RD. Meta-analysis of psychological interventions for chronic low back pain. Health Psychol. 2007;26:1–9. https://doi.org/10.1037/0278-6133.26.1.1
28. Yan Q. Psychoneuroimmunology: systems biology approaches to mind-body medicine. Springer International Publishing; 2016. https://doi.org/10.1007/978-3-319-45111-4
29. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71
30. Bramer WM, Rethlefsen ML, Kleijnen J, Franco OH. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. Syst Rev. 2017;6. https://doi.org/10.1186/s13643-017-0644-y
31. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5. https://doi.org/10.1186/s13643-016-0384-
32. Furlan JC, Singh J, Hsieh J, Fehlings MG. Reviews methodology of systematic reviews and recommendations. 2011.
33. Cumpston MS, McKenzie JE, Thomas J, Brennan SE. The use of 'PICO for synthesis' and methods for synthesis without meta-analysis: protocol for a survey of current practice in systematic reviews of health interventions. F1000Res. 2021;9:678.
34. The Joanna Briggs Institute. Critical appraisal tools | JBI. 2023 https://jbi.global/critical-appraisal-tools
35. Monnaatsie M, Biddle SJH, Khan S, Kolbe-Alexander T. Physical activity and sedentary behaviour in shift and non-shift workers: a systematic review and meta-analysis. Prev Med Rep. 2021;24. https://doi.org/10.1016/J.PMEDR.2021.101597
36. Lutgendorf SK, Costanzo ES. Psychoneuroimmunology and health psychology: an integrative model. Brain Behav Immun. 2003;17:225–32. https://doi.org/10.1016/S0889-1591(03)00033-3
37. Jibb LA, Birnie KA, Nathan PC, Beran TN, Hum V, Victor JC, et al. Using the MEDiPORT humanoid robot to reduce procedural pain and distress in children with cancer: a pilot randomized controlled trial. Pediatr Blood Cancer. 2018;65.
38. McCullough A, Ruehrdanz A, Jenkins MA, Gilmer MJ, Olson J, Pawar A, et al. Measuring the effects of an animal-assisted intervention for pediatric oncology patients and their parents: a multisite randomized controlled trial. J Pediatr Oncol Nurs. 2018;35:159–77. https://doi.org/10.1177/1043454217748586
39. Gerçeker GÖ, Bektaş M, Aydınok Y, Ören H, Ellidokuz H, Olgun N. The effect of virtual reality on pain, fear, and anxiety during access of a port with huber needle in pediatric hematology-oncology patients: randomized controlled trial. Eur J Oncol Nurs. 2021;50.
40. Genik LM, McMurtry CM, Marshall S, Rapoport A, Stinson J. Massage therapy for symptom reduction and improved quality of life in children with cancer in palliative care: a pilot study. Complement Ther Med. 2020;48.
41. Gürcan M, Atay Turan S. The effectiveness of mandala drawing in reducing psychological symptoms, anxiety and depression in hospitalised adolescents with cancer: a randomised controlled trial. Eur J Cancer Care. 2021;30. https://doi.org/10.1111/ecc.13491
42. Cheng KKF, Tan LML. A pilot study of the effect of a home-based multimodal symptom-management program in children and adolescents undergoing chemotherapy. Cancer Rep. 2021;4. https://doi.org/10.1002/cnr2.1336
43. Çelebioğlu A, Gürol A, Yildirim ZK, Büyükavci M. Effects of massage therapy on pain and anxiety arising from intrathecal therapy or bone marrow aspiration in children with cancer. Int J Nurs Pract. 2015;21:797–804. https://doi.org/10.1111/ijn.12298
44. Liu H, Gao X, Hou Y. Effects of mindfulness-based stress reduction combined with music therapy on pain, anxiety, and sleep quality in patients with osteosarcoma. Brazilian Journal of Psychiatry. 2019;41:540–5. https://doi.org/10.1590/1516-4446-2018-0346
45. Silva NB, Osó Rio FL. Impact of an animal-assisted therapy programme on physiological and psychosocial variables of paediatric oncology patients. PLoS One. 2018;13. https://doi.org/10.1371/journal.pone.0194731
46. Hsiao HJ, Chen SH, Jaing TH, Yang CP, Chang TY, Li MY, et al. Psychosocial interventions for reduction of distress in children with leukemia during bone marrow aspiration and lumbar puncture. Pediatr Neonatol. 2019;60:278–84. https://doi.org/10.1016/j.pedneo.2018.07.004
47. Shoshani A, Mifano K, Czamanski-Cohen J. The effects of the Make a Wish intervention on psychiatric symptoms and health-related quality of life of children with cancer: a randomised controlled trial. Qual Life Res. 2016;25: 1209–18. https://doi.org/10.1007/s11136-015-1148-7
48. Lam KKW, Li WHC, Chung OK, Ho KY, Chiu SY, Lam HS, 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 Counsel. 2018;101:1947. https://doi.org/10.1016/j.pec.2018.07.008, 56.
49. Jacobs S, Mowbray C, user Cates LM, Baylor A, Gable C, Skora E, et al. Pilot study of massage to improve sleep and fatigue in hospitalized adolescents with cancer. Pediatr Blood Cancer. 2016;63:880–6. https://doi.org/10.1002/pbc.25902
50. Li WHC, Ho KY, Lam KKW, Lam HS, Chui SY, Chan GCF, 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. https://doi.org/10.1016/j.ijnurstu.2018.04.007
51. Zhang P, Mo L, Torres J, Huang X. Effects of cognitive behavioral therapy on psychological adjustment in Chinese pediatric cancer patients receiving chemotherapy: a randomized trial. Medicine (United States). 2019;98. https://doi.org/10.1097/MD.0000000000016319
52. Altay N, Kilicarslan-Toruner E, Sari Ç. The effect of drawing and writing technique on the anxiety level of children undergoing cancer treatment. Eur J Oncol Nurs. 2017;28:1–6. https://doi.org/10.1016/j.ejon.2017.02.007
53. Hasanah I, Mulatsih S, Haryanti F, Haikal Z. Effect of music therapy on cortisol as a stress biomarker in children undergoing IV-line insertion. J Taibah Univ Med Sci. 2020;15. https://doi.org/10.1016/j.jtumed.2020.03.007
54. Lopes-Junior LC, Silveira DSC, Olson K, Bomfim EO, Veronez LC, Santos JC, et al. Clown intervention on psychological stress and fatigue in pediatric patients with cancer undergoing chemotherapy. Cancer Nurs. 2020;43:290–9. https://doi.org/10.1097/NCC.0000000000000690
55. Tsai YL, Tsai SC, Yen SH, Huang KL, Mu PF, Liou HC, et al. Efficacy of therapeutic play for pediatric brain tumor patients during external beam radiotherapy. Child's Nerv Syst. 2013;29:1123–9. https://doi.org/10.1007/s00381-013-2099-3
56. Sherwood L. Human physiology: from cells to systems. 9th ed. Cengage Learning; 2016.
57. Randazzo D, Peters KB. Psychosocial distress and its effects on the health-related quality of life of primary brain tumor patients. CNS Oncol. 2016;5: 241–9. https://doi.org/10.2217/CNS-2016-0010
58. Schneiderman N, Ironson G, Siegel SD. Stress and health: psychological, behavioral, and biological determinants. Annu Rev Clin Psychol. 2005;1: 607–28. https://doi.org/10.1146/annurev.clinpsy.1.102803.144141
59. Coughtrey A, Millington A, Bennett S, Christie D, Hough R, Su MT, et al. The effectiveness of psychosocial interventions for psychological outcomes in pediatric oncology: a systematic review. J Pain Symptom Manag. 2018;55: 1004–17. https://doi.org/10.1016/j.jpainsymman.2017.09.022
60. Calcaterra V, Veggiotti P, Palestrini C, de Giorgis V, Raschetti R, Tumminelli M, et al. Post-operative benefits of animal-assisted therapy in pediatric surgery: a randomised study. PLoS One. 2015;10. https://doi.org/10.1371/journal.pone.0125813
61. Altschuler EL. Animal-assisted therapy for post-traumatic stress disorder: lessons from "case reports" in media stories. Mil Med. 2018;183:11–3. https://doi.org/10.1093/milmed/usx073
62. Braun C, Stangler T, Narveson J, Pettingell S. Animal-assisted therapy as a pain relief intervention for children. Complement Ther Clin Pract. 2009;15:105–9. https://doi.org/10.1016/j.ctcp.2009.02.008
63. Feng Y, Lin Y, Zhang N, Jiang X, Zhang L. Effects of animal-assisted therapy on hospitalized children and teenagers: a systematic review and meta-analysis. J Pediatr Nurs. 2021;60:11–23. https://doi.org/10.1016/j.pedn.2021.01.020
64. Cunningham NR, Kashikar-Zuck S, Coghill RC. Brain mechanisms impacted by psychological therapies for pain: identifying targets for optimization of treatment effects. Pain Rep. 2019;4. https://doi.org/10.1097/PR9.0000000000000767
65. Chand SP, Kuckel DP, Huecker MR. Cognitive behavior therapy. StatPearls Publishing; 2023.
66. Patil PP, Karale R, Mohite VR, Naregal P. Effectiveness of art therapy on level of stress and anxiety among pediatric oncology patients. Sri Lanka Journal of Child Health. 2021;50:459–64. https://doi.org/10.4038/sljch.v50i3.9696

67. Śliwka A, Kaszuba M, Piliński R, Pieniążek M, Batkiewicz M, Marciniak K, et al. The comparison between pulmonary rehabilitation with music therapy and pulmonary rehabilitation alone on respiratory drive, cortisol level and asthma control in patients hospitalized with asthma exacerbation. J Asthma. 2020:1–10. https://doi.org/10.1080/02770903.2020.1789874
68. Kühlmann AYR, Van Rosmalen J, Staals LM, Keyzer-Dekker CMG, Dogger J, De Leeuw TG, et al. Music interventions in pediatric surgery (The music under surgery in children study): a randomized clinical trial. Anesth Analg. 2020;130:991–1001. https://doi.org/10.1213/ANE.0000000000003983
69. Agrawal AK, Robertson S, Litwin L, Tringale E, Treadwell M, Hoppe C, et al. Virtual reality as complementary pain therapy in hospitalized patients with sickle cell disease. Pediatr Blood Cancer. 2019;66:e27525. https://doi.org/10.1002/pbc.27525
70. Eijlers R, Dierckx B, Staals LM, Berghmans JM, van der Schroeff MP, Strabbing EM, et al. Virtual reality exposure before elective day care surgery to reduce anxiety and pain in children. Eur J Anaesthesiol. 2019;36:728–37. https://doi.org/10.1097/EJA.0000000000001059
71. Hinic K, Kowalski MO, Holtzman K, Mobus K. The effect of a pet therapy and comparison intervention on anxiety in hospitalized children. J Pediatr Nurs. 2019;46:55–61. https://doi.org/10.1016/j.pedn.2019.03.003
72. Chester SJ, Tyack Z, de Young A, Kipping B, Griffin B, Stockton K, et al. Efficacy of hypnosis on pain, wound-healing, anxiety, and stress in children with acute burn injuries: a randomized controlled trial. Pain. 2018;159:1790–801. https://doi.org/10.1097/j.pain.0000000000001276
73. Lee A, Moulton D, Mckernan L, Russell A, Slaughter JC, Acra S, et al. Clinical hypnosis in pediatric crohn's disease: a randomized controlled pilot study. J Pediatr Gastroenterol Nutr. 2021;72:e63–70. https://doi.org/10.1097/MPG.0000000000002980
74. Carlson LE, Toivonen K, Flynn M, Deleemans J, Piedalue KA, Tolsdorf E, et al. The role of hypnosis in cancer care. Curr Oncol Rep. 2018;20.
75. Chen PY, Liu YM, Chen ML. The effect of hypnosis on anxiety in patients with cancer: a meta-analysis. Worldviews Evid Based Nurs. 2017;14:223–36. https://doi.org/10.1111/wvn.12215
76. Provençal SC, Bond S, Rizkallah E, El-Baalbaki G. Hypnosis for burn wound care pain and anxiety: a systematic review and meta-analysis. Burns. 2018;44:1870–81. https://doi.org/10.1016/j.burns.2018.04.017
77. Rennick JE, Stremler R, Horwood L, Aita M, Lavoie T, Majnemer A, et al. A pilot randomized controlled trial of an intervention to promote psychological well-being in critically ill children: soothing through touch, reading, and music. Pediatr Crit Care Med. 2018;19:e358–66. https://doi.org/10.1097/PCC.0000000000001556
78. Vagnoli L, Bettini A, Amore E, de Masi S, Messeri A. Relaxation-guided imagery reduces perioperative anxiety and pain in children: a randomized study. Eur J Pediatr. 2019. https://doi.org/10.1007/s00431-019-03376-x
79. Kim SH, Kim SJ, Dukyoo J, Oh HJ. The effects of a humor intervention on the physiological, physical, and psychological responses of school-aged children with atopic dermatitis in South Korea: a pilot study. J Pediatr Nurs. 2018;39:e21. https://doi.org/10.1016/j.pedn.2018.01.001, 9.
80. Coşkuntürk AE, Gözen D. The effect of interactive therapeutic play education program on anxiety levels of children undergoing cardiac surgery and their mothers. J PeriAnesthesia Nurs. 2018;33:781–9. https://doi.org/10.1016/j.jopan.2017.07.009
81. Zengin M, Yayan EH, Düken ME. The effects of a therapeutic play/play therapy program on the fear and anxiety levels of hospitalized children after liver transplantation. J PeriAnesthesia Nurs. 2021;36:81–5. https://doi.org/10.1016/j.jopan.2020.07.006
82. Li WHC, Chung JOK, Ho KY, Kwok BMC. Play interventions to reduce anxiety and negative emotions in hospitalized children. BMC Pediatr. 2016;16:36. https://doi.org/10.1186/s12887-016-0570-5
83. Akgün Kostak M, Kutman G, Semerci R. The effectiveness of finger puppet play in reducing fear of surgery in children undergoing elective surgery: a randomised controlled trial. Collegian. 2021;28:415–21. https://doi.org/10.1016/j.colegn.2020.10.003
84. Deshpande R, Rajesh Shah M. Effectiveness of play therapy on pain and anxiety in children post surgery. Int J Health Sci Res. 2019;9:84.
85. Susanty E, Sijbrandij M, van Dijk W, Srisayekti W, de Vries R, Huizink AC. The effects of psychological interventions on neurocognitive functioning in post-traumatic stress disorder: a systematic review. Eur J Psychotraumatol. 2022;13. https://doi.org/10.1080/20008198.2022.2071527
86. Weekly T, Riley B, Wichman C, Tibbits M, Weaver M. Impact of a massage therapy intervention for pediatric palliative care patients and their family caregivers. J Palliat Care. 2019;34:164–7. https://doi.org/10.1177/0825859718810727
87. Rodríguez-Mansilla J, González-Sánchez B, Torres-Piles S, Martín JG, Jiménez-Palomares M, Bellino MN. Effects of the application of therapeutic massage in children with cancer: a systematic review. Rev Lat Am Enfermagem. 2017;25. https://doi.org/10.1590/1518-8345.1774.2903
88. Field T. Pediatric massage therapy research: a narrative review. Children. 2019;6. https://doi.org/10.3390/children6060078
89. Finn S, Fancourt D. The biological impact of listening to music in clinical and nonclinical settings: a systematic review. Prog Brain Res. 2018;237:173–200. https://doi.org/10.1016/bs.pbr.2018.03.007. Elsevier B.V.
90. Rokade PB. Release of endomorphin hormone and its effects on our body and moods: a review. Internationa Conference on Chemical, Biological and Environment Sciences; 2011:431127.
91. Branson SM, Boss L, Padhye NS, Trötscher T, Ward A. Effects of animal-assisted activities on biobehavioral stress responses in hospitalized children: a randomized controlled study. J Pediatr Nurs. 2017;36:84–91. https://doi.org/10.1016/j.pedn.2017.05.006
92. Salzmann S, Euteneuer F, Laferton JAC, Auer CJ, Shedden-Mora MC, Schedlowski M, et al. Effects of preoperative psychological interventions on catecholamine and cortisol levels after surgery in coronary Artery Bypass Graft patients: the randomized controlled PSY-HEART trial. Psychosom Med. 2017;79:806–14. https://doi.org/10.1097/PSY.0000000000000483
93. Ding Y, Yin H, Wang S, Meng Q, Yan M, Zhang Y, et al. Effectiveness of clown intervention for pain relief in children: a systematic review and meta-analysis. J Clin Nurs. 2022;31:3000–10. https://doi.org/10.1111/jocn.16195
94. Lopes-Júnior LC, Bomfim E, Olson K, Neves ET, Silveira DSC, Nunes MDR, et al. Effectiveness of hospital clowns for symptom management in paediatrics: systematic review of randomised and non-randomised controlled trials. BMJ. 2020;371. https://doi.org/10.1136/bmj.m4290
95. Herawati C, Suwandono A, Putra ST, Rahmi FL, Syukur MA, Sakti H, et al. Effect of psychoeducation-modification on the improvement of spiritual response, perception stigma, anxiety level and cortisol levels among Lepers. Indian J Public Health Res Dev. 2019;10:1873. https://doi.org/10.5958/0976-5506.2019.03826.9
96. Chang C, Tsai G, Hsieh CJ. Psychological, immunological and physiological effects of a Laughing Qigong Program (LQP) on adolescents. Complement Ther Med. 2013;21:660–8. https://doi.org/10.1016/j.ctim.2013.09.004
97. Alarcón-Yaquetto DE, Tincopa JP, Guillén-Pinto D, Bailon N, Cárcamo CP. Effect of augmented reality books in salivary cortisol levels in hospitalized pediatric patients: a randomized cross-over trial. Int J Med Inform. 2021;148:104404. https://doi.org/10.1016/j.ijmedinf.2021.104404
98. Brockington G, Gomes Moreira AP, Buso MS, Gomes da Silva S, Altszyler E, Fischer R, et al. Storytelling increases oxytocin and positive emotions and decreases cortisol and pain in hospitalized children. Proc Natl Acad Sci USA. 2021;118. https://doi.org/10.1073/pnas.2018409118
99. Hoge EA, Bui E, Palitz SA, Schwarz NR, Owens ME, Johnston JM, et al. The effect of mindfulness meditation training on biological acute stress responses in generalized anxiety disorder. Psychiatr Res. 2018;262:328–32. https://doi.org/10.1016/j.psychres.2017.01.006
100. Kenne Sarenmalm E, Mårtensson LB, Andersson BA, Karlsson P, Bergh I. Mindfulness and its efficacy for psychological and biological responses in women with breast cancer. Cancer Med. 2017;6:1108–22. https://doi.org/10.1002/cam4.1052
101. Yang M, Zhang Z, Nice EC, Wang C, Zhang W, Huang C. Psychological intervention to treat distress: an emerging frontier in cancer prevention and therapy. Biochim Biophys Acta Rev Cancer. 2022;1877:188665. https://doi.org/10.1016/J.BBCAN.2021.188665
102. Almigbal TH, Almutairi KM, Fu JB, Vinluan JM, Alhelih E, Alonazi WB, et al. Assessment of psychological distress among cancer patients undergoing radiotherapy in Saudi Arabia. Psychol Res Behav Manag. 2019;12:691–700. https://doi.org/10.2147/PRBM.S209896
103. Rodriguez EM, Dunn MJ, Zuckerman T, Vannatta K, Gerhardt CA, Compas BE. Cancer-related sources of stress for children with cancer and their parents. J Pediatr Psychol. 2012;37:185–97. https://doi.org/10.1093/jpepsy/jsr054

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Review Article

Benefits of Music Intervention on Anxiety, Pain, and Physiologic Response in Adults Undergoing Surgery: A Systematic Review and Meta-analysis

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SUMMARY

Purpose: Evidence on factors influencing the variations of music's effect on anxiety and pain in surgical patients is unclear. We aimed to elucidate the effects of music intervention on anxiety and pain throughstudy characteristics.

Methods: We conducted a search on the PubMed, CINAHL, Embase, Cochrane, and Web of Science databases from March 7 to April 21, 2022, for randomized controlled trials (RCTs) for the effect of music intervention on anxiety, pain, and physiological responses in surgical patients. We included studies published within the last 10 years. We assessed the risk of bias in the study using the Cochrane risk of bias tool for randomized trials and performed meta-analyses using a random-effects model for all outcomes. We used change-from-baseline scores as summary statistics and computed bias-corrected standardized mean differences (Hedges'g) for anxiety and pain outcomes and mean differences (MD) for blood pressure and heart rate.

Results: Of the 454 records retrieved, 30 RCTs involving 2280 participants were found to be eligible. Music intervention was found to be superior to standard care in reducing anxiety (Hedges' g = −1.48, 95% confidence interval: −1.97 to −0.98), pain (Hedges's g = −0.67, −1.11 to −0.23), systolic blood pressure (MD = −4.62, −7.38 to −1.86), and heart rate (MD = −3.37, −6.65 to −0.10) in surgical patients. The impact of music on anxiety and pain relief varied significantly depending on the duration of the intervention. The largest effect was observed in interventions lasting between 30 and 60 minutes, with a decrease in anxiety and pain.

Conclusions: Music intervention is an effective way to reduce anxiety, pain, and physiological responses in surgical patients. Future reviews examining the influence of different types of surgery on the effects of music would add to the body of knowledge in this field. This study has been registered on the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42022340203, with a registration date of July 4, 2022.

Introduction

Surgical patients often experience perioperative anxiety and moderate to severe postoperative pain, despite pharmacological measures to reduce these symptoms [1]. Current perioperative interventions primarily rely on pharmacological approaches, such as anesthetic and analgesic medications, which can have adverse effects [2]. Therefore, non-pharmacological interventions that can complement pharmacological measures are crucial for reducing psychophysiological stress and opioid use [3]. Music intervention

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has been proposed as a non-pharmacological approach to alleviate perioperative anxiety and pain, as benzodiazepines and opioids, the common pharmacological interventions, have common adverse effects [4].

Music intervention is a non-pharmacological measure that has no known adverse effects and is a relatively inexpensive and easily applicable intervention [1]. Many trials have suggested statistically significant beneficial effects of perioperative music intervention on anxiety [5–12], pain [13–18], and physiological parameters [19–22]. Perioperative music intervention has been recognized as beneficial for reducing the consumption of intraoperative sedatives and postoperative opioids in a variety of surgical populations [1].

Most systematic reviews on music intervention for perioperative anxiety and pain have focused on specific surgical populations and reported positive effects [1,23,24]. Most reviews of music interventions for perioperative anxiety and pain have primarily relied on self-reported measures, with little evidence available on physiological responses. Furthermore, while the evidence on anxiety and pain has shown significantly large effects, there has also been substantial heterogeneity in those effects.

The evidence from the only meta-analysis on music intervention in mixed surgical populations is outdated and reports moderating variables that potentially influence the effect of music intervention, including the timing of intervention, type of anesthesia, and type of music intervention [4]. However, the effects of other moderating factors that potentially influence the heterogeneity of music intervention effects still require further investigation.

The purpose of this review is twofold. First, we aim to investigate the effects of music intervention on operative anxiety, pain, and physiological responses in patients undergoing surgery. Second, we aim to identify the effects of possible influencing variables on the heterogeneity of intervention effects, specifically participants and intervention characteristics.

Methods

Research design

This research employs a systematic review and meta-analysis to evaluate the effects of music intervention on operative anxiety and pain in surgical patients. This review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement—reporting guidelines relevant to this research design [25].

Eligibility criteria

We specified eligibility criteria based on the PICOS framework (population, intervention, comparator, outcome, and study design) for study characteristics as follows: Population: We included adult patients (age ≥18 years) undergoing any surgical procedures, excluding invasive or non-invasive diagnostic procedures. Intervention: Perioperative music interventions, regardless of genre, duration, frequency, or timing of delivery, were included. Comparator: We excluded any other comparator interventions purporting to reduce operative anxiety and/or pain and included operative care without any music intervention, such as standard care, routine care, usual care, or placebo. Outcomes: The primary outcomes were operative anxiety and pain, which were measured by standardized or validated instruments. The secondary outcomes were physiological parameters of anxiety and pain, such as systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Studies were excluded if the outcomes were not measured or reported as inappropriate data to calculate our preplanned effects measures, such as mean difference (MD) or standardized mean difference (SMD). Study design: We included randomized controlled trials (RCTs) that examined the efficacy of music intervention on operative anxiety, pain, or vital signs in surgical patients.

We also specified eligibility criteria with regard to reporting characteristics. As the recent systematic review and meta-analysis on this topic [4] screened publications between 1980 and 2016, we restricted studies to those published in the last 10 years (from January 2012 to March 2022) to ensure updated evidence and minimize duplication. We limited studies to those published in English and on humans.

Information sources and search strategy

We systematically searched for eligible articles in the title, abstract, and keyword search fields in the following databases: PubMed/Medline, Cochrane Central Register of Controlled Trials, CINAHL, Embase, and Web of Science from March 7 to April 21, 2022.

We developed a search strategy based on the PICO framework. We first determined the keywords, including music intervention, anxiety, pain, and surgery. We then identified search terms focusing on these keywords using synonyms, derivatives, and MeSH thesaurus terms. This was done by reviewing references on this topic. The search strategy was reviewed and pilot-searched in the pre-planned databases by the review authors. The strategy was then finalized through discussion and agreement among the reviewers.

We searched for the following search terms and derivatives of these terms, including MeSH thesaurus terms (surgery or operative or operation or operate* orsurgical oroperative intervention orinvasive procedure* oroperative procedure* oroperation* or perioperative procedure* or intraoperative procedure* or perioperative procedure* or preoperative procedure*) and (music intervention or acoustic stimulation or intervention, Music or music) and (anxiety or angst or hypervigilance or nervousness or anxiousness or stress or physiological response or pain or vital sign* or blood pressure*). We applied additional filters to the search strategy as follows: randomized controlled trial, published in the last 10 years, and written in English. The approach to study identification in this systematic review is transparently reported in the Online Supplementary Material (H).

Selection and data collection process

Four reviewers independently assessed each record retrieved through a multiple-stage process. We first screened titles and abstracts and then identified records for full-text review. Any disagreements were discussed and resolved by consensus among all reviewers.

We developed data collection forms for extracting study characteristics and outcome data and pilot tested them on five randomly selected studies. Any problems were discussed and appropriately refined by consensus among all review authors. The data were independently extracted by two review authors and checked by the other two authors. Any disagreements were resolved by discussion and consensus among all authors.

Data items

Eligible outcomes were categorized as follows: *primary outcomes:* self-rated anxiety and self-rated pain; and *secondary outcomes:* physiological parameters of anxiety and pain, including systolic blood pressure, diastolic blood pressure, and heart rate. We anticipated that individual studies would report multiple results for

each outcome, such as results using multiple methods or tools to measure the same outcome or data from multiple time points for the same outcome. If studies reported outcome data measured by validated or standardized tools, any measure of anxiety or pain was eligible for inclusion. If multiple results from different time points for the same outcome were reported, we selected the results from the first post-intervention time point. The outcome data of the first post-intervention time point would have a stronger intervention effect than the subsequent data.

We collected the following data: *report details:* author, year, and country; *participants details:* type of surgery, randomized and analyzed sample sizes in the intervention and control groups; *intervention details:* type, genre, timing (before, during, or after surgery), session, and duration of music intervention; *outcomes details:* outcome measures, instruments used, and outcome data, i.e. means and standard deviations for baseline, post-intervention, and change scores between baseline and post-intervention scores; *comparator details:* usual, standard, routine care, or other similar operative care; and *research design details:* sampling and treatment assignment mechanisms, and length of follow-up.

Study risk of bias assessment

We assessed the risk of bias in the included studies by focusing on the main outcomes of each study. We used the revised Cochrane risk of bias tool for randomized trials (RoB 2) [26] to assess the risk of bias. The RoB 2 tool comprises five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported result.

An overall risk of biased judgment for an individual trial result was reached by summarizing across all domains based on the suggested rule in the RoB 2 tool. If a trial was judged to be at low risk of bias for all domains of the main outcome(s), an overall risk of bias was judged to be low. If a trial was judged to raise some concerns in at least one domain but not be at high risk of bias in any other domain for the result, it was judged to raise some concerns. However, if a study was judged to be at high risk of bias in at least one domain or to raise some concerns for multiple domains in a way that substantially lowers confidence in the result, it was judged to be at high risk of overall bias.

Two review authors independently assessed the risk of bias in each study. The other two authors checked the risk of bias in each study. Any discrepancies were resolved through discussion and consensus among all authors.

Effect measures

Since the included studies for music intervention used different scales to measure self-rated anxiety and pain, we used the bias-corrected SMD effect measure, specifically Hedges' g, and 95% confidence intervals (CIs) in pairwise meta-analyses. However, since blood pressure and heart rate were measured on the same scale, we estimated the MD and 95% CIs for these outcomes. We interpreted the effect size according to the following thresholds: Hedges' g $\leq$ 0.39 as small, 0.4 to 0.79 as medium, and $\geq$0.8 as large [27].

Synthesis method

1) Eligibility for synthesis

We categorized participants based on the type of surgery they underwent and the duration of the music intervention for subgroup analysis and meta-regression on anxiety and pain. To categorize the participants accurately, we classified them based on the specific surgical field. The categorization was done according to the reported surgeries in the trials. The categories include: patients who underwent spinal anesthesia, patients who underwent obstetrics or gynecologic surgery, patients who underwent urologic surgery, patients who underwent eye, ear, nose, or throat surgery, patients who underwent thoracic or cardiovascular surgery, patients who underwent breast surgery, patients who underwent general surgery, patients who underwent awake craniotomy, and post-operative patients in the intensive care unit.

We excluded studies that investigated patients undergoing dental procedures or invasive procedures other than surgery. We also categorized the duration of music intervention delivery in the included trials as follows: 1. below 30 minutes; 2. 30 to 60 minutes; 3. over 60 minutes continuously through the operative period; and 4. 30 minutes per day for six months.

2) Data conversion

We used the change from baseline values in summary statistics, including the mean and standard deviation (SD) of the outcome measurements (anxiety, pain, blood pressure, and heart rate), to prepare the data for presentation and synthesis. If trials did not report changes from baseline values, we calculated the change means and SDs using the descriptions in Chapter 6 of the Cochrane Handbook for Systematic Reviews of Interventions [28]. We obtained the change mean value by subtracting the baseline from the post-intervention value. To obtain the SDs for the mean change values, we used the baseline and post-intervention data, as well as the change means and SDs from a similar study that was included in the review.

3) Tabulation and graphical methods

We compiled a table summarizing the key characteristics of each study included in our review. This table includes the following information: first author, year of publication, country of origin, study design, sample sizes of intervention groups that were randomized and analyzed, type of surgery, type of music used, timing the of music intervention (i.e. preoperative, intra-operative, or postoperative), comparator intervention, outcomes, and instruments used.

To present the results of our syntheses, we used forest plots that show summary statistics, effect estimates, and the precision of each study, as well as the overall effect, precision, and heterogeneity statistics. We also represented the results of our sensitivity test using a forest plot. To display the reporting bias assessment results, we presented a funnel plot, which shows the standard error and SMD of each study. Finally, we presented the certainty assessment in the Summary of Findings table, which provides information on outcome domains, the number of follow-up participants, the certainty of the evidence, and anticipated absolute effects.

4) Statistical synthesis methods

As the effects of music intervention are assumed to be highly variable depending on study characteristics such as surgery type, duration, session, and timing of music intervention, as well as study design artifacts, we used a random-effects model and the inverse variance method for meta-analysis. To identify and quantify statistical heterogeneity, we first visually inspected the results, followed by assessing the formal statistical test for heterogeneity. We used the Chi-squared test and p-value to test for observed variance, τ^2 for between-study variance, and I^2 for the proportion of

between-study variance out of the observed variance. We used the restricted maximum-likelihood (REML) estimator to calculate between-study variance (τ^2). If the statistical test for heterogeneity resulted in I^2 over 50% and a p-value for Chi-squared below 0.1, we judged the effects to be substantially heterogeneous.

We conducted meta-analyses using the 'meta' and 'metafor' packages in R software version 4.0.2 [29]. Additionally, to assess the certainty of evidence, we imported the results from Review Manager 5.4 [30] into the GRADEpro program [31].

5) Methods to explore heterogeneity

We performed subgroup analysis and meta-regression to explore possible causes of statistical heterogeneity in intervention effects on anxiety and pain. According to the Cochrane Handbook for Systematic Reviews of Interventions version 6.3 [32], there should be at least ten studies available for each characteristic modeled in a subgroup analysis or meta-regression. If a substantial number of studies were available, we planned to conduct subgroup analyses and meta-regressions based on the type of surgery, duration of the music intervention, and assessment of the risk of bias.

In the meta-analysis on anxiety, which included 24 studies, we performed two subgroup analyses based on the type of surgery and duration of music intervention. For pain, we analyzed 13 studies and conducted one subgroup analysis on the duration of music intervention. We also used meta-regression to estimate the variance in heterogeneity for the intervention effects on anxiety and pain, respectively. We compared subgroup effects using statistical tests for interaction for subgroup analyses.

Sensitivity Analyses

A sensitivity analysis was conducted to assess the influence of the study with a high risk of bias on the robustness of the synthesized results on anxiety. However, as there were no studies with an overall high risk of bias, we did not perform a sensitivity analysis for the other outcomes, including pain and vital signs.

Reporting Bias Assessment

We used funnel plots to graphically assess the risk of bias due to missing results arising from reporting biases. If asymmetry was identified in the funnel plot, we performed Egger's regression to statistically test the asymmetry, provided there were at least ten studies in the synthesis. As funnel plot asymmetry was identified, we applied the trim-and-fill method to adjust funnel plot asymmetry in anxiety and pain.

Two reviewers (EN and HL) independently assessed reporting bias, and any disagreements between assessors were resolved by discussion and consensus among all authors. When we assessed reporting bias, we considered any poor methodological quality or true clinical heterogeneity that might lead to funnel plot asymmetry other than reporting bias.

Certainty Assessment

We used the GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation) and GRADEpro GDT software [31] to assess the certainty of the body of evidence. Two authors (EN and HL) independently assessed the certainty of the evidence and resolved any disagreements through discussion and consensus. Initially, we specified the study design, i.e. randomized controlled trials, and assessed the five factors that can reduce the quality of evidence: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Then, the GRADE system rated the certainty of the evidence for each outcome across studies as high, moderate, low, or very low. We presented the results of certainty assessments in the Summary of Findings table. For certainty assessment, we referred to the descriptions in sections 3, 4, and 5 of the GRADE handbook for grading the quality of evidence and strength of recommendations [33].

Results

Study selection

The database search retrieved 454 trials. After removing 254 duplicates, the titles and abstracts of the remaining 200 trials were assessed for eligibility. Following a title and abstract screening, 146 records were removed. Out of the remaining 54 records that were sought for retrieval, 45 records were actually retrieved. Subsequently, 45 trials were assessed for eligibility, and 15 were excluded after a detailed evaluation of their full-text articles. The list of the excluded trials was presented in the Online Supplementary Material (I).

Finally, 30 trials were included in the review, and their list is presented in the Online Supplementary Material (A). Details of the search, selection process, and reasons for excluding full-text articles are shown in Figure 1.

Study characteristics

The details of the key characteristics of each included study are presented in the Online Supplementary Material (B). All studies were randomized controlled trials published in English. The included studies involved 2,280 participants.

The studies were conducted in hospital settings for surgery and in the following countries: China or Taiwan (eight trials), the USA (five trials), Turkey or Iran (nine trials), as well as Brazil, South Korea, Malaysia, Italy, and Israel. The music intervention comprised folk, traditional, modern Western, natural sound, relaxing, or the patients' favorite music. The intervention was given at different times, such as pre, post, intraoperative periods, or a combination of two or more of these periods.

Risk of bias in studies

We assessed the risk of bias in studies by focusing on the main outcomes in each included study. As the outcome assessors were unable to be blinded to the intervention assignment (music intervention vs. control treatment) and the outcomes were participant-reported, there is a potential for bias influenced by knowledge of the intervention received. This could lead to a judgment of 'some concerns' in the assessment of the risk of bias in the domain of outcome measurement, which in turn should prompt some concerns in the overall risk of bias.

As a result, 29 trials were judged to raise some concerns about the overall risk of bias, which accounted for 96.7% of all included trials, and only one trial was judged to be at an overall high risk of bias, accounting for 3.3%. The summary table of the bias risk assessment is presented in the Online Supplementary Material (C1), and the risk of bias graph is available in C2.

Effect of music intervention on anxiety

Figure 2A displays the summary statistics (mean, SD, and sample size) for each included study for both the music intervention and control groups, as well as the bias-corrected standardized mean difference (Hedges' g) and its 95% confidence interval for the

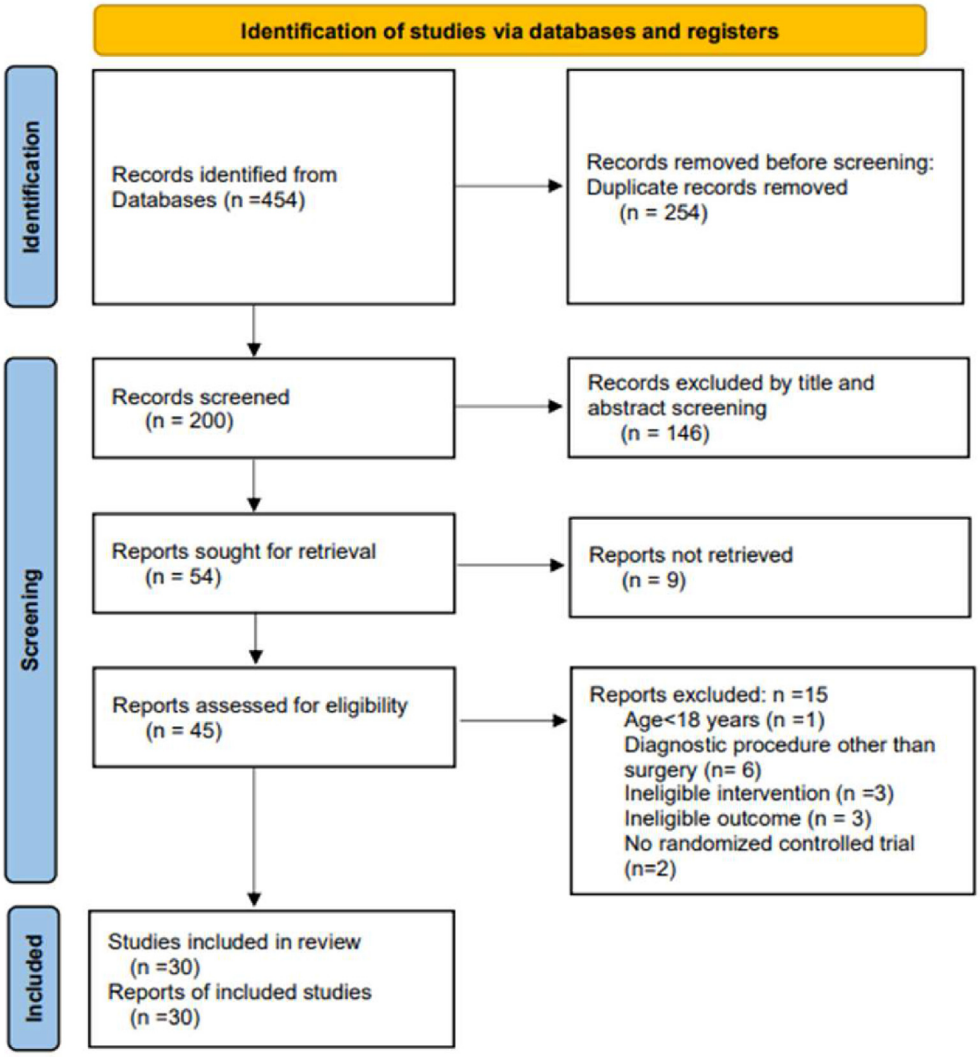

Figure 1. PRISMA 2020 Flow Diagram Displaying the Search and Selection.

anxiety outcome. All data for each included study were obtained from the primary reference of the journal article, unless otherwise specified. The effect estimates (Hedges' g) for each study ranged from −0.13 (95% CI: −0.46 to 0.18) to −6.08 (95% CI: −7.02 to −5.13), displaying substantial heterogeneity.

Twenty-four randomized controlled trials (RCTs) compared patient-reported operative anxiety directly between the music intervention and standard care groups. These RCTs enrolled 1,916 patients undergoing surgeries and used a variety of validated or standardized instruments. Twenty-three of the trials were judged to raise some concerns, and only one trial was deemed to have a high overall risk.

The pooled analysis showed that music intervention was significantly associated with lower perioperative anxiety (Hedges' g = −1.48, 95% CI: −1.97 to −0.98) compared to standard care. However, substantial heterogeneity was identified within this synthesis ($I^2 = 92.7\%$, $\chi^2 = 316.03$, df = 23, $p < .001$).

Effect of music intervention on pain

Figure 2B presents summary statistics, effect estimates, and precisions for each group in the pain meta-analysis for each study. Unless otherwise specified, data for each study were obtained from the primary reference of the journal article. The effect estimates (Hedges's g) ranged from 0.28 (CI: −0.21 to 0.77) to −2.61 (CI: −3.32 to −1.91), displaying substantial heterogeneity.

Thirteen RCTs compared postoperative pain between the music intervention and control groups. These RCTs enrolled 951 patients undergoing surgeries in surgical units and used various validated pain instruments. Thirteen of the trials were judged to raise concerns regarding the overall risk of bias. No studies were deemed to be at high overall risk of bias.

The synthesis results showed that music intervention was associated with significantly lower postoperative pain (Hedges's g = −0.67, 95% CI: −1.11 to −0.23) than standard care. The consistency statistics showed substantial heterogeneity (I2 = 87.4%, $\chi 2 = 95.45$, df = 12, $p < .001$).

Effects of music intervention on physiologic parameters

The results of individual studies and syntheses for these outcomes are presented in Figure 2C. Unless otherwise specified, all data for each included study were extracted from the primary references of journal articles. The effect estimate MD for each study ranged from −10.48 (95% CI: −14.7 to −6.26) to 3.28 (95% CI: −4.79 to 11.35) for systolic blood pressure (SBP), −14.40 (95% CI: −18.63 to −10.17) to 4.97 (95% CI: −0.12 to 10.06) for diastolic blood

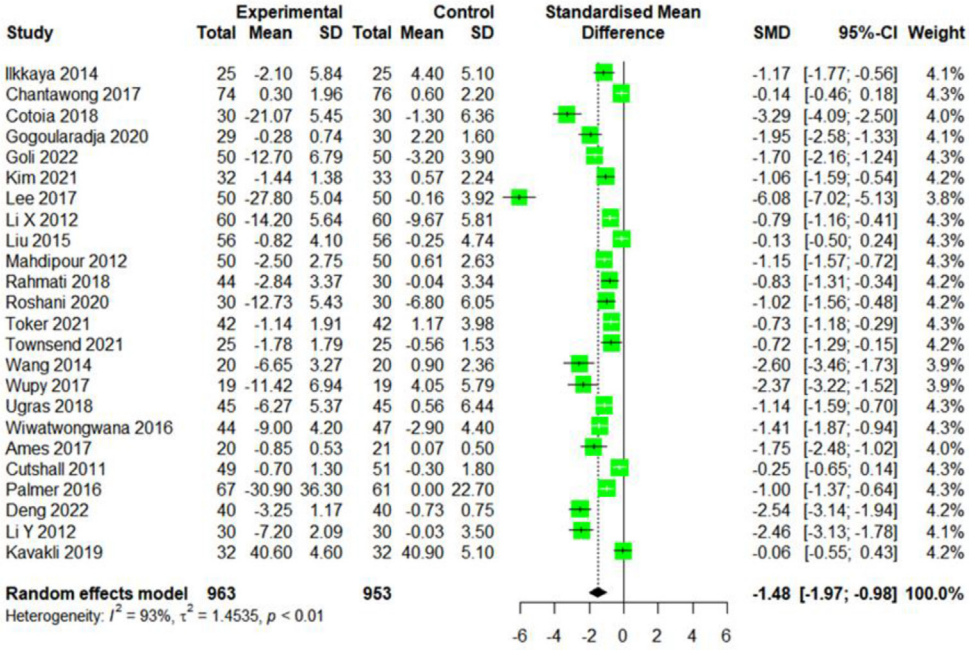

Figure 2. A. Forest Plot for the Effect of Music Therapy on Anxiety. Note. CI: confidence interval, SD: standard deviation, SMD: standardized mean difference. B. Forest Plot for the Efficacy of Music on Pain. Note. CI: confidence interval, SD: standard deviation, SMD: standardized mean difference. C. Forest Plots for the Effect of Music on Vital Signs. Note. CI = confidence interval; DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure; SD = standard deviation, MD = mean difference.

pressure (DBP), and −16.68 (95% CI: −21.28 to −12.08) to 2.42 (95% CI: −1.35 to 6.19) for heart rate (HR), respectively.

Nine RCTs compared SBP, DBP, and HR between the music and standard care groups, and these RCTs enrolled 707 patients undergoing surgery. Seven of the trials were judged to have a low overall risk of bias. One trial was found to raise some concerns due to deviations from intended interventions, while another trial was deemed to be at high overall risk due to high risk of randomization process and some concern of risk of deviations from intended interventions.

The results of the syntheses displayed that music intervention was associated with significantly lower SBP (MD = −4.62, 95% CI = −7.38 to −1.86) and lower HR (MD = −3.37, 95% CI: −6.65 to −0.10) than standard care. Music intervention was associated with lower DBP (MD = −3.43, 95% CI: −7.26 to 0.39) than standard care, but it was not significant. The heterogeneity statistics for all physiological parameters showed substantial heterogeneity (SBP: I2 = 46%, $\chi 2$ = 14.75, df = 8, p < .064; DBP: I2 = 87%, $\chi 2$ = 61.70, df = 8, p < .001; HR: I2 = 82.9%, $\chi 2$ = 46.88, df = 8, p<. 001).

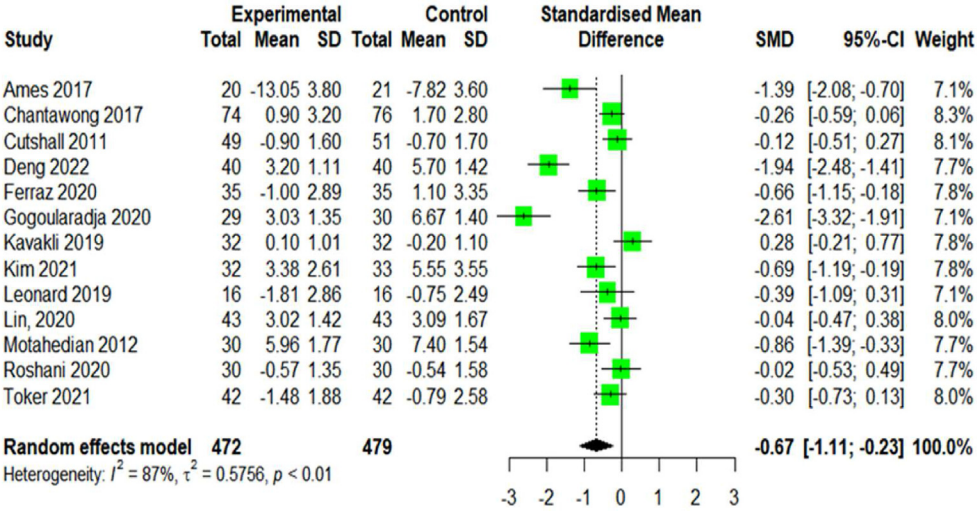

Figure 2B. (*continued*).

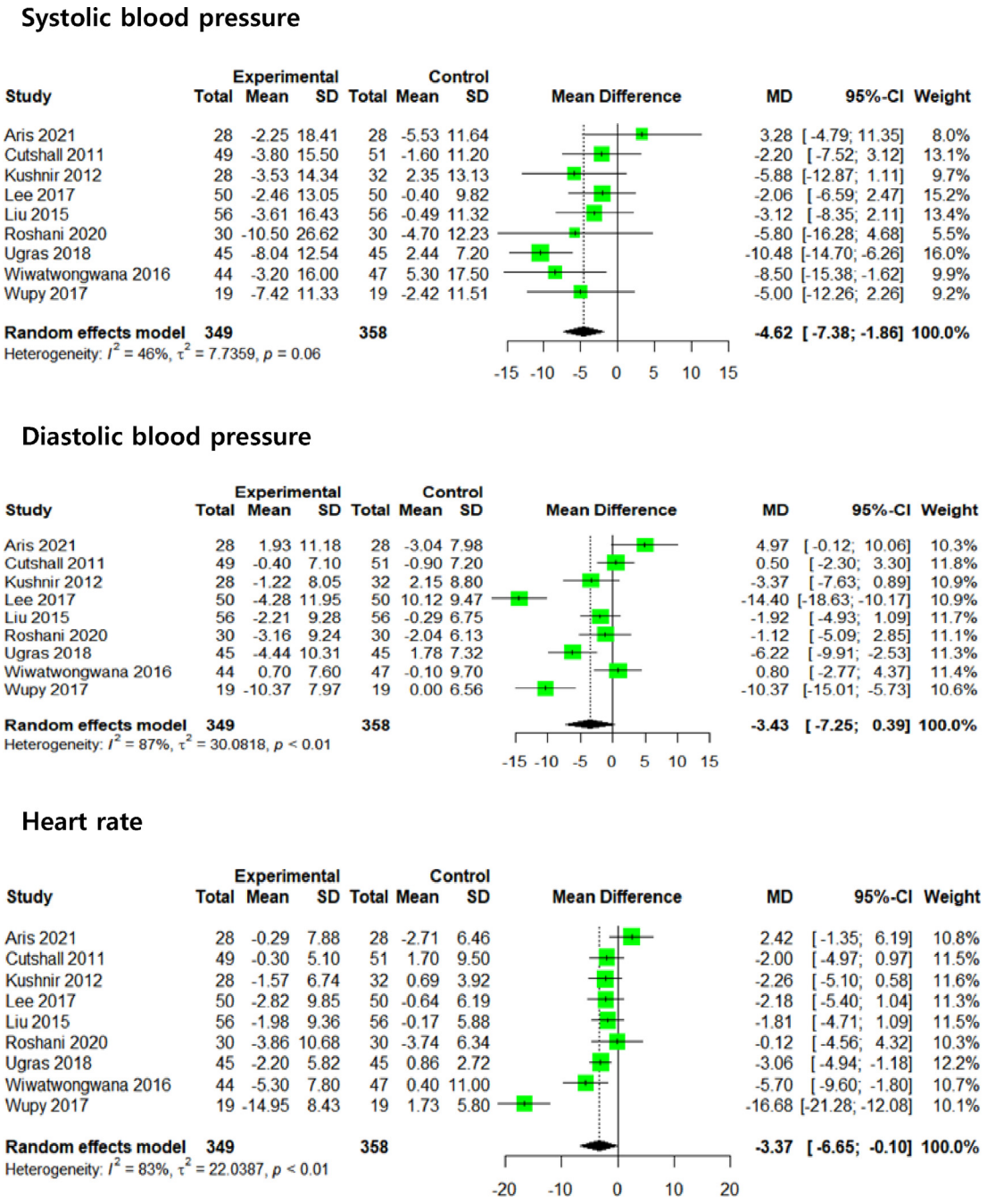

Figure 2C. (*continued*).

Subgroup analysis and meta-regression

The subgroup analysis of anxiety by surgery type revealed that the music intervention was significantly more effective in reducing anxiety compared to the comparators within each subgroup of patients. The summary estimates, precision, and statistics of heterogeneity for each subgroup are presented in the Online Supplementary Material D.

Substantial and large mean effects were observed among patients who underwent surgery under spinal anesthesia, with a SMD of −3.5 (95% CI: −5.14 to −1.86). Patients who underwent obstetric or gynecologic surgeries also showed significant effects (SMD: −1.43, 95% CI: −2.57 to −0.30), as did patients who underwent urologic surgery (SMD: −2.47, 95% CI: −4.08 to −0.86). On the other hand, relatively small to medium mean effects were observed in patients who underwent cardiovascular or thoracic surgery, with a SMD of −0.53 (95% CI: −1.52 to 0.47), and among patients who had general surgery (SMD: −0.77, 95% CI: −2.36 to 0.81), without reaching statistical significance. Most of the subgroup analyses revealed substantial heterogeneity in the effects of music. A test for the interaction between music effects and surgery type, conducted using a random effects model, indicated no statistical significance (Qb = 12.20, df = 8, p = .142).

The regression analysis indicated that the different mean effects among surgery-type subgroups were not statistically significant (QM (df = 8) = 12.20, p = .142). However, the analysis revealed that

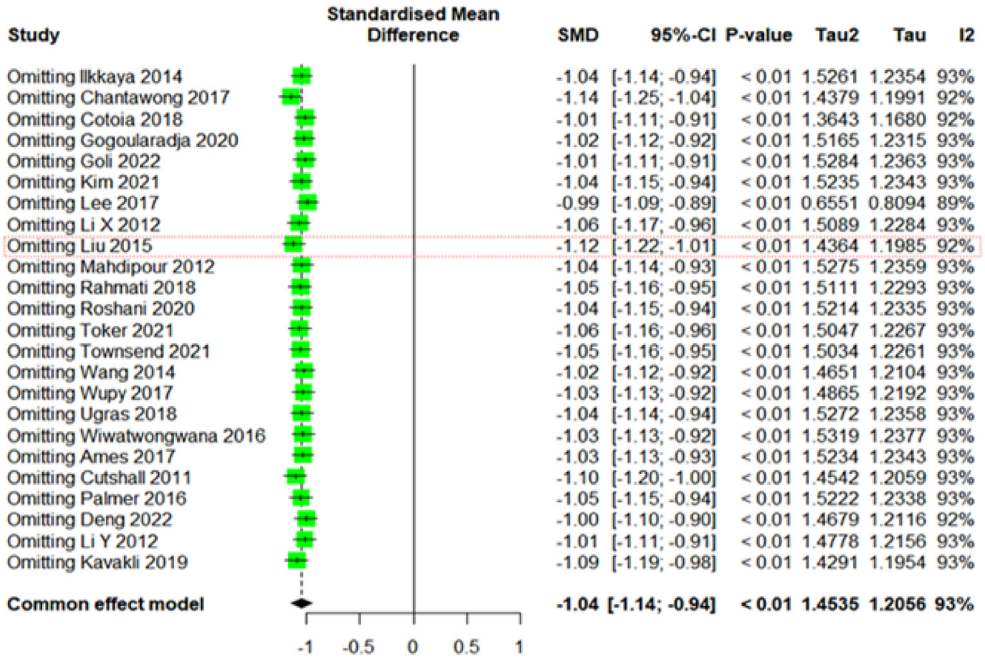

Figure 3. Forest Plot for Sensitivity Analysis on the Music Effect for Anxiety: omitting the study with high overall risk (Liu 2015; indicated by the red line) changed the overall effect from −1.04 to −1.12 using the common effect model (Default Model). Note. CI = confidence interval, SD = standard deviation, SMD = standardized mean difference.

the type of surgery accounted for 14.7% of the heterogeneity in music's effects on anxiety.

The subgroup analysis on anxiety by the duration of intervention revealed that the mean effect (Hedges' g) was −2.09 (95% CI: −2.68 to −1.49) in patients who listened to music for 30 to 60 minutes, −0.79 (95% CI: −1.54 to −0.05) for continuous music listening (from preoperative to postoperative period), and −0.69 (95% CI: −1.90 to 0.52) for less than 30 minutes (see Supplementary Material E). The test for subgroup differences using the random effects model showed that the different mean effects between subgroups were statistically significant (Q = 8.83, df = 2, p = .012). The meta-regression confirmed this result (QM (df = 2) = 8.83, p = .012), and the duration the of music intervention accounted for 24.4% of the heterogeneity of the music effect on anxiety.

As the number of studies included in the pain meta-analysis was thirteen, we performed only one subgroup analysis and meta-regression by the duration of the intervention (see Supplementary Material F). The subgroup analysis showed that the effect was −1.34 (Hedges' g, −1.95 to −0.73) in patients receiving music for 30 to 60 minutes, −0.31 (−0.9 to 0.29) in patients listening to music continuously, and −0.24 (−1.20 to 0.72) for music for less than 30 minutes. Lin et al's findings [23] on music intervention for 30 minutes every day for six months showed an effect of −0.04 (95% CI: −0.47 to 0.38). In summary, music intervention has the most significant effect among participants receiving it for 30 to 60 minutes. The test for subgroup differences showed marginal statistical significance (Q = 7.67, df = 3, p = .053). The meta-regression analysis confirmed the result of the test for subgroup differences (QM = 7.67, df = 3, p = .053), and the duration of the music intervention accounted for 30.4% of the heterogeneity of effects on pain.

Sensitivity analyses

The sensitivity analysis revealed that omitting the study with a high overall risk of bias [34] using the default common effect model (see Figure 3) changed the overall effect from Hedges' g = −1.04 (95% CI: −1.14 to −0.94) to −1.12 (95% CI: −1.22 to −1.01). The effect estimate of the study with an overall high risk of bias [34] was g = −0.13 (95% CI: −0.50 to 0.24), which is much smaller than the mean effect (g = −1.04, 95% CI: −1.14 to −0.94). However, the inclusion of this study did not significantly inflate the overall effect. Thus, our decision to include the study with a high risk of bias in the synthesis appears to have only a minor influence on the robustness of the synthesized results on anxiety. Sensitivity analysis was not conducted for other outcomes (i.e. pain, blood pressure, and heart rate) because no study with an overall high risk of bias was included in the syntheses of those outcomes.

Risk of reporting biases in syntheses

The funnel plot for the effect of music on anxiety appears asymmetrical, as it seems empty in the lower-right area (Figure 4A). This lower-right region is the space for studies with small samples and small effects, indicating that studies with small samples and effects are missing. Egger's regression test to assess funnel plot asymmetry showed statistical significance (t = −6.26, df = 22, p < .001). The trim-and-fill method to adjust for funnel plot asymmetry using the common effect model showed that the overall effect was g = −0.76 SD (−0.85 to −0.67), combining 32 studies with 8 added studies, while the mean effect combining 24 trials was g = −1.04 (−1.14 to −0.94) (see Figure 4B). This result suggests small study effects and a possible risk of bias due to missing studies arising from reporting or sampling biases. Therefore, we considered the evidence on anxiety to be of low quality due to reporting bias and selection bias.

The funnel plot for the effect of music on pain appears somewhat asymmetric (see online Supplementary Material G1). Egger's regression test confirmed statistically significant funnel plot asymmetry (t = −2.43, df = 11, p = .033). However, the trim-and-fill method showed the same mean effect as the primary mean effect (g = −0.5, −0.63 to −0.37), combining 13 studies with no added study (see online Supplementary Material G2). Since the reporting

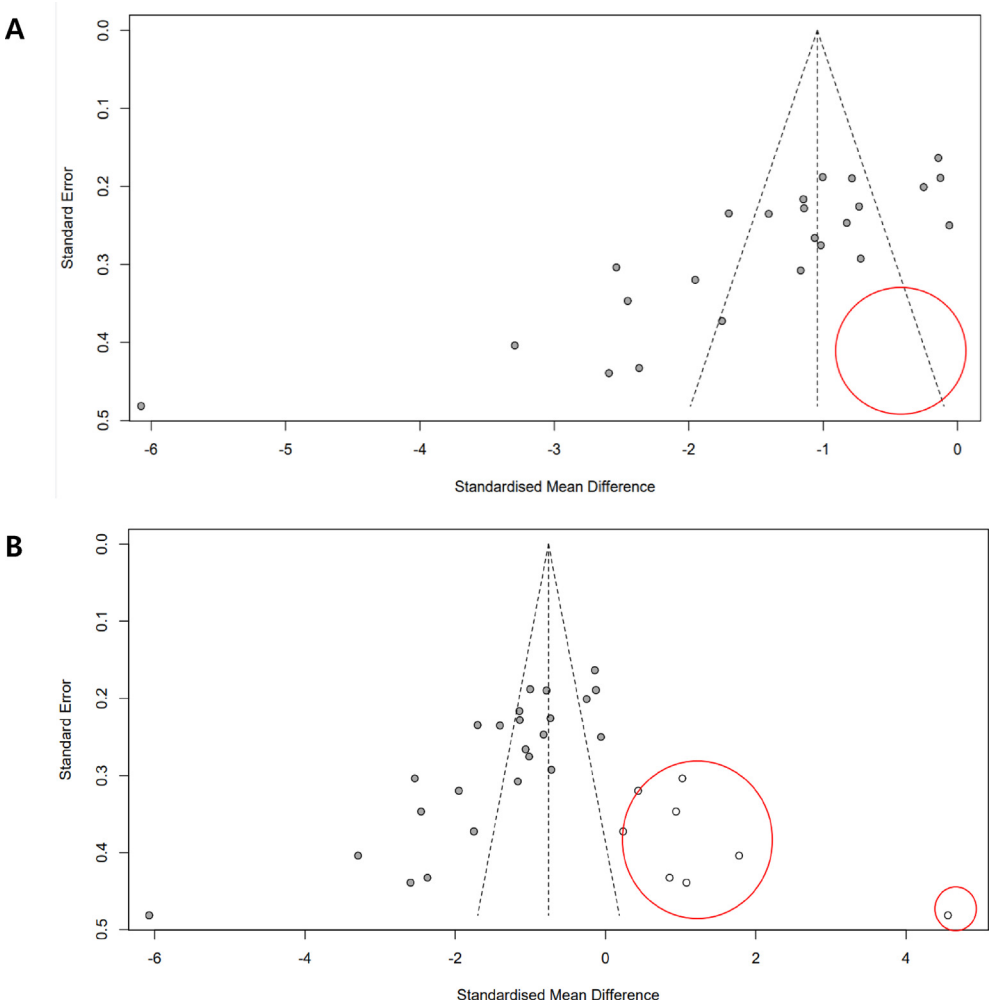

Figure 4. Funnel Plot for the Music Effect on Anxiety. A. Funnel Plot for the Music Effect on Anxiety: the red circle indicates assumed missing small-sample studies with small effects. B. Funnel Plot after Trimfill for the Music Effect on Anxiety: the red circle indicates 8 filled studies that were assumed to be missing.

bias on the pain evidence is not clear, we cannot conclude the efficacy of the music intervention in terms of patients reporting pain.

Certainty of evidence

The anxiety score in the music intervention groups was, on average, SMD = 1.48 SD (95% CI: −1.97 to −0.98) lower than that in the usual care groups. The evidence suggests that music intervention leads to a large reduction in anxiety compared to usual care, but with low certainty. The evidence was downgraded twice, once for unexplained heterogeneity of effects and once for publication bias. Table 1 presents the GRADE summary of findings table, which provides information on the certainty of evidence for all outcomes, with footnotes explaining judgments.

The pain score in the music intervention groups was, on average, SMD = 0.67 SD (95% CI: −1.11 to −0.23) lower than that in the comparator groups. The evidence suggests that music intervention reduces postoperative pain compared with standard care but with low certainty. The evidence was downgraded twice, once for unexplained inconsistency of effects and once for publication bias.

The systolic blood pressure in the music groups was, on average, MD = 4.62 lower (95% CI: −7.48 to −1.86) than that in the standard care groups. The evidence suggests that music intervention slightly reduces systolic blood pressure compared with standard care, with high certainty. The evidence was not downgraded in the judgment of certainty of evidence.

The diastolic blood pressure in the music intervention groups was, on average, MD = 3.43 lower (95% CI: −7.25 to 0.39, which is not significant) than in the usual care groups. Compared with usual care, the evidence suggests music intervention likely results in little to no difference in diastolic blood pressure with moderate certainty. The evidence was downgraded one step for unexplained heterogeneity of results.

The heart rate in the music intervention groups was, on average, MD = 3.37 lower (95% CI: −6.65 to −0.10) than in the usual care groups. Compared with usual care, moderately certain evidence suggests music intervention likely results in a slight reduction in heart rate. The evidence was downgraded one step for unexplained heterogeneity.

Discussion

A general interpretation of the results

This systematic review and meta-analysis identified a statistically significant reduction in operative anxiety, pain, systolic blood pressure, and heart rate in adults who received perioperative music

Table 1 *The GRADE Summary of Findings Table for Music Intervention.*

Patient or population: patients undergoing surgery; **Setting**: any hospital settings; **Intervention**: music intervention; **Comparison**: standard care				
Outcomes	N of participants (studies)	Certainty of the evidence (GRADE)	Anticipated absolute effects	
			Risk with standard care	Risk difference with music therapy
Anxiety	1916 (24 RCTs)	⨁⨁◯◯ Low[a,b]	–	SMD **1.48 SD lower** (1.97 lower to 0.98 lower)
Pain	951 (13 RCTs)	⨁⨁◯◯ Low[c,d]	–	SMD **0.67 SD lower** (1.11 lower to 0.23 lower)
SBP	707 (9 RCTs)	⨁⨁⨁⨁ High	**The mean SBP was -0.56**	MD **4.62 lower** (7.38 lower to 1.86 lower)
DBP	707 (9 RCTs)	⨁⨁⨁◯ Moderate[e]	**The mean DBP was 0.85**	MD **3.43 lower** (7.25 lower to 0.39 higher)
HR	707 (9 RCTs)	⨁⨁⨁◯ Moderate[f]	**The mean HR was -0.21**	MD **3.37 lower** (6.65 lower to 0.1 lower)

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI = confidence interval; MD = mean difference; RCT = randomized controlled trial; SMD = standardised mean difference; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate.

GRADE Working Group grades of evidenceHigh certainty: we are very confident that the true effect lies close to that of the estimate of the effect.**Moderate certainty**: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.**Low certainty**: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.**Very low certainty**: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

[a] The heterogeneity statistics indicated high heterogeneity ($Tau^2 = 1.45$; $I^2 = 93\%$; $Chi^2 = 316.03$, df = 23, $p < .001$). The meta-regression analysis revealed that surgery type accounted for 14.69% of the total between-studies variance, the duration of music accounted for 24.4%, and the sample size accounted for 3.4%. However, the residual heterogeneity was not sufficiently explained. Based on the observed heterogeneity, the certainty of the evidence was downgraded by one level.

[b] The funnel plot of 24 trials revealed asymmetry, which was further confirmed by Egger's regression analysis. Due to the suspected presence of publication bias, the certainty of the evidence was downgraded by one level.

[c] The heterogeneity statistics indicated significant heterogeneity ($Tau^2 = 0.58$, $Chi^2 = 95.45$, df = 12, $p < .001$, $I^2 = 87.4\%$). Meta-regression demonstrated that the duration of the music intervention explained 30.4% of the total between-study variance. However, the residual heterogeneity remains unexplained. As a result, the certainty of the evidence was downgraded by one level.

[d] The funnel plot of 13 trials displayed asymmetry, indicating a potential small study bias, which was confirmed by Egger's regression. Due to the suspected publication bias, the certainty of the evidence was downgraded by one level.

[e] The heterogeneity statistics revealed significant heterogeneity ($Tau^2 = 30.08$, $Chi^2 = 61.7$, df = 8, $p < .001$, $I^2 = 87\%$). Due to insufficiently explained heterogeneity, the certainty of the evidence was downgraded by one level.

[f] The heterogeneity statistics indicated significant heterogeneity ($Tau^2 = 22.04$, $Chi^2 = 46.88$, df = 8, $p < .001$, $I^2 = 82.9\%$). Due to unexplained heterogeneity in effects, the certainty of the evidence was downgraded by one level.

intervention. The average effect of music intervention on anxiety and pain was −1.48 SD (95% CI: −1.97 to −0.98) and −0.67 SD (95% CI: −1.11 to −0.23), respectively, compared to standard care. Perioperative music intervention resulted in a large reduction in anxiety and a moderate reduction in pain in surgical patients. These findings are consistent with recent systematic reviews on the effect of music on reducing operative anxiety and pain in surgical patients [1,4,24,35].

Although our findings are largely consistent with previous reviews, indicating that perioperative music intervention is effective in reducing anxiety and pain, our findings on perioperative anxiety are much larger than those reported in previous reviews. Previous reviews have indicated moderate effects, with SMD of −0.4 SD in orthopedic surgery [24], MD of −0.69 in surgery patients [4], SMD of −0.68 in cardiac surgery [35], and SMD of −0.5 in cardiac surgery [1]. One reason for the discordant results could be the possibility of a small study effect due to missing results in the synthesis of our evidence, which might have resulted in the inflation of the average effect. Another possible issue is that our anxiety data were based on change scores from baseline to post-intervention scores, which could generate larger effect sizes.

The evidence on pain is consistent with previous reviews, indicating that music is effective in reducing postoperative pain, and the overall effect size remains in line with other evidence. For example, MDs of −0.5 in surgery patients [4], SMDs of −0.74 SD in cardiac surgery [35], SMDs of −0.51 SD in cardiac surgery [1], SMDs of −0.27 SD in orthopedic surgery [24], and SMDs of −0.42 SD in abdominal surgery [36], respectively.

The findings of this review suggest a robust body of evidence investigating the effects of music intervention on operative anxiety and pain. However, there are several important questions that require further investigation. Although the subgroup analysis on anxiety by type of surgery was not significant, it indicated substantial variability in the mean effects across different types of surgery or anesthesia. Further reviews that focus on determining whether the effects of music intervention differ based on the type of surgery or anesthesia would enhance our understanding of the knowledge base on this topic.

Our findings on physiological parameters indicated that music intervention worked to decrease SBP and HR with statistical significance. Considering the certainty of the evidence, perioperative music intervention results in a slight decrease in SBP and likely results in a slight decrease in HR.

These results are inconsistent with recent meta-analyses showing that music interventions are not effective in decreasing SBP and HR in adult patients undergoing orthopedic surgery [24] and cardiac surgery [1]. These reviews reported trivial, small, unimportant effects, or no effects. One possible reason for the previous evidence could be the lack of statistical power due to the small number of studies included in syntheses. For instance, Patiyal *et al* [24] reported findings on SBP and HR from three RCTs with a total of 134 orthopedic surgery patients, and Kakar *et al.* [1] reported findings on SBP from four RCTs with 289 cardiac surgery patients and HR from five RCTs with a total of 347 cardiac surgery patients. The small number of included studies and the limited number of participants might have contributed to the lack of statistical power and the failure to detect the true effect. In contrast to previous review findings, our study revealed significant but small effects on SBP and HR. The previous findings might have been influenced by a lack of statistical power due to the synthesis of a small number of studies. Therefore, to better understand the effect of music on vital signs, we recommend high-quality primary studies assessing

music's impact on vital signs using RCTs and systematic reviews. Our results on DBP are consistent with previous reviews [1,24], indicating that music intervention alone may not sufficiently decrease DBP in surgical patients. Given the limitations of our study and previous reviews due to the small number of studies, we suggest conducting RCTs and meta-analyses to examine the music effect on SBP in surgical patients.

Limitations of the evidence and review process

The assessment of the certainty of the evidence indicates appreciable limitations in the evidence on anxiety and pain, including substantial heterogeneity of effects and strongly suspected publication bias. The statistics of heterogeneity on anxiety and pain showed highly heterogeneous results, and exploration for reasons showed that two factors (i.e., type of surgery and the duration of music intervention) accounted for a portion of heterogeneity, but the substantial amount of between-study variance was not adequately explained. The funnel plot and Egger's regression on anxiety and pain outcomes strongly suggest publication bias. We limited studies to published articles written in English and accessible full-text articles, which might have contributed to missing results.

The evidence on DBP and HR also has limitations, with substantial heterogeneity between study variances. The music effects might be inconsistent across music intervention types, surgery types, or methodological features. Because we did not limit the type of surgery, type, and duration of the music, inconsistencies in treatment effects might be presented.

We restricted eligibility to studies published in English only. Furthermore, we were unable to access all potentially eligible study reports, so we included accessible full-text studies only. Due to these limitations of the review process, we might have missed some of the potentially eligible publications. However, we are confident that these limitations would not change the overall findings of this review.

Conclusions

Evidence from this review suggests that music intervention has significant beneficial effects on relieving anxiety, pain, and physiological responses, specifically systolic blood pressure and heart rate, in surgical patients. Moreover, the findings that music intervention for 30–60 minutes has the largest effect on both operative anxiety and pain should be a primary consideration for planning music intervention to alleviate operative anxiety and pain.

Future reviews investigating the influence of surgery types on the effects of music would enhance our knowledge in this area. Additionally, high-quality primary studies assessing the impact of music on vital signs through randomized controlled trials and systematic reviews would help advance our understanding of the effects of music on physiological responses.

Registration and protocol

This systematic review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42022340203. The protocol for the systematic review and meta-analysis is available at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022340203.

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Conflict of interest

The authors declare that they have no competing interests.

Availability of data, code, and other materials

The data supporting the review findings are available upon submitting a reasonable request to the corresponding author.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.05.002.

References

1. Kakar E, Billar RJ, van Rosmalen J, Klimek M, Takkenberg JJM, Jeekel J. Music intervention to relieve anxiety and pain in adults undergoing cardiac surgery: a systematic review and meta-analysis. Open Heart. 2021;8(1):e001474. https://doi.org/10.1136/openhrt-2020-001474. PMID: 33495383; PMCID: PMC7839877.
2. Soffin EM, Lee BH, Kumar KK, Wu CL. The prescription opioid crisis: role of the anaesthesiologist in reducing opioid use and misuse. Br J Anaesth. 2019;122(6):e198–208. https://doi.org/10.1016/j.bja.2018.11.019
3. Ginsberg JP, Raghunathan K, Bassi G, Ulloa L. Review of perioperative music medicine: mechanisms of pain and stress reduction around surgery. Front Med. 2022;9:821022. https://doi.org/10.3389/fmed.2022.821022. PMID: 35187004. PMCID: PMC8854756.
4. Kühlmann AYR, de Rooij A, Kroese LF, van Dijk M, Hunink MGM, Jeekel J. Meta-analysis evaluating music interventions for anxiety and pain in surgery. Br J Surg. 2018;105(7):773–83. https://doi.org/10.1002/bjs.10853
5. Ames N, Shuford R, Yang L, Moriyama B, Frey M, Wilson F, et al. Music listening among postoperative patients in the intensive care unit: a randomized controlled trial with mixed-methods analysis. Integr Med Insights. 2017;12:1178633717716455. https://doi.org/10.1177/1178633717716455. PMID: 28904523; PMCID: PMC5588801.
6. Cooke M, Chaboyer W, Schluter P, Hiratos M. The effect of music on preoperative anxiety in day surgery. J Adv Nurs. 2005;52(1):47–55. https://doi.org/10.1111/j.1365-2648.2005.03563.x
7. Cotoia A, Dibello F, Moscatelli F, Sciusco A, Polito P, Modolo A, et al. Effects of Tibetan music on neuroendocrine and autonomic functions in patients waiting for surgery: a randomized, controlled study. Anesthesiol Res Pract. 2018;2018:9683780. https://doi.org/10.1155/2018/9683780. PMID:29692808; PMCID: PMC5859866.
8. Ilkkaya NK, Ustun FE, Sener EB, Kaya C, Ustun YB, Koksal E, et al. The effects of music, white noise, and ambient noise on sedation and anxiety in patients under spinal anesthesia during surgery. J Perianesth Nurs. 2014;29(5):418–26. https://doi.org/10.1016/j.jopan.2014.05.008. PMID: 25261145.
9. Palmer JB, Lane D, Mayo D, Schluchter M, Leeming R. Effects of music therapy on anesthesia requirements and anxiety in women undergoing ambulatory breast surgery for cancer diagnosis and treatment: a randomized controlled trial. J Clin Oncol. 2015;33(28):3162–8. https://doi.org/10.1200/JCO.2014.59.6049. Epub 2015 Aug 17. PMID: 26282640; PMCID: PMC4979095.
10. Vachiramon V, Sobanko JF, Rattanaumpawan P, Miller CJ. Music reduces patient anxiety during Mohs surgery: an open label randomized controlled trial. Dermatol Surg. 2013;39(2):298–305. https://doi.org/10.1111/dsu.12047
11. Wang Y, Dong Y, Li Y. Perioperative psychological and music interventions in elderly patients undergoing spinal anesthesia: effect on anxiety, heart rate variability, and postoperative pain. Yonsei Med J. 2014;55(4):1101–5. https://doi.org/10.3349/ymj.2014.55.4.1101
12. Wu PY, Huang ML, Lee WP, Wang C, Shih WM. Effects of music listening on anxiety and physiological responses in patients undergoing awake craniotomy. Compl Ther Med. 2017;32:56–60. https://doi.org/10.1016/j.ctim.2017.03.007
13. Deng C, Xie Y, Liu Y, Li Y, Xiao Y. Aromaintervention plus music intervention improve pain intensity and anxiety scores in patients with breast cancer during perioperative periods: a randomized controlled trial. Clin Breast Cancer. 2022;22(2):115–20. https://doi.org/10.1016/j.clbc.2021.05.006
14. Ferraz MCL, Santana-Santos E, Pinto JS, Nunes Ribeiro CJ, Santana J, Alves JAB, et al. Analgesic effect of music during wound care among patients with diaphyseal tibial fractures: randomized controlled trial. Eur J Pain. 2021;25(3):541–9. https://doi.org/10.1002/ejp.1692
15. Gogoularadja A, Bakshi SS. A randomized study on the efficacy of music intervention on pain and anxiety in nasal septal surgery. Int Arch Otorhinolaryngol. 2020;24(2):E232–6. https://doi.org/10.1055/S-0039-3402438. PMID: 32296470; PMCID: PMC7153921.
16. Kim S, Jeong H. Effects of patient-selected music listening on the pain, and anxiety of patients undergoing hemodialysis: a randomized controlled trial. Healthcare (Basel). 2021;9(11):1437.

https://doi.org/10.3390/healthcare9111437. PMID: 34828484. PMCID: PMC8625598.
17. Leonard H. Live music intervention during rehabilitation after total knee arthroplasty: a randomized controlled trial. J Music Ther. 2019;56(1):61–89. https://doi.org/10.1093/jmt/thy022
18. Motahedian E, Movahedirad S, Hajizadeh E, Lak M. The effect of music intervention on postoperative pain intensity in patients under spinal anesthesia. Iran J Crit Care Nurs. 2012;5(3):139–44.
19. Cutshall SA, Bauer BA, Anderson PG, Prinsen SK, Wentworth LJ, Olney TJ, et al. Effect of the combination of music and nature sounds on pain and anxiety in cardiac surgical patients: a randomized study. Alternative Ther Health Med. 2011;17(4):16–23. PMID: 22314630.
20. Kushnir J, Friedman A, Ehrenfeld M, Kushnir T. Coping with preoperative anxiety in cesarean section: physiological, cognitive, and emotional effects of listening to favorite music. Birth. 2012;39(2):121–7. https://doi.org/10.1111/j.1523-536X.2012.00532.x. PMID: 23281860.
21. Uğraş GA, Yıldırım G, Yüksel S, Öztürkçü Y, Kuzdere M, Öztekin SD. The effect of different types of music on patients' preoperative anxiety: a randomized controlled trial. Compl Ther Clin Pract. 2018;31:158–63. https://doi.org/10.1016/j.ctcp.2018.02.012. PMID: 29705448.
22. Wiwatwongwana D, Vichitvejpaisal P, Thaikruea L, Klaphajone J, Tantong A, Wiwatwongwana A. The effect of music with and without binaural beat audio on operative anxiety in patients undergoing cataract surgery: a randomized controlled trial. Eye (Lond). 2016;30(11):1407–14. https://doi.org/10.1038/eye.2016.160. PMID: 27740618. PMCID: PMC5108018.
23. Lin CL, Hwang SL, Jiang P, Hsiung NH. Effect of music intervention on pain after orthopedic surgery-a systematic review and meta-analysis. Pain Pract. 2020;20(4):422–36. https://doi.org/10.1111/papr.12864
24. Patiyal N, Kalyani V, Mishra R, Kataria N, Sharma S, Parashar A, et al. Effect of music intervention on pain, anxiety, and use of opioids among patients underwent orthopedic surgery: a systematic review and meta-analysis. Cureus. 2021;13(9):e18377. https://doi.org/10.7759/cureus.18377. PMID: 34725621; PMCID: PMC8555445.
25. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160. https://doi.org/10.1136/bmj.n160
26. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898. PMID: 31462531.
27. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. New York: Lawrence Erlbaum Associates; 1988. p. p26.
28. Higgins JPT, Li T, Deeks JJ. Chapter 6: choosing effect measures and computing estimates of effect. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al., editors. Cochrane handbook for systematic reviews of interventions version 6.3. 2022 (updated February 2022). Cochrane www.training.cochrane.org/handbook
29. R Core Team. R. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2020. Available from: https://www.R-project.org/
30. The Cochrane Collaboration. Review manager (RevMan) [computer program]. London: Cochrane; 2020. Available from https://community.cochrane.org/help/tools-and-software/Version 5.4
31. GRADEpro GDT. GRADEpro guideline development tool [software]. McMaster University and Evidence Prime; 2022. Available from: gradepro.org
32. Deeks JJ, Higgins JPT, Altman DG. Chapter 10: analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al., editors. Cochrane handbook for systematic reviews of interventions version 6.3. 2022 (updated February 2022). Cochrane www.training.cochrane.org/handbook
33. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group; 2013. Updated October 2013 https://gdt.gradepro.org/app/handbook/handbook.html
34. Liu Y, Petrini MA. Effects of music intervention on pain, anxiety, and vital signs in patients after thoracic surgery. Compl Ther Med. 2015;23(5):714–8. https://doi.org/10.1016/j.ctim.2015.08.002
35. Chandrababu R, Ramesh J, Sanatombi Devi E, Nayak BS, George A. Effectiveness of music on anxiety and pain among cardiac surgery patients: a quantitative systematic review and meta-analysis of randomized controlled trials. Int J Nurs Pract. 2021;27(4):e12928. https://doi.org/10.1111/ijn.12928. PMID: 33759286.
36. Dale VH. The impact of perioperative music on abdominal surgery patients' experience of postoperative pain: a systematic review and meta-analysis. J Perioperat Pract. 2021;31(1-2):31–43. https://doi.org/10.1177/1750458920943375. PMID: 32894995.

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Research Article

Increased Parasympathetic Activity as a Fall Risk Factor Beyond Conventional Factors in Institutionalized Older Adults with Mild Cognitive Impairment

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SUMMARY

Purpose: This study aimed to investigate autonomic nervous function during the orthostatic challenge and its relationship with depression and fall, and to elucidate fall-associated factors, including autonomic function, executive function, and depression among institutionalized older adults with mild cognitive impairment (MCI).

Methods: This study employed a descriptive cross-sectional design. Fall experiences in the current institutions were researched. Heart rate variability (HRV) during the orthostatic challenge was measured. Executive function was evaluated using the semantic verbal fluency test and clock drawing test. Depression was assessed using the Geriatric Depression Scale.

Results: Of the 115 older adults, 17 (14.8%) experienced falls in the current institution. None of the HRV indices during the orthostatic challenge showed any significant changes except for the standard deviation of normal RR intervals ($p = .037$) in the institutionalized older adults with MCI. None of the HRV indices was significantly related to the depressive symptoms. Multivariate logistic regression analysis showed that normalized high frequency on lying was independently associated with falls (OR = 1.027, $p = .049$) after adjusting for other conventional fall risk factors although executive function and depressive symptoms were not significant factors for falls.

Conclusions: Institutionalized older adults with MCI were vulnerable to autonomic nervous modulation, especially to sympathetic modulation, during the orthostatic challenge, which was not associated with depressive symptoms. As increased resting parasympathetic activity seemed to play a key role in association with falls, autonomic nervous function assessment should be considered for fall risk evaluation.

Introduction

Falls are one of the major adverse events that lead to negative consequences such as unintentional injuries and death in older adults [1]. Although nurses are making tremendous efforts to prevent falls among institutionalized older adults, 50.2% of institutionalized older adults still suffered from falls for a year, an average of 1.3 falls per 1.57 persons [2,3]. As institutionalized older adults are deconditioned with multiple chronic diseases and on various medications, special attention is needed to consider their physiological state for fall risk factors. However, there is a lack of literature considering the underlying physiological conditions in institutionalized older adults.

Mild cognitive impairment (MCI) is a clinical entity characterized by slight cognitive impairment without functional dependence [4], which is associated with 1.53 times higher odds of fall-related injury [5]. Further, older adults with MCI have reported reduced executive function [6]. Executive function—a cognitive subdomain—is an important mediating factor between visual acuity and postural stability, especially in cognitively impaired older adults [7], and is an important factor for daily life activities [8]. Recent studies have shown that executive function is a key cognitive domain involved in gait or postural control [9,10] and is closely related to falls in community-dwelling older adults [11]. As institutionalized older adults with MCI are more likely to have pronounced executive dysfunction, it is necessary to investigate their executive function as a risk factor for falls in institutionalized older adults.

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In addition to cognition, autonomic dysfunction can be considered a risk factor for falls in older adults. With increasing age, the overall ability of cardiac autonomic modulation declines constantly [12]; consequently, blood pressure regulation reduces [13], which, in turn, causes hypotensive episodes and falls [14]. A previous study also reported that autonomic dysfunction is common in patients with MCI [15]. Moreover, as institutionalized older adults with MCI have several chronic diseases and take various medications, including antihypertensives and antidepressants, they may be subject to the exaggerated risk of orthostatic intolerance and falls. Thus, their autonomic nervous function during orthostatic challenge should be assessed and evaluated in association with falls.

Depression has also been suggested as a risk factor for falls in community-dwelling older adults although there are some controversies in institutionalized adults. In a meta-analysis, the authors demonstrated that depressive symptoms were significant predictors of falls [16], whereas Susilowati et al. [17] found no significant relationship between depressive symptoms and falls among institutionalized older adults. Furthermore, considering a recent meta-analysis showing that heart rate variability (HRV) was found to be reduced among depressed older adults [18], HRV may mediate between depressive symptoms and falls. Therefore, it is necessary to examine depressive symptoms and HRV in relation to falls in institutionalized older adults.

This study aimed to investigate the autonomic nervous function during the orthostatic challenge and to explore the involvement of depressive symptoms in autonomic nervous function. This study also aimed to elucidate the associations between autonomic nervous function, cognitive function, including the executive function domain, and depressive symptoms with falls among institutionalized older adults with MCI.

Methods

Study design and participants

This descriptive cross-sectional study investigated autonomic nervous function during the orthostatic challenge using HRV to explore the involvement of autonomic nervous function in depressive symptoms and analyzed associations of autonomic nervous function, cognitive function, and depressive symptoms with falls. The conceptual models of this study were illustrated in Figure 1.

A convenience sample of 115 institutionalized older adults aged ≥65 years was recruited from four regional geriatric hospitals in South Korea from July 2017 to February 2020. Older adults with the following characteristics were included: those who complained of decreased memory in answering the question, “Do you feel like your memory is becoming worse?” [19]; who did not have dementia with scores greater than 1.5SD below the mean on the Mini-Mental Status Examination for Dementia Screening (MMSE-DS) score regarding age, gender, and education as suggested by a previous study [20]; who could communicate and walk around by themselves or with little assistance from one caregiver; who had been institutionalized for more than 1 week. Older adults with current arrhythmias on the EKG were excluded. The participant selection process was illustrated in Figure 2.

Based on Long's suggestion for a regression model with binary outcomes of at least 10 cases per estimated parameter [21], the minimum number of participants required for this study was 90, with the expectation of nine predictors included in the regression model.

Study measures

General characteristics such as years of education, marital status, subjective financial status, smoking, and drinking were obtained via interviews. Clinical information, including age, gender, admission date, and diagnosed disease information, was acquired from medical records.

Fall and fall risk

A fall was defined as an event that resulted in a person coming to rest inadvertently on the ground, floor, or any other such lower level with or without injury [22]. Fall experience in the current institution was assessed with the question, “Have you fallen in the current institution?” Fall situations when the fall occurred in current institutions were also asked. Fall experience and fall situations in the current institutions were verified by caregivers at patients’ bedsides to ensure the reliability of patient responses. Further, fall risk was assessed using the Bobath Memorial Hospital Fall Risk Assessment Scale Short Form (BMFRAS-SF) [23]. It has four items: past fall history, level of physical activity, number of fall risk factors, and number of fall-risk-increasing medications. Each item has a 4-point scale ranging from 0 to 3, with a total score of 12. Individuals with a score greater than 5 are considered to have a high fall risk [23]. It has been shown to have a good sensitivity of 86.7% and a specificity of 67.9% [23].

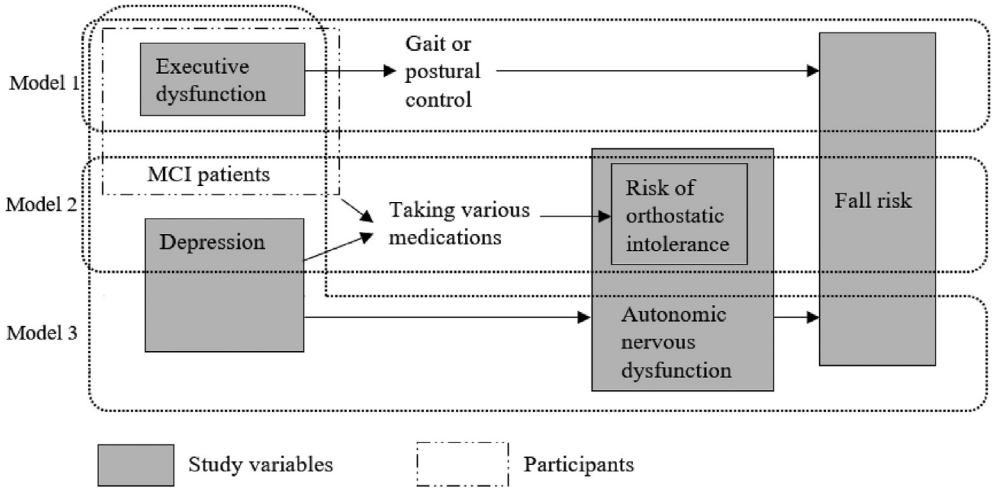

Figure 1. Conceptual Model of This Study.

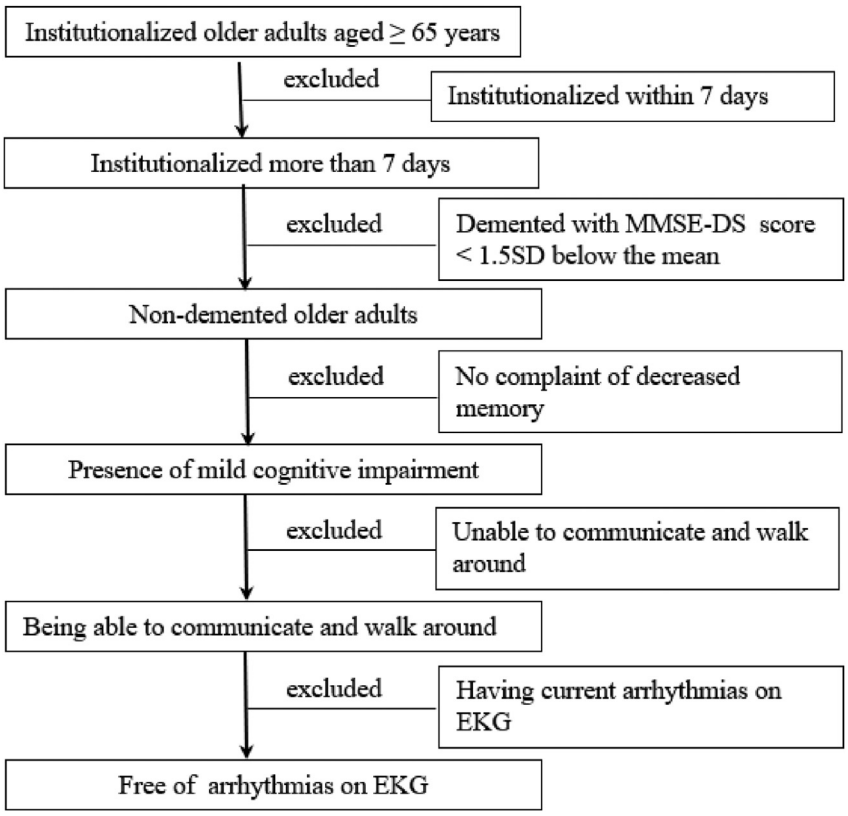

Figure 2. Process of Participant Selection.

Heart rate variability

For autonomic nervous system function, HRV was measured using Heart Rhythm Scanner 3.0 (Biocom Technologies, Poulsbo, USA) [24] in the participants' room. HRV was measured between 9 a.m. and 11 a.m. to minimize bias from HRV diurnal variation. Caffeine, nicotine, and alcohol intake were restricted from 12 h before the measurement to evaluate HRV accurately. Further, three-channel electrocardiogram electrodes were attached to the inner part of both wrists to measure HRV. It was measured for 5 min in the participant's lying position after 5 min of rest, and for another 5 min in their sitting position after 5 min of resting, as 5 min are believed necessary for adjustment to the posture [25].

The software Heart Rhythm Scanner 5.4.1. version (Biocom Technologies, Poulsbo, USA) was used, developed according to standards and mathematical procedures set forth by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. HRV was analyzed both in the time domain—the standard deviation of the normal RR intervals (SDNN), root mean square of the differences between adjacent RR intervals (RMSSD)—and the frequency domain—normalized high frequency (nHF), normalized low frequency (nLF), and LF/HF ratio—on each of the two measurements. SDNN is the index of the heart's response to changing workloads and was measured in milliseconds, with higher SDNN indicating better cardiac response to changing workloads [26]. RMSSD is the primary time-domain measure used to estimate vagally mediated changes reflected in HRV, with higher RMSSD indicating greater activity of parasympathetic nervous system [27]. nLF indicates the contribution of the low frequency in the total power, excluding the contribution of very low frequency (VLF), and reflects sympathetic activity dominantly. nHF indicates the contribution of the high frequency in the total power, excluding the contribution of VLF, and is mediated almost entirely by parasympathetic nerve activity. The LF/HF ratio verifies the balance between sympathetic and parasympathetic nervous activities.

Orthostatic hypotension

Orthostatic hypotension (OH) was defined as a decrease in systolic blood pressure (SBP) of at least 20 mmHg or a decrease in diastolic blood pressure (DBP) of at least 10 mmHg within 3 min of standing from a supine position [25]. To evaluate OH, brachial BP was measured using an electronic sphygmomanometer (HEM-907, Omron, Kyoto, Japan). After the participants rested for 5 min in the lying position, brachial BP was measured. Subsequently, the participants sat on the bed, and brachial BP was measured within 3 min.

General cognitive function and executive function

The Mini Mental Status Examination for Dementia Screening (MMSE-DS) was used to evaluate overall cognitive function [20]. The MMSE-DS comprises 19 items, including tests of orientation, attention, memory, language, and visual-spatial skills. The total score was 30, with higher scores indicating better cognitive function.

Executive function, one of the cognitive domains, is defined as complex cognitive abilities that enable the identification of goals, mental planning, behavior organization, and planning actions to achieve these goals [28]. To evaluate executive function, the semantic verbal fluency (VF) test and clock drawing test (CDT) were used. VF reflects multiple dimensions of executive function of the frontal and temporal lobes, and starts to be damaged from the beginning of Alzheimer disease [29]. For the VF test, participants were asked to speak as many names as possible in an animal category for 1 min; subsequently, the number of correct animal names was counted with higher counts indicating better executive function [30]. The CDT evaluates cognitive abilities, including

auditory and visual comprehension, concentration, visuospatial abilities, abstract conceptualization, and executive control [31]. For CDT, participants were asked to draw a clock on paper and mark a specific time on it. The Rouleau scoring system was used to calculate the CDT score [32]. The total score ranges from 0 to 10, with higher scores indicating better executive function.

Depressive symptoms

Depressive symptoms were evaluated using the 15-item Geriatric Depression Scale Short Form (GDS-SF) [33]. Each item has a binary response format (yes/no), with scores ranging from 0 to 15. A higher score indicates more severe depressive symptoms. Depression was considered present when the score was equal to or greater than 6. The Korean version of the GDS-SF has been shown to have good validity [34]. The Crombach's α of the GDS-SF was .80 previously [35], and .82 in this study.

Procedures and ethical considerations

This study was approved by the institutional review board of Inha University (Approval No. 161118-1AR). To recruit participants, the researcher contacted the directors of four regional geriatric hospitals conveniently selected to receive approval for data collection. The directors extracted the names of older adults who met the inclusion criteria and provided the list to the researcher. The researcher then visited the patients to explain the study purpose and procedure and obtain written consent from each participant. The patients were given time to consider participation or discuss it with their family. When necessary, the researcher explained the study purpose and procedure to their family via phone call or in person. The older adults who voluntarily decided to participate in this study were included. Subsequently, a research assistant measured HRV and orthostatic BP, and assessed general information and depressive symptoms via one-on-one interviews for approximately 40 min. Clinical information, including diseases diagnosed and medication taken, was collected by reviewing participants' electronic medical records. Participants who completed all procedures were given a small gift as a reward.

Before visiting the participants, three research assistants were educated on data collection protocols over an hour in advance. In addition, they visited four participants together to observe data collection procedures in the beginning and coordinated the details of the protocols through discussion with the others to ensure reliability.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 25 for Windows (IBM, Armonk, USA). All continuous variables were first assessed for normality using the Shapiro–Wilk test. In descriptive statistics, the mean with standard deviation and median with interquartile range were demonstrated for variables with normal distribution and those without it, respectively. The paired *t*-test and Wilcoxon signed-rank test were used to compare HRV indices during the orthostatic challenge. Because the changes in HRV indices during the orthostatic challenge did not show normal distribution, ranked ANCOVA was used to compare changes in HRV during the orthostatic challenge adjusted for antidepressant medication with presence of depression. For ranked ANCOVA, the residuals of ranked changes in HRV indices during orthostatic challenge adjusted for antidepressants use were calculated, which was analyzed depending on the presence of depression using ANOVA. For univariate analyses for association between study variables and fall experience in the current institutions, chi-square tests, *t*-test, and the Mann-Whitney U test were used. Multiple logistic regression was used to identify the influence of cognitive function, autonomic nervous function, and depression on falls, including age, sex, and other fall risk factors with p value < .10 in the univariate analysis to avoid deleting less significant factors that may have practical and clinical reasoning [36,37]. The level of statistical significance was set at $p < .05$. The Hosmer–Lemeshow goodness-of-fit statistic was used to check the model fit.

Results

One hundred and fifteen older adults participated in this study. The mean age of the participants was 78.0 years old (SD = 8.20), and 73 (63.5%) were female (Table 1). The median education years was 7 years with the interquartile range of 6, and 34 (29.5%) reported themselves in poor financial status. Most participants did not smoke or drink. The average duration of admission was 302.0 days. The most common disease diagnosed was hypertension (40.1%), followed by musculoskeletal diseases (24.5%) such as arthritis and osteoporosis.

Among the 115 participants, 17 (14.8%) had experienced falls in the current institutions (Table 1). Further, 49 (40.8%) were classified

Table 1 *Descriptive Statistics of Participants Characteristics and Study Variables (n = 115).*

Variables		*n* (%)
Age (years)	Mean (SD)	78.00 (8.20)
Gender	Men	42 (36.5)
	Women	73 (63.5)
Education years	Median (IQR)	7.00 (6.00)
Marital status	Married	45 (39.1)
	Widowed	65 (56.5)
	Single	3 (2.6)
	Divorced	2 (1.7)
Subjective financial status	Good	8 (7.0)
	Average	73 (63.5)
	Poor	34 (29.5)
Smoking	Never	80 (69.6)
	Previous smoker	34 (29.5)
	Current smoker	1 (0.9)
Drinking alcohol	Previous drinker	59 (51.3)
	Never	53 (46.1)
	Sometimes	3 (2.6)
Admission duration (days)	Mean (SD)	302.04 (146.83)
Underlying illness diagnosed[a]	Hypertension	77 (40.1)
	Musculoskeletal disease	47 (24.5)
	Stroke	34 (17.7)
	Cancer	16 (8.3)
	Kidney disease	9 (4.7)
	Parkinson disease	9 (4.7)
Fall experience in current hospitals	Yes	17 (14.8)
	No	98 (85.2)
Fall situation (n = 17)	Losing one's balance	5 (29.4)
	Losing one's footing	4 (23.5)
	Changing position	3 (17.6)
	Walking on stairs	3 (17.6)
	Others	2 (11.8)
Fall risk score	High risk	49 (40.8)
	Low risk	66 (57.4)
Previous fall for 1 year before admission	Yes	41 (35.7)
	No	74 (64.3)
MMSE-DS	median (IQR)	23.00 (8.75)
Verbal fluency	mean (SD)	8.51 (4.07)
Clock drawing test	median (IQR)	8.00 (5.00)
Depressive symptoms	median (IQR)	7.00 (3.00)
	Yes (≥6)	92 (80.0)
	No (<6)	23 (20.0)
Orthostatic hypotension	Yes	14 (12.2)
	No	101 (87.8)

Note. IQR = interquartile range; MMSE-DS = mini-mental status examination for dementia screening; SD = standard deviation.
[a] Multiple diagnoses allowed to secondary diagnosis.

into the high fall risk group based on the BMFRAS-SF. While the median scores of the MMSE-DS and CDT were 23.0 and 8.0, respectively, the mean score of the VF test was 8.51. Moreover, 92 participants (80.0%) had depression, with a GDS≥6.

For HRV during the orthostatic challenge, SDNN significantly increased from 18.50 millisecond to 20.30 millisecond ($p = .037$) (Table 2). nHF decreased from 46.9% to 41.6%, while nLF increased from 54.5% to 58.9%, which was not significant. The other HRV indices showed no significant changes during the orthostatic challenge. None of the HRV indices was significantly related to the presence of depression (Table 2).

In univariate analyses, older adults with fall experience in current institutions were significantly younger than those without fall experience ($p = .041$) (Table 3). The MMSE-DS score ($p = .008$) and VF score ($p = .036$) were significantly higher in older adults with fall experience in current institutions than in those without it. However, the CDT score was lower in older adults with fall experience in current institutions although the difference was not significant. Among HRV indices, nHF on lying was significantly higher in older adults with fall experience in current institutions than in those without it ($p = .047$). There were no significant differences in high fall risk assessed on BMFRAS-SF, presence of OH, and presence of depression between older adults with fall experience in current institutions and those without it.

In the multivariate logistic regression analysis, age, sex, and factors with p values less than .10 were included. Only nHF on lying was independently associated with falls (OR = 1.03, 95%CI: 1.000–1.055 $p = .049$) (Table 3). The Hosmer–Lemeshow goodness of fit was not significant ($\chi^2 = 9.019$, $p = .341$), indicating adequate model fit.

Discussion

This study was conducted to investigate the autonomic nervous function during the orthostatic challenge using HRV measurement, explore the involvement of autonomic nervous function in depressive symptoms, and elucidate the association of cognitive function, including executive function, autonomic nervous function, and depressive symptoms, with falls.

In this study, surprisingly, older adults who experienced falls in current institutions were the ones with higher MMSE-DS scores, better VF, and younger age. This result contradicts the prior finding that cognitive impairment and older age have also been shown to be intrinsic risk factors for falls [38]. The first thing to be considered is that the participants have received general fall preventive care in current institutions; the healthcare personnel have already taken care of those with lower cognition and older age. Second, older adults with older age and lower cognitive functions may have refrained from walking around to have a lower chance of falling. Mendes da Costa et al. [39] pointed out that older adults with older age restricted their activity more than those with younger age owing to fear of falling. Lastly, older age and lower general cognitive ability may not increase risk of falls in institutionalized older adults with MCI. A recent meta-analysis study by Hopkins et al. [40] showed that fall-related factors were physical performances such as gait and dual-tasking ability, rather than age or general cognitive function, in older adults with MCI, consistent with the finding that the association of age and cognitive ability with falls disappeared in the multivariate analysis. Furthermore, they addressed that there were no effective fall intervention programs to reduce falls for MCI patients in previous studies. Therefore, another strategy focusing on physical performance training and cognitive training targeting for dual-task ability or working memory are needed for healthcare personnel to prevent further falls among institutionalized MCI older adults with relatively higher cognitive function and younger age.

All of the participants had significantly increased SDNN upon sitting, which is an appropriate transition to increased cardiac reactivity. However, the increase in nLF and decreased nHF during the orthostatic challenge did not reach a significant level, indicating attenuated sympathetic/parasympathetic modulation. This is consistent with a previous study [41], which addressed autonomic dysfunction in both sympathetic and parasympathetic modulation among community-dwelling older adults with MCI. Although sympathetic modulation is believed to play an important role in postural control [42] and maintained in some healthy older adults [43], notably, a smaller increase in nLF was prominent among the institutionalized older adults with MCI in this study. Thus, it seems that the institutionalized older adults with MCI were vulnerable to sympathetic modulation with a reduced capacity to accelerate cardiac function during the orthostatic challenge. Failing to redistribute autonomic balance during the orthostatic challenge has also given rise to diminished quality of life [44]. Therefore, more attention should be paid to autonomic dysfunction in institutionalized older adults with MCI.

When exploring HRV in relation to falls, however, it was nHF on lying that was significantly higher in older adults with fall experience in current institutions than in those without fall experience although its significant level was somewhat marginal. In addition, its influence outweighed that of cognitive function and others on fall experience in current institutions. This is somewhat different from the study of Razjouyan et al. [45] who suggested that nHF was

Table 2 *Changes of Heart Rate Variability During Orthostatic Challenge and its Relation With Depression.*

HRV during orthostatic challenge		median (IQR)	Z[a]	p	Residuals of changes in HRV during orthostatic challenge[c] mean (SD)	Depression		Z	p
						Yes ($n = 92$)	No ($n = 23$)		
SDNN (millisecond)	Lying	18.50 (19.10)	−2.09	.037	△ in SDNN	−1.82 (26.52)	7.30 (24.96)	1.616	.286
	Sitting	20.30 (23.95)							
RMSSD (millisecond)	Lying	12.60 (26.10)	−0.49	.628	△ in RMSSD	−0.32 (26.77)	1.29 (28.51)	0.034	.855
	Sitting	12.70 (24.90)							
nHF (%), mean (SD)	Lying	46.9 (23.83)	1.99[b]	.050	△ in nHF	0.96 (26.77)	−3.77 (26.48)	0.762	.386
	Sitting	41.6 (22.97)							
nLF (%), mean (SD)	Lying	54.5 (23.76)	−1.59[b]	.114	△ in nLF	1.53 (26.65)	−5.98 (26.34)	0.301	.586
	Sitting	58.9 (22.65)							
LF/HF (a.u)	Lying	1.20 (2.10)	−0.66	.510	△ in LF/HF	2.36 (25.83)	−9.44 (34.58)	1.742	.192
	Sitting	1.40 (2.60)							

Note. HRV = heart rate variability; IQR = interquartile range; nHF = normalized high frequency; nLF = normalized low frequency; RMSSD = root mean square of the successive differences; SD = standard deviation; SDNN = standard deviation of normal RR intervals.

[a] Wilcoxon signed rank test.

[b] t-test.

[c] Adjusted for taking antidepressants.

Table 3 *Associated Factors of Fall Experience in Current Hospitals (n = 115).*

Variables		Univariate analysis				Multivariate analysis		
		Fall experience in current hospitals, *n* (%)		Mann-Whitney's U or χ^2	*p*	Fall experience in current hospitals, Yes		
		Yes (*n* = 17)	No (*n* = 98)			Exp(B)	CI	*p*
Age, mean (SD)		74.29 (7.16)	78.62 (8.23)	2.04[a]	.044	0.98	0.896–1.080	.735
Gender	Men	6 (35.3)	36 (36.7)	0.01	.915	–	–	–
	Women	11 (64.7)	62 (63.3)			1.29	0.324–5.091	.721
Education years, median (IQR)		9.00 (6.00)	9.00 (6.00)	812.00	.765	–	–	–
Admission duration		792.50 (1180.75)	311.00 (896.00)	22.00	.282	–	–	–
Previous fall before admission	Yes	8 (47.1)	33 (33.3)	1.20	.274	–	–	–
	No	9 (52.9)	65 (66.7)			–	–	–
Fall risk	High risk	13 (76.5)	52 (53.1)	3.23	.060[b]	5.23	0.992–27.542	.051
	Low risk	4 (23.5)	46 (46.9)			–	–	–
MMSE-DS, median (IQR)		26.50 (4.75)	22.00 (15.00)	504.00	.008	1.10	0.919–1.321	.293
Verbal fluency, mean (SD)		10.41 (4.00)	8.19 (4.01)	−2.12[a]	.036	1.04	0.816–1.329	.744
Clock drawing test, median (IQR)		7.50 (4.00)	8.00 (9.00)	624.00	.424	–	–	–
Depressive symptoms	Yes	13 (76.5)	79 (80.2)	0.13	.748	–	–	–
	No	4 (23.5)	19 (19.8)			–	–	–
Orthostatic hypotension	Yes	1 (5.9)	13 (13.1)	0.72	.689[b]	–	–	–
	No	16 (94.1)	85 (86.9)			–	–	–
Heart rate variability								
SDNN (millisecond) median (IQR)	Lying	18.00 (27.40)	20.30 (19.00)	609.50	.956	–	–	–
	Sitting	21.60 (34.03)	20.70 (25.05)	548.50	.552	–	–	–
RMSSD (millisecond)	Lying	12.00 (34.90)	12.60 (23.30)	597.50	.861	–	–	–
median (IQR)	Sitting	13.90 (38.48)	12.80 (20.55)	450.00	.112	–	–	–
nHF (%), mean (SD)	Lying	58.69 (22.07)	44.92 (23.89)	−2.01[a]	.047	1.03	1.000–1.055	.049
	Sitting	39.96 (25.35)	41.82 (22.37)	0.29[a]	.774	–	–	–
nLF (%), mean (SD)	Lying	48.31 (24.92)	55.67 (23.76)	1.09[a]	.277	–	–	–
	Sitting	60.03 (25.37)	58.77 (22.14)	−0.20[a]	.843	–	–	–
LF/HF (a.u), median (IQR)	Lying	1.00 (2.20)	1.30 (2.10)	552.00	.529	–	–	–
	Sitting	1.15 (2.20)	1.80 (2.80)	553.50	.586	–	–	–
Constant		–	–	–	–	0.00		.208

Note. IQR: interquartile range; MMSE-DS: mini-mental status examination for dementia screening; nHF: normalized high frequency; nLF: normalized low frequency; RMSSD: root mean square of the successive differences; SD: standard deviation; SDNN: standard deviation of normal RR intervals.

[a] *t*-test.

[b] Fisher's exact test.

low in patients with a high fall risk. This discrepancy may be due to the fact that most participants in the previous study were adults and young older adults. As parasympathetic modulation appeared to be maintained during the aging process, whereas other HRV indices were reduced [46], parasympathetic modulation in older adults might be preserved more than sympathetic modulation, which contributes to fall occurrence. Indeed, LF/HF in the prior study was approximately 3.8, which is much greater than 1.3 in this study. Moreover, institutionalized older adults may be on medications that reinforce parasympathetic activity and weaken sympathetic activity, such as antidepressants and various antihypertensives. Thus, increased parasympathetic activity during lying likely plays a key role in the occurrence of falls in institutionalized older adults. On the other hand, there was no significant difference in the presence of OH between older adults with fall experience in current institutions and those without it. There have been controversies regarding OH as a significant risk factor for falls [47]. A recent meta-analysis reported that OH was associated with time to fall incidence, not with fall occurrence itself [48], in line with the findings of this study. Considered together, autonomic nervous function assessment based on HRV is likely more sensitive than OH assessment for evaluating fall risk in institutionalized older adults with MCI.

In this study, depressive symptoms were not associated with falls. This is contrary to a prior result that depression increased the risk of falls in community-dwelling older adults [49]. This may be because of the severity of the depressive symptoms. The participants in the prior study were relatively low depressed, with a prevalence of depression of only 10.0% and free-living in community settings. However, in the study [49], 86.4% of older adults were depressed, with a GDS >5. Further, Kamińska, Brodowski, and Karakiewicz [50] suggested there was no difference in depressive symptoms between fallers and nonfallers, but depressive symptoms were involved in the number of falls. Therefore, depressive symptoms seem to have little relevance to fall occurrence in institutionalized older adults with severe depression.

In addition, depressive symptoms were not related to changes of HRV during orthostatic challenge in this study, whereas Luo et al. [51] addressed reduced HRV function in older adults with depression. This difference might come from the type of antidepressant medications that were taken by some depressive older adults. Some of prior studies addressed antidepressant agents from different classes may differentially impact HRV, addressing tricyclic antidepressants decrease HRV and selective serotonin reuptake inhibitors do not or do so to a lesser extent [52,53]. In this study, taking antidepressants was adjusted but type of antidepressants was not, which may lead to the inconsistency. Because the involvement of antidepressants in HRV alterations in depressive patients is still somewhat debatable, further research is needed to investigate the different effect of antidepressants on HRV in older adults with depression.

This study has certain limitations. First, fall occurrence was retrospectively investigated in a small number of older adults who experienced falls. Prospective research with larger sample sizes is needed to follow up fall occurrence to identify contributing factors to falls in the future. Second, the measurement of HRV was as short as 5 min and performed only once. However, as HRV measurement for 5 min was reported to be stable compared to that for 24 h [54] and performed in a relatively consistent time frame, it would be worthy of being accepted. Third, the effects of medications could not be controlled for HRV although those were controlled for falls.

Further research is needed to determine the types of antidepressants, antihypertensives, and other cardiac medications that affect autonomic nervous activity. Finally, we cannot help pointing out missing variable bias because only seven predictors were included in the final logistic regression model, which may lead to no predictor except for the one marginally significant factor, nHF on lying.

Conclusion

In this study, fall experience in current institutions was significantly associated with younger age and better cognitive function. Therefore, another strategy is needed for healthcare personnel to prevent further falls among MCI older adults with younger age and higher general cognitive function. Further, institutionalized older adults with MCI had attenuated sympathetic/parasympathetic modulation, and higher nHF on lying was independently associated with fall experience in current institutions. Thus, parasympathetic function based on HRV assessment should be considered as a significant factor for evaluating fall risk. Depression was not significantly associated with HRV or falls. In the future, studies with prospective fall follow-up in a large population considering medications, and their effects on a relationship between depression and HRV are needed.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.05.001.

References

1. World Health Organization. Falls [Internet]. Geneva, Switzerland: World Health Organization; 2022 [cited 2023 January 12]. Available from: https://www.who.int/news-room/fact-sheets/detail/falls
2. Vlaeyen E, Poels J, Colemonts U, Peeters L, Leysens G, Delbaere K, et al. Predicting falls in nursing homes: a prospective multicenter cohort study comparing fall history, staff clinical judgment, the care home falls screen, and the fall risk classification algorithm. J Am Med Dir Assoc. 2021;22(2):380–7. https://doi.org/10.1016/j.jamda.2020.06.037
3. Castaldo A, Giordano A, Antonelli Incalzi R, Lusignani M. Risk factors associated with accidental falls among Italian nursing home residents: a longitudinal study (FRAILS). Geriatr Nurs. 2020;41(2):75–80. https://doi.org/10.1016/j.gerinurse.2019.06.003
4. Petersen RC. Clinical practice. Mild cognitive impairment. N Engl J Med. 2011;364(23):2227–34. https://doi.org/10.1056/NEJMcp0910237
5. Smith L, Jacob L, Kostev K, Butler L, Barnett Y, Pfeifer B, et al. Mild cognitive impairment is associated with fall-related injury among adults aged ≥65 years in low- and middle-income countries. Exp Gerontol. 2021;146:111222. https://doi.org/10.1016/j.exger.2020.111222
6. Corbo I, Casagrande M. Higher-level executive functions in healthy elderly and mild cognitive impairment: a systematic review. J Clin Med. 2022;11(5):1204. https://doi.org/10.3390/jcm11051204
7. Hunter SW, Divine A, Madou E, Omana H, Hill KD, Johnson AM, et al. Executive function as a mediating factor between visual acuity and postural stability in cognitively healthy adults and adults with Alzheimer's dementia. Arch Gerontol Geriatr. 2020;89:104078. https://doi.org/10.1016/j.archger.2020.104078
8. Santos Henriques RPD, Tomas-Carus P, Filipe Marmeleira JF. Association between neuropsychological functions and activities of daily living in people with mild cognitive impairment. Exp Aging Res. 2022:1–15. https://doi.org/10.1080/0361073X.2022.2133292
9. Savica R, Wennberg AM, Hagen C, Edwards K, Roberts RO, Hollman JH, et al. Comparison of gait parameters for predicting cognitive decline: the Mayo clinic study of aging. J Alzheimers Dis. 2017;55(2):559–67. https://doi.org/10.3233/JAD-160697
10. Muir-Hunter SW, Clark J, McLean S, Pedlow S, Van Hemmen A, Montero Odasso M, et al. Identifying balance and fall risk in community-dwelling older women: the effect of executive function on postural control. Physiother Can. 2014;66(2):179–86. https://doi.org/10.3138/ptc.2013-16
11. Smith TO, Neal SR, Peryer G, Sheehan KJ, Tan MP, Myint PK. Orientation and verbal fluency in the English Longitudinal Study of Ageing: modifiable risk factors for falls? Int Psychogeriatr. 2019;31(10):1491–8. https://doi.org/10.1017/S1041610218002065
12. Dorey TW, Jansen HJ, Moghtadaei M, Jamieson KL, Rose RA. Impacts of frailty on heart rate variability in aging mice: roles of the autonomic nervous system and sinoatrial node. Heart Rhythm. 2021;18(11):1999–2008. https://doi.org/10.1016/j.hrthm.2021.07.069
13. Baker SE, Limberg JK, Ranadive SM, Joyner MJ. Neurovascular control of blood pressure is influenced by aging, sex, and sex hormones. Am J Physiol Regul Integr Comp Physiol. 2016;311(6):R1271–5. https://doi.org/10.1152/ajpregu.00288.2016
14. Hohtari-Kivimäki U, Salminen M, Vahlberg T, Kivelä SL. Orthostatic hypotension is a risk factor for falls among older adults: 3-year follow-up. J Am Med Dir Assoc. 2021;22(11):2325–30. https://doi.org/10.1016/j.jamda.2021.07.010
15. Collins O, Dillon S, Finucane C, Lawlor B, Kenny RA. Parasympathetic autonomic dysfunction is common in mild cognitive impairment. Neurobiol Aging. 2012;33(10):2324–33. https://doi.org/10.1016/j.neurobiolaging.2011.11.017
16. Kvelde T, McVeigh C, Toson B, Greenaway M, Lord SR, Delbaere K, et al. Depressive symptomatology as a risk factor for falls in older people: systematic review and meta-analysis. J Am Geriatr Soc. 2013;61(5):694–706. https://doi.org/10.1111/jgs.12209
17. Susilowati IH, Nugraha S, Sabarinah S, Peltzer K, Pengpid S, Hasiholan BP. Prevalence and risk factors associated with falls among community-dwelling and institutionalized older adults in Indonesia. Malays Fam Physician. 2020;15(1):30–8.
18. Brown L, Karmakar C, Gray R, Jindal R, Lim T, Bryant C. Heart rate variability alterations in late life depression: a meta-analysis. J Affect Disord. 2018;235:456–66. https://doi.org/10.1016/j.jad.2018.04.071
19. Jessen F, Wiese B, Bachmann C, Eifflaender-Gorfer S, Haller F, Kölsch H, et al. Prediction of dementia by subjective memory impairment: effects of severity and temporal association with cognitive impairment. Arch Gen Psychiatr. 2010;67(4):414–22. https://doi.org/10.1001/archgenpsychiatry.2010.30
20. Han JW, Kim TH, Hjhoo JH, Park JH, Kim JL, Ryu SH, et al. A normative study of the Mini-mental state examination for dementia screening (MMSE-DS) and its short form(SMMSE-DS) in the Korean elderly. J Korean Geriatr Psychiatry. 2010;14:27–37.
21. Long JS. Regression models for categorical and limited dependent variables. Thousand Oaks: Sage Publications Inc.; 1997. p. p54.
22. World Health Organization. Falls [Internet]. Switzerland: World Health Organization; 2016 [cited 2023 January 12]. Available from: http://www.who.int/mediacentre/factsheets/fs344/en/
23. Song KY, Park MH, Chaung SK, Park HJ. Validation of the short form Bobath memorial hospital fall risk assessment scale at a specialized geriatric hospital in Korea. J Korean Public Health Nurs. 2014;28(3):495–508. https://doi.org/10.5932/JKPHN.2014.28.3.495
24. Yamasaki Y, Kodama M, Matsuhisa M, Kishimoto M, Ozaki H, Tani A, et al. Diurnal heart rate variability in healthy subjects: effects of aging and sex difference. Am J Physiol. 1996;271(1 Pt 2):H303–10. https://doi.org/10.1152/ajpheart.1996.271.1.H303
25. Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W, Tassinari M. EFNS guidelines on the diagnosis and management of orthostatic hypotension. Eur J Neurol. 2006;13(9):930–6. https://doi.org/10.1111/j.1468-1331.2006.01512.x
26. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health. 2017;5:258. https://doi.org/10.3389/fpubh.2017.00258
27. Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. Front Psychol. 2014;5:1040. https://doi.org/10.3389/fpsyg.2014.01040
28. Diamond A. Executive functions. Annu Rev Psychol. 2013;64:135–68. https://doi.org/10.1146/annurev-psych-113011-143750
29. Aita SL, Beach JD, Taylor SE, Borgogna NC, Harrell MN, Hill BD. Executive, language, or both? An examination of the construct validity of verbal fluency measures. Appl Neuropsychol Adult. 2019;26(5):441–51. https://doi.org/10.1080/23279095.2018.1439830
30. Lucas JA, Ivnik RJ, Smith GE, Bohac DL, Tangalos EG, Graff-Radford NR, et al. Mayo's older Americans normative studies: category fluency norms. J Clin Exp Neuropsychol. 1998;20(2):194–200. https://doi.org/10.1076/jcen.20.2.194.1173
31. Shulman KI. Clock-drawing: is it the ideal cognitive screening test? Int J Geriatr Psychiatr. 2000;15(6):548–61. https://doi.org/10.1002/1099-1166(200006)15:6<548::AID-GPS242>3.0.CO;2-U
32. Rouleau I, Salmon DP, Butters N, Kennedy C, McGuire K. Quantitative and qualitative analyses of clock drawings in Alzheimer's and Huntington's disease. Brain Cognit. 1992;18(1):70–87. https://doi.org/10.1016/0278-2626(92)90112-y
33. Sheik J, Yesavage J. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clin Gerontol. 1986;5:165–72. https://doi.org/10.1300/J018v05n01_09

34. Cho MJ, Bae JN, Suh GH, Hahm HJ, Kim JK, Lee DW, et al. Validation of geriatric depression scale, Korean version (GDS) in the assessment of DSM-III-R major depression. Psychiatry Investig. 1999;38(1):48–63. https://doi.org/10.1016/j.jpsychores.2004.01.004
35. Park YH, Choi-Kwon S, Park KA, Suh M, Jung YS. Nutrient deficiencies and depression in older adults according to sex: a cross sectional study. Nurs Health Sci. 2017;19(1):88–94. https://doi.org/10.1111/nhs.12315
36. Hosmer DW, Lemeshow S, Sturdivant RX. Applied logistic regression. New York: John Wiley & Sons, Incorporated; 2013.
37. Chowdhury MZI, Turin TC. Variable selection strategies and its importance in clinical prediction modelling. Fam Med Community Health. 2020;8:e000262. https://doi.org/10.1136/fmch-2019-000262
38. Ma Y, Li X, Pan Y, Zhao R, Wang X, Jiang X, et al. Cognitive frailty and falls in Chinese elderly people: a population-based longitudinal study. Eur J Neurol. 2021;28(2):381–8. https://doi.org/10.1111/ene.14572
39. Mendes da Costa E, Pepersack T, Godin I, Bantuelle M, Petit B, Levêque A. Fear of falling and associated activity restriction in older people. Results of a cross-sectional study conducted in a Belgian town. Arch Publ Health. 2012;70(1):1. https://doi.org/10.1186/0778-7367-70-1
40. Hopkins J, Hill K, Jacques A, Burton E. Prevalence, risk factors and effectiveness of falls prevention interventions for adults living with mild cognitive impairment in the community: a systematic review and meta-analysis. Clin Rehabil. 2023;37(2):215–43. https://doi.org/10.1177/02692155221129832
41. Nicolini P, Ciulla MM, Malfatto G, Abbate C, Mari D, Rossi PD, et al. Autonomic dysfunction in mild cognitive impairment: evidence from power spectral analysis of heart rate variability in a cross-sectional case-control study. PLoS One. 2014;9(5):e96656. https://doi.org/10.1371/journal.pone.0096656
42. Sibley KM, Mochizuki G, Lakhani B, McIlroy WE. Autonomic contributions in postural control: a review of the evidence. Rev Neurosci. 2014;25(5):687–97. https://doi.org/10.1515/revneuro-2014-0011
43. Perseguini NM, Takahashi AC, Rebelatto JR, Silva E, Borghi-Silva A, Porta A, et al. Spectral and symbolic analysis of the effect of gender and postural change on cardiac autonomic modulation in healthy elderly subjects. Braz J Med Biol Res. 2011;44(1):29–37. https://doi.org/10.1590/s0100-879x2010007500137
44. Kanbara K, Morita Y, Hasuo H, Abe T. The association between heart rate variability and quality of life in patients with functional somatic syndrome and healthy controls. Appl Psychophysiol Biofeedback. 2021;46(3):279–85. https://doi.org/10.1007/s10484-021-09515-1
45. Razjouyan J, Grewal GS, Rishel C, Parthasarathy S, Mohler J, Najafi B. Activity monitoring and heart rate variability as indicators of fall risk: proof-of-concept for application of wearable sensors in the acute care setting. J Gerontol Nurs. 2017;43(7):53–62. https://doi.org/10.3928/00989134-20170223-01
46. Reardon M, Malik M. Changes in heart rate variability with age. Pacing Clin Electrophysiol. 1996;19(11):1863–6. https://doi.org/10.1111/j.1540-8159.1996.tb03241.x
47. Shaw BH, Borrel D, Sabbaghan K, Kum C, Yang Y, Robinovitch SN, et al. Relationships between orthostatic hypotension, frailty, falling and mortality in elderly care home residents. BMC Geriatr. 2019;19(1):80. https://doi.org/10.1186/s12877-019-1082-6
48. Hartog LC, Schrijnders D, Landman GWD, Groenier K, Kleefstra N, Bilo HJG, et al. Is orthostatic hypotension related to falling? A meta-analysis of individual patient data of prospective observational studies. Age Ageing. 2017;46(4):568–75. https://doi.org/10.1093/ageing/afx024
49. Menant JC, Wong AK, Trollor JN, Close JC, Lord SR. Depressive symptoms and orthostatic hypotension are risk factors for unexplained falls in community-living older people. J Am Geriatr Soc. 2016;64(5):1073–8. https://doi.org/10.1111/jgs.14104
50. Kamińska MS, Brodowski J, Karakiewicz B. Fall risk factors in community-dwelling elderly depending on their physical function, cognitive status and symptoms of depression. Int J Environ Res Publ Health. 2015;12(4):3406–16. https://doi.org/10.3390/ijerph120403406
51. Luo Y, Zhang S, Zheng R, Xu L, Wu J. Effects of depression on heart rate variability in elderly patients with stable coronary artery disease. J Evid Base Med. 2018;11(4):242–5. https://doi.org/10.1111/jebm.12310
52. Alvares GA, Quintana DS, Hickie IB, Guastella AJ. Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. J Psychiatry Neurosci. 2016;41(2):89–104. https://doi.org/10.1503/jpn.140217
53. Licht CM, Naarding P, Penninx BW, van der Mast RC, de Geus EJ, Comijs H. The association between depressive disorder and cardiac autonomic control in adults 60 years and older. Psychosom Med. 2015;77(3):279–91. https://doi.org/10.1097/PSY.0000000000000165
54. Min KB, Min JY, Paek D, Cho SI, Son M. Is 5-minute heart rate variability a useful measure for monitoring the autonomic nervous system of workers? Int Heart J. 2008;49(2):175–81. https://doi.org/10.1536/ihj.49.175

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Research Article

Educational Program with Text Messaging for Community-Dwelling Patients with Hypertension: A Pilot Randomized Controlled Trial

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SUMMARY

Purpose: Controlling blood pressure minimizes the risk of cardiovascular events among patients with hypertension. Despite regular follow-ups, the hypertension management for patients aged ≥45 years is limited as evidenced from a decreased control rate. This pilot study aimed to test a theory-guided educational program for community-dwelling patients with hypertension.

Methods: Sixty-nine patients with hypertension aged ≥45 years and having high blood pressure (>130/80 mmHg) were recruited in this two-arm pilot randomized controlled trial. Participants in the intervention group underwent a program guided by the Health Promotion Model, whereas those in the control group received usual care. Data were collected at baseline, week 8, and week 12 and used to assess the blood pressure, pulse pressure, self-efficacy, and adherence to hypertension management. Data were analyzed using a generalized estimating equation based on the intention-to-treat principle. Process evaluation was conducted to assess the feasibility and acceptability of the educational program.

Results: The results obtained using the generalized estimating equation revealed that the educational program led to reduction in the systolic blood pressure ($\beta = -7.12$, $p = .086$) and pulse pressure ($\beta = -8.20$, $p = .007$) and to improve self-efficacy ($\beta = 2.61$, $p = .269$) at week 12. The program had a small-to-moderate effect on the reduction of systolic blood pressure (effect size = −0.45) and pulse pressure (effect size = −0.66) and self-efficacy (effect size = 0.23). The participants were highly satisfied with the educational program.

Conclusions: The educational program was found to be feasible and acceptable and may be incorporated into current hypertension management practices at the community level.

Trial registration: ClinicalTrials.gov with identifier: NCT04565548.

Introduction

Hypertension, defined as persistent elevated blood pressure (BP), affects more than 1 billion people worldwide [1]. Uncontrolled hypertension can lead to various adverse outcomes, including heart diseases, stroke, and chronic kidney disease [2]. According to the Global Burden of Diseases study, hypertension is the leading global risk factor accounting for 10.8 million attributable deaths worldwide in 2019 [3]. Thus, many national and international institutions, including the American Heart Association and the International Society of Hypertension, have developed guidelines for hypertension management and continue to post regular updates [4–7]. These guidelines recommend medication and lifestyle modifications (i.e., healthy eating, regular exercise, maintaining optimal body weight, smoking cessation, and limited alcohol consumption) to effectively control BP. However, the Noncommunicable Disease Risk Factor Collaboration reported that only 50% of the treated patients with hypertension achieved a controlled BP, that is, a systolic blood pressure (SBP) of <140 mmHg and diastolic blood pressure (DBP) of <90 mmHg [8]. The Macau Health Bureau also reported that 49.9% of the treated patients with hypertension achieved a controlled BP and that this rate was decreased in patients aged ≥45 years [9]. Moreover, the BP control

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rate among treated Chinese patients with hypertension was only 37.5%, and the rate was decreased in patients aged ≥45 years.

Nonadherence to hypertension management (i.e., medication and lifestyle modifications) is a major limiting factor for BP control [2,4]. A systematic review of 61 observational studies revealed a medication adherence rate of 55.3% among patients with hypertension [10]. A couple of studies reported low adherence to lifestyle modifications (23.6%–27.4%) [11,12]. Furthermore, a secondary analysis of a national dataset revealed that the rate of adherence to lifestyle modifications among patients with hypertension was as low as 1.7% [13]. The national data showed that patients with hypertension tended not to practice lifestyle modifications (odds ratio 0.48–0.53) [14]. Of note, health education can effectively improve adherence to medication and lifestyle modifications and significantly reduce SBP and DBP among patients with hypertension [15–17]. Furthermore, a meta-analysis showed that health education could significantly enhance self-efficacy among patients with hypertension [18]. Supportive techniques, such as written materials and text messaging, can enhance the effects of health education on hypertension management [19,20]. However, evidence on the theoretical framework of hypertension studies is insufficient, and this has limited our understanding of the associated behavioral changes [16,21,22].

On the other hand, the analysis of 169,613 individuals aged 40–69 years found that pulse pressure was a significant predictor of new onset of hypertension-related adverse outcomes [23], but very limited study assessed the pulse pressure among patients with hypertension.

Taking together, the currently available hypertension management for patients to achieve a controlled BP is insufficient. Although health education could be an effective intervention in terms of hypertension management, evidence on theory-guided interventions is limited. This pilot study aimed to test a theory-guided educational program for community-dwelling patients with hypertension.

Methods

Aims

This study aimed to test the preliminary effects of a theory-guided educational program on hypertension management and compare the effects of this program with those of usual care among patients with hypertension. The following outcomes were compared: BP, pulse pressure, self-efficacy in hypertension management, and adherence to hypertension management. Moreover, process evaluation was conducted to examine the feasibility (recruitment rate and retention rate) and acceptability (participant satisfaction and usefulness of the program for hypertension management) of the program.

Study design

This two-arm, prospective, multicenter, pilot randomized controlled trial (RCT) was conducted in accordance with the Consolidated Standards of Reporting Trials statement was followed [24]. The study was registered with the ClinicalTrials.gov (identifier: NCT04565548) before the baseline data collection. Eligible participants were randomly assigned to either an intervention group or a control group in a 1:1 ratio and were followed up twice (at weeks 8 and 12).

Setting and sample

The study was conducted at four community centers (two in Macau and two in Shenzhen) that offer various health-related activities to both members and nonmembers in communities. Macau and Shenzhen are located in the Greater Bay Area in southern China; these two cities were selected because they share similar cultural traditions and eating habits [25]. The staff of the centers called their members to come for screening, and posters of this study were posted in visible public areas for those interested nonmembers.

By estimating a medium effect (Eta squared = 0.05), Hertzog suggested a 2-arm pilot study should include 35 participants per group to achieve a power of 80.0% at a 5.0% level of significance in a two-tailed repeated measure [26].

Inclusion and exclusion criteria

The criteria for inclusion in this study were as follows: (1) age ≥45 years; (2) a diagnosis of hypertension and use of at least one anti-hypertensive drug; (3) ability to use a mobile phone to read text messages; (4) SBP of 131–159 mmHg or DBP of 81–99 mmHg (as a BP of <130/80 mmHg helps patients with hypertension to significantly lower their risk of cardiovascular events [27,28]); and (5) a Mini-Cog score of ≥3 (cognitive competence was required to understand the contents of the educational program; this threshold indicates a lower likelihood of cognitive impairment [29]).

Randomization and allocation concealment

In each study venue, the eligible participants were randomly assigned. The permuted block randomization, with a block size of four, was used. The allocation sequence was computer generated using an online tool (http://www.randomization.com) by an independent assistant who was not affiliated with the study. Small cards indicating the group allocation were placed in sequentially numbered, opaque, sealed envelopes. The participants opened the envelopes after the completion of baseline data collection. The participants from different groups visiting the same community center were then called to join the group health education on different date and time to minimize subject contamination.

Interventions material

Intervention group

The participants in the intervention group received an educational program that was developed according to the framework of the Health Promotion Model [30]. The program consisted of health education, a summary leaflet, and text messaging to increase the participants' cognition with respect to hypertension management–related adherence behaviors. The construct-matched interventions and methods are shown in supplementary material, Table S1. Some interactive elements, such as practice for measuring BP and discussion on healthy cooking, were added to the health education component. Integration of hypertension management into daily life was emphasized. For example, a daily alarm was set in the health education to remind taking medication regularly. Natural herbs, such as star anise and clove, were introduced to substitute the use of salt. Some packed foods were provided to practice how to

read and understand the food label. Also, an indoor 6-min exercise was practiced together that facilitated participants to do exercise at anywhere and anytime. The health education content was adopted from the educational manual developed by the World Health Organization [31] and was validated by five experts in the fields of community nursing, family medicine, nutrition, and academics with a good content validity index (0.85). The leaflet summarized the hypertension-related knowledge, and quick response (QR) codes were added to enable the participants to practice some exercises at their convenience. The text message content was adopted from other hypertension studies and international organizations, with modifications made at the local level [32–34]. Practical aspects were focused. For example, a message of adding one fist-sized fruit and four taels (unit of measurement used in China) of vegetable in each lunch, and dinner was delivered. Making healthy choice when eating outside was also included in the pool of text messages.

One face-to-face group health education was conducted in groups of 4–8 after baseline data collection and group allocation. This session was administered by the first author, a registered nurse, who did not participate in data collection. The session lasted for 45 min, and a leaflet was given to the participants at the end. Weekly one-way text messages were sent to the participants' mobile phones for 12 weeks. Each message covered a behavior taxonomy, and each participant received the standardized content.

Control group

The differences and similarities of interventions between intervention and control groups were summarized in supplementary material, Table S2. In brief, the participants in the control group received a face-to-face group health education session, administered by an independent community nurse. The content was directly adopted from the government (usual care) in the form of lecture with no interactive element. After routine health education, a leaflet from the government was given to the participants. Text messages related to general health practices, such as washing of the hands after coughing or sneezing, were delivered to the participants every week for 12 weeks.

Study outcomes

The study outcomes included BP (primary outcome), pulse pressure, self-efficacy in hypertension management, adherence to hypertension management, and process evaluation.

BP, including SBP and DBP, was measured using a validated upper-arm BP monitor manufactured by Rossmax (model AU941) [35]. A standardized BP measurement procedure was adopted from the Chinese Guidelines for Prevention and Treatment of Hypertension [7]. In brief, the research assistant (RA) placed an appropriately sized cuff on the participant's upper arm at the heart level. Two BP readings (1-min apart) were obtained from the same arm. SBP and DBP were recorded as the means of two BP readings.

Pulse pressure, which is the difference between SBP and DBP, was the secondary outcome in this study.

Self-efficacy was measured on a 10-point Likert scale, namely, Self-Efficacy for Managing Chronic Disease (SEMCD). The SEMCD comprises six items with a higher score indicating a higher level of self-efficacy [36]. The Chinese version of SEMCD showed good internal consistency (0.88–0.98) [37,38] and was feasible for assessing Chinese patients with hypertension [37] and Chinese older adults [39].

The Treatment Adherence Questionnaire for Patients with Hypertension (TAQPH) was used to measure adherence to hypertension management. TAQPH comprises 28 items measured on a 4-point Likert scale [40]. The total score ranged from 28 to 112, and a higher score indicates a higher level of adherence behavior. TAQPH, which was originally written in Chinese, has good reliability (internal consistency = 0.86; test-retest reliability = 0.82) and construct validity (goodness of fit index = 0.99; root mean squared error of approximation = 0.038) and can explain 62.5% of variance in adherence to hypertension management among patients [40].

The process evaluation included assessment of the recruitment rate, retention rate, and participants' satisfaction with the program. A numerical program satisfaction rating scale was adopted from Ashe et al [41] and van Berckel et al [42]. This was an 11-point scale and was scored from 0 to 10, with 0 indicating not satisfied and 10 indicating highly satisfied. The 11-point scale was also used to rate the usefulness of the program components (health education, leaflet, and text messaging) for hypertension management.

Demographic data (e.g., age, gender, and education level), family history, and medical consultations were collected at baseline.

Ethical consideration

This study was approved by the Human Subjects Ethics Subcommittee of the Hong Kong Polytechnic University before the baseline data collection (Approval no. HSEARS20200821002-02).

Data collection

Trained RAs explained the study details to the potential participants and assessed their eligibility. Next, written informed consent was obtained from the participants, and RAs collected the participants' baseline data before the start of the intervention. The interventions were provided according to the randomization assignment and protocol. The same set of study outcomes was obtained at the follow-ups after the health education session. In summary, data collection was completed at three time points by RAs who were blinded to the group allocation: baseline (T0), week 8 (T1), and week 12 (T2).

Data analysis

SPSS for Windows (version 26; IBM) was used for data analysis. Baseline characteristics were examined using the Chi-square test or Fisher's exact test for categorical variables. The Shapiro-Wilk test and Levene's test were used to examine the normality and homogeneity of the continuous data. An independent t-test was used if the assumptions were not violated; otherwise, Mann–Whitney U test was used. The generalized estimating equation (GEE) based on the intention-to-treat principle was used to estimate the effects of the educational program on SBP, DBP, pulse pressure, self-efficacy, and adherence to hypertension management between two groups at T0, T1, and T2. Two-tailed tests were used for all data analyses, and significance was set at $P < .05$. The last observation carried forward was used to handle the missing data. Effect size was used to evaluate the clinical importance of all continuous variables and was determined as follows: small = 0.2; moderate = 0.5; and large = 0.8 [43].

Results

The study was conducted between February and December 2021. Figure 1 presents a diagram of the flow of participants through the trial. A total of 150 individuals were screened for eligibility; 18 individuals denied participation before screening, and 51 individuals did not meet the eligibility criteria. Eighty-one

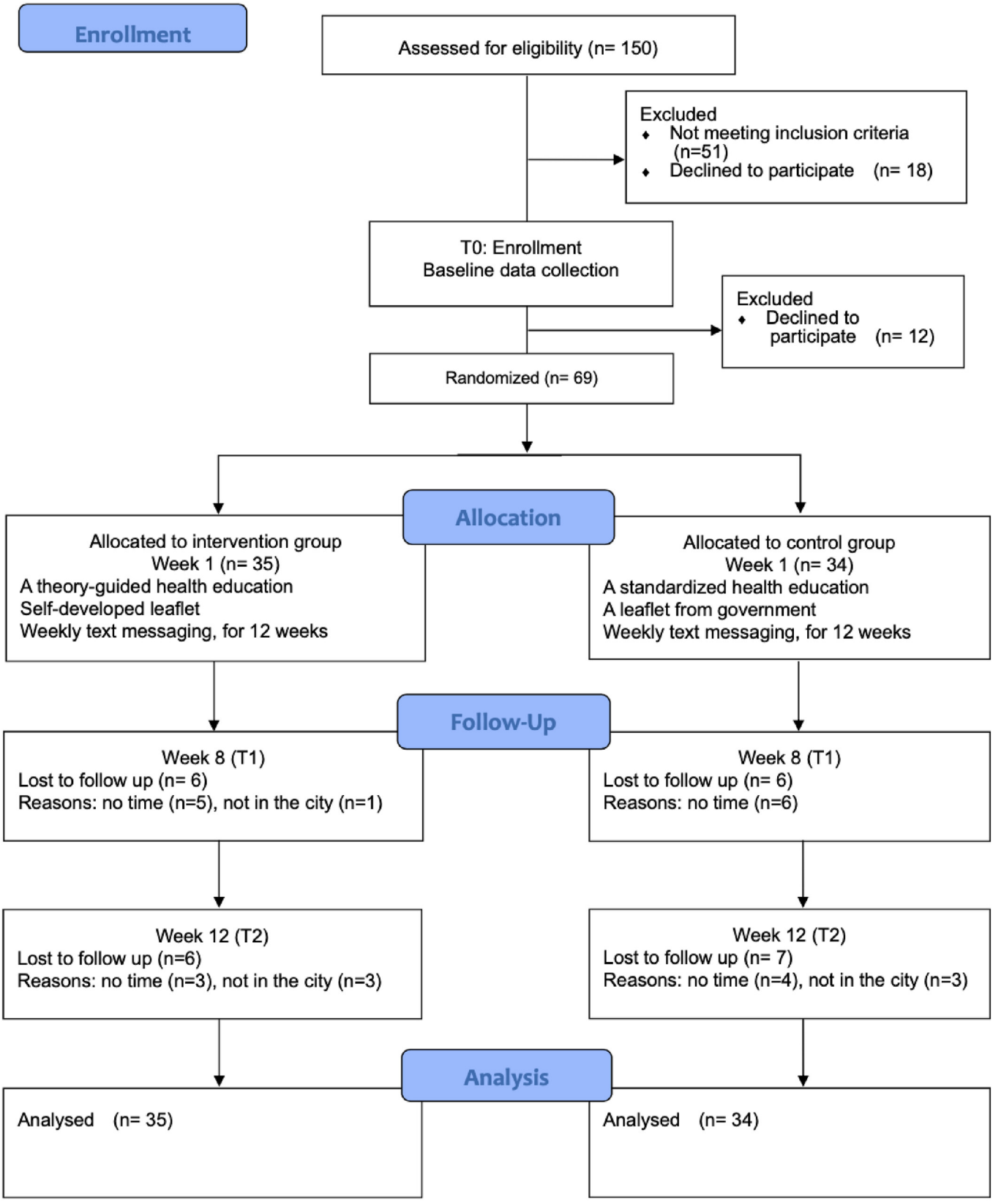

Figure 1. Flow of Participants through the Trial.

Table 1 *Participant Characteristics and Outcome Variables at Baseline.*

Variables	Intervention ($n = 35$), n (%)	Control ($n = 34$), n (%)	Chi-square (df)/Mann-Whitney /t-test	p
Age (yr),[a] mean (SD)	66.82 (10.5)	67.97 (9.5)	602.0	.937
Gender			2.02 (1)	.155
Men	7 (20.0)	12 (35.3)		
Women	28 (80.0)	22 (64.7)		
Marital status			0.29 (1)	.590
Married	27 (77.1)	28 (82.4)		
Others	8 (22.9)	6 (17.6)		
Work status			0.004 (1)	.947
Working	8 (22.9)	8 (23.5)		
Unemployed or retried	27 (77.1)	26 (76.5)		
Education level			0.06 (3)	.995
No formal education	7 (20.0)	6 (17.7)		
Primary school	8 (22.8)	8 (23.5)		
Junior secondary	10 (28.6)	10 (29.4)		
Senior secondary and above	10 (28.6)	10 (29.4)		
Family history of hypertension			0.46 (2)	.792
Yes	21 (60.0)	18 (52.9)		
No	7 (20.0)	9 (26.5)		
Unclear	7 (20.0)	7 (20.6)		
Diagnosed with hypertension			2.08 (3)	.554
<4 yr	7 (20.0)	12 (35.3)		
5–9 yr	8 (22.9)	6 (17.6)		
10–14 yr	7 (20.0)	5 (14.7)		
≥15 yr	13 (37.1)	11 (32.4)		
Kind of medications used every day,[a] mean (SD)	3.00 (1.86)	3.05 (1.80)	612.0	.839
Change of prescription over the last 3 months[b]				.477
Yes	3 (8.6)	5 (14.7)		
No	32 (91.4)	29 (85.3)		
Outcome variables, mean (SD)				
Systolic blood pressure[a]	146.64 (9.99)	145.38 (9.20)	549.50	.588
Diastolic blood pressure	78.75 (9.07)	82.17 (10.73)	*1.43*	.157
Pulse pressure	67.88 (12.12)	63.20 (10.68)	*−1.69*	.093
SEMCD (range 6–60)	43.65 (8.16)	43.32 (9.25)	*−0.15*	.874
TAQPH (range 28 −112)[a]	92.94 (10.28)	91.94 (10.25)	566.50	.736

Note. SD = standard deviation; SEMCD = self-efficacy for managing chronic disease; TAQPH = treatment adherence questionnaire for patients with hypertension. Italicized values were the results of t test analysis.
[a] Mann-Whitney U test.
[b] Fisher's exact test.

individuals met the eligibility criteria, but 12 of those denied participation after screening. Finally, 69 individuals were included and randomly assigned to either the intervention group ($n = 35$) or the control group ($n = 34$). Both groups included participants from Macau and Shenzhen. No significant difference was noted in the demographic data of the individuals who completed the study and those who dropped out of the study. The recruitment rate was 85.2% (69/81).

Participant characteristics and baseline outcomes

The characteristics of the participants in the intervention and control groups are listed in Table 1. The mean participant age was 67.39 ± 9.98 years. The majority of the participants were women (72.5%) and married (79.7%). Most of the participants were unemployed or retired (76.8%). Most of the participants (81.2%) had completed primary school or higher. Appropriately 56.5% of the participants had a family history of hypertension. Nearly 52.2% of the participants had hypertension for more than 10 years. No statistically significant difference in any of these parameters was noted between the two groups.

For all outcome variables at baseline (T0), no statistical significance was noted between both groups (Table 1). The mean SBP of the participants in both groups was similar. Although the mean DBP was higher in the control group than in the intervention group, the difference was not statistically significant. The mean pulse pressure in the intervention and control groups was 67.88 mmHg and 63.20 mmHg, respectively. The mean SEMCD and TAQPH scores were similar in both groups.

Effect of the educational program on the study outcomes

The means and standard deviations of the outcomes and effect sizes were summarized in Table 2. Compared with that in the control group, the educational program in the intervention group produced a small effect size to improve self-efficacy (effect size = 0.230), a small-to-moderate effect size to reduce SBP (effect size = −0.450), a moderate effect size to reduce pulse pressure (effect size = −0.667), and a very small effect size on the remaining outcomes.

Figure 2 shows the changes of all outcomes across T0, T1, and T2. The SBP and pulse pressure in the intervention group reduced the most at T1 but returned at T2, like a V-shape (Figure 2A and C). The DBP in the intervention group was decreased gradually (Figure 2B), whereas an increasing trend was noted in the change of self-efficacy at T1 and T2 (Figure 2D). The overall treatment adherence in the intervention group was merely unchanged (Figure 2E).

Table 2 *Results of Study Outcomes at Follow-ups.*

Variables, mean (SD)	Intervention ($n = 35$)	Control ($n = 34$)	Effect size
Systolic blood pressure			
Week 8	132.65 (11.29)	135.78 (15.63)	−0.20
Week 12	136.00 (14.25)	140.31 (18.70)	−0.45
Diastolic blood pressure			
Week 8	76.75 (9.01)	76.83 (11.72)	0.59
Week 12	76.03 (9.63)	77.44 (9.56)	0.08
Pulse pressure			
Week 8	55.67 (11.83)	58.94 (13.98)	−0.79
Week 12	60.00 (14.48)	62.87 (15.45)	−0.66
SEMCD			
Week 8	43.86 (7.89)	44.14 (11.19)	−0.07
Week 12	45.65 (7.45)	43.66 (7.88)	0.23
TAQPH			
Week 8	92.82 (9.61)	92.32 (9.43)	−0.07
Week 12	92.96 (8.74)	91.14 (11.51)	0.04

Note. SD = standard deviation; SEMCD = self-efficacy for managing chronic disease; TAQPH = treatment adherence questionnaire for patients with hypertension.

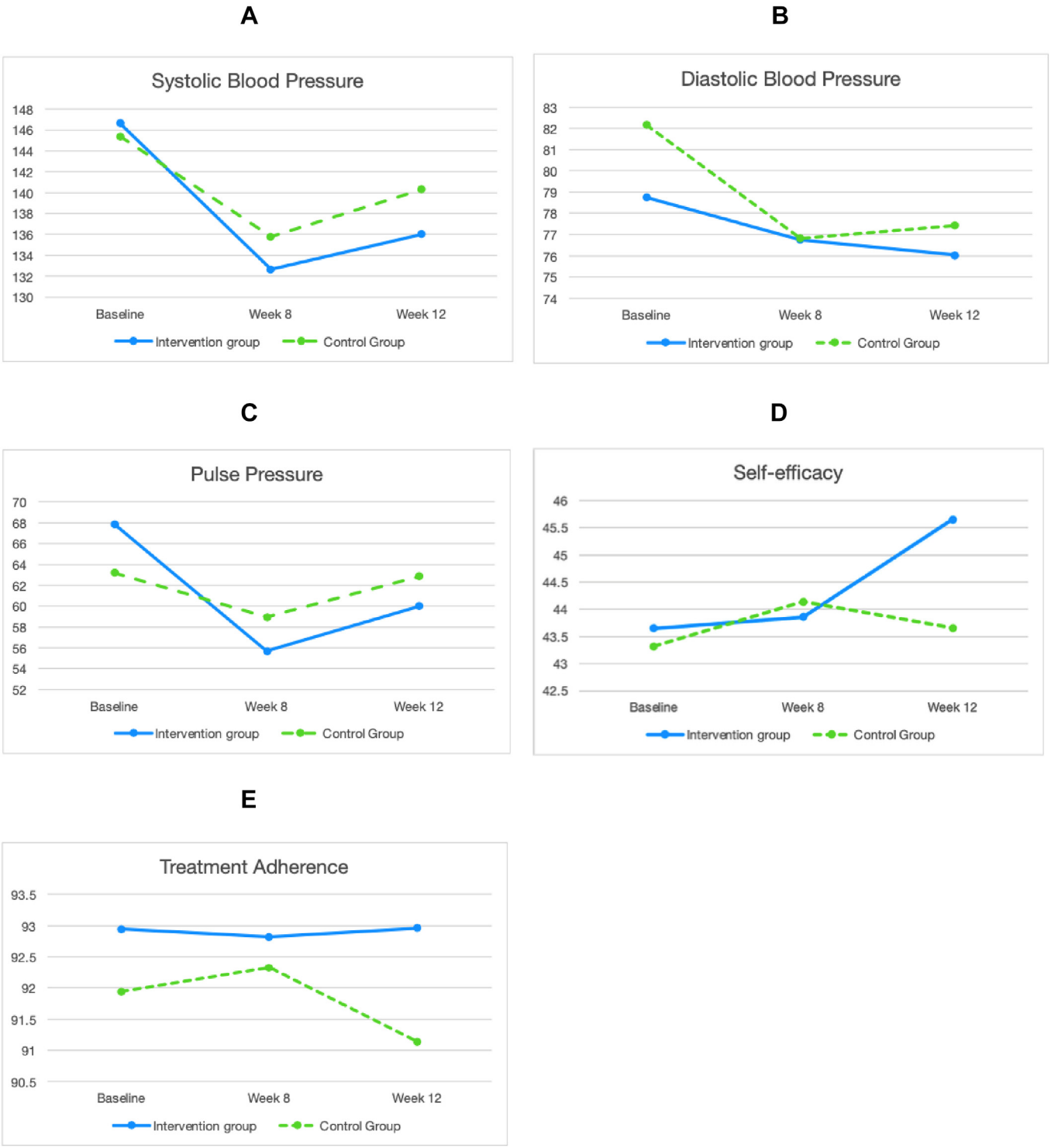

Figure 2. The Changes of Outcome Variables at Week 8 (T1) and Week 12 (T2): (A) systolic blood pressure, (B) diastolic blood pressure, (C) pulse pressure, (D) self-efficacy, and (E) treatment adherence.

The GEE results of the outcomes across T0, T1, and T2 between the two groups are presented in Table 3. At T1, the reduction of DBP in the control group was significantly greater than that in the intervention group ($\beta = 4.826$, $p = .017$); however, at T2, the reduction of DBP in both the groups was not statistically significant. The GEE results revealed that the reduction in pulse pressure was greater in the intervention group than in the control group at both T1 and T2 and that the differences were statistically significant (T1: $\beta = -8.175$, $p = .006$; T2: $\beta = -8.203$, $p = .007$). The GEE results of the remaining outcomes were not statistically significant.

Process evaluation

The feasibility of the program was evaluated based on the recruitment rate (85.2%, 69/81) and the overall retention rate at T2 (81.2%, 56/69; Figure 1). Program acceptability was shown in

Table 3 *Results of the Generalized Estimating Equation Analysis.*

Variables	Beta	95% Confidence interval		*p*
		Upper	Lower	
Systolic blood pressure				
Group	1.26	−3.20	5.72	.580
T1	−10.19	−15.62	−4.76	<.001*
T2	−3.57	−9.10	1.95	.205
Group*T1	−3.41	−10.68	3.86	.358
Group*T2	−7.13	−15.26	1.00	.086
Diastolic blood pressure				
Group	−3.42	−8.05	1.21	.148
T1	−5.70	−8.85	−2.55	<.001*
T2	−3.01	−6.06	0.03	.052
Group*T1	4.82	0.87	8.78	.017*
Group*T2	0.34	−3.86	4.54	.872
Pulse pressure				
Group	4.68	−0.63	9.99	.084
T1	−4.69	−8.54	−0.84	.017*
T2	0.17	−3.89	4.34	.934
Group*T1	−8.17	−13.96	−2.38	.006*
Group*T2	−8.20	−14.20	−2.20	.007*
SEMCD				
Group	0.33	−3.72	4.39	.872
T1	0.31	−2.99	3.61	.856
T2	−0.15	−3.49	3.18	.928
Group*T1	0.55	−4.15	5.25	.818
Group*T2	2.61	−2.02	7.24	.269
TAQPH				
Group	1.00	−3.77	5.77	.681
T1	−0.08	−3.61	3.43	.961
T2	−1.01	−5.89	3.87	.685
Group*T1	0.29	−4.42	4.99	.904
Group*T2	0.77	−4.90	6.45	.789

Note. SEMCD = self-efficacy for managing chronic disease; TAQPH = treatment adherence questionnaire for patients with hypertension.
*$p < .05$.

supplementary material, Table S3. The overall satisfaction with the program was 8.79 of 10. Regarding the content of the program for hypertension management, the participants agreed that the content of the health education, leaflet, and text message was useful and sufficient. No adverse event was reported.

Discussion

This study aimed to test the preliminary effects of a theory-guided educational program on hypertension management. No significant differences were noted in the baseline characteristics and outcomes between the intervention and control groups. The educational program had a small-to-moderate effect on the reduction of the participants' SBP and pulse pressure and the improvement of self-efficacy at T2. Compared with the baseline, the SBP, DBP, and pulse pressure were decreased at T2 after the educational program; the self-efficacy was increased, and the treatment adherence was merely unchanged. The results of the GEE analysis indicated that the reduction of pulse pressure in the intervention group was statistically significant at T1 and T2. The recruitment and retention rates were good, indicating that the educational program was feasible. The good satisfaction and content scores indicated the program was highly appreciated.

The reduction of SBP and pulse pressure and improvement of self-efficacy in this study could be related to the design of the educational program. The demonstrations and practices in the health education allowed the participants to have a mastery experience, which could enhance their self-efficacy [44]. The discussion could help them overcome difficulties in their daily hypertension management, whereas they could share their experience and learn from peers. A systematic review found that the peer support interventions could have a small effect to reduce SBP but not DBP [45]. Furthermore, the QR codes on the leaflet and the practical information of text messages could reinforce the practice to integrate hypertension management into daily life.

Although the reduction in SBP was not statistically significant, the reduction noted upon group health education was similar to that noted through individual health education. In the RCTs conducted by Wan et al [46] and Jahan et al [47], individual health education with text messaging was administered to the participants in the intervention group; the net SBP reduction in the intervention group at week 12 was 9.86 mmHg and 9.00 mmHg, respectively. As evident from the net SBP reduction at week 12 in the present study (146.64 − 136.00 = 10.64 mmHg), group health education with interactive elements in this study resulted in a better SBP reduction than individual health education. Furthermore, group health education was cost-effective because one interventionist could attend to multiple participants per session. The nonsignificant SBP reduction results might be attributable to the small sample size of the present study. The nonsignificant DBP reduction results might be attributable to the low baseline DBP value among the participants in the intervention group had been in the optimal level of DBP [27,28].

Pulse pressure also was evaluated in recent hypertension studies. Nolan et al [48] developed a web-based educational program comprising videos, online reading material, and monitoring forms; they reported that the program could significantly decrease pulse pressure at 16 weeks. Similarly, Chen et al [49] developed and implemented a web-based educational program comprising videos and monitoring forms and noted a significant decrease in pulse pressure at 12 weeks. However, compared with the present study, the aforementioned studies required the participants to have a greater level of digital competence. The present study was comparatively simple as the participants were only required to attend one group health education session and read a message every week. Despite this, the educational program in this study significantly reduced the pulse pressure of patients with hypertension to an optimal range [50].

In this study, the participants' self-efficacy showed a positive improvement after the educational program, although the change was not statistically significant. Although Chen et al [49] noted a significant improvement in the participants' self-efficacy at 12 weeks using SEMCD, it can be argued that the baseline self-efficacy of their participants (33.66 ± 9.11) was lower than that of the participants in this study (43.65 ± 8.16). Moreover, the old age of the participants in this study might be responsible for the nonsignificant changes in the self-efficacy because behavioral changes were found to have a small effect on improving self-efficacy among older adults [51]. Finally, the TAQPH score in this study was high. A ceiling effect was suggested, which might limit the effect of the educational program on overall treatment adherence and cause a nonsignificant result in GEE analysis [52].

Limitations

This study has some limitations. The results should be interpreted cautiously because of the small sample size. It remains unclear whether the program would be effective for uninterested, excluded, or younger people with hypertension. The participants may have recognized their group allocations based on the text message content. Moreover, participants from different groups visiting the same community center may have communicated with each other. However, such communication was limited because the centers had reduced their activities during the COVID-19 pandemic, and the health education sessions and follow-ups for the

intervention and control groups were scheduled on different dates to minimize subject contamination. Furthermore, both SEMCD and TAQPH were administrated by trained RAs and self-reported by the participants; hence, the high scores could be related to the social desirability bias [52].

Implications

The results of this pilot RCT, that is, the effect sizes and process evaluation, provide valuable information for further research. The construct-matched interventions may be applicable to other hypertension studies guided by the Health Promotion Model. A reinforcement educational intervention, such as health education session or phone call, at week 8 is recommended and should be included in future studies. A website link could be included in the text messages to enable the patients to watch videos related to hypertension management [53]. Furthermore, the follow-up duration should be increased to assess the sustainable effects of the educational program. Given the significant reduction in pulse pressure noted in this study, future studies should examine whether the educational program is suitable for people at risk of cardiovascular diseases. However, the overall adherence to hypertension management was unchanged. Record of exercise and diet might help participant monitor their lifestyle behaviors. Other objective measures can be used in future studies; for example, daily step counts can be used to monitor whether the patient adheres to the recommended activity level. Blood lipid profile and glucose might be the indicators of healthy diet.

This study also has implications in clinical practice. Because the educational program is feasible and acceptable in the community setting, it can be added to current hypertension management practices at the community level. For example, after health education, weekly text messages can be delivered to patients with hypertension to increase their engagement with hypertension management practices. The program is also fit for communities with limited personnel, training, and economic resources. The construct-matched interventions and methods shown in Table S1 listed out the essentials in applications of health promotion model for patients with hypertension.

In brief, the interactive elements in the health education and the use of technology, that is, QR code and text messages, showed a favorable effect to improve the health of patients with hypertension in the pilot study. The results of process evaluation showed that the program was highly appreciated, and the retention rate and effect size of outcome variables provided accurate sample size calculation for future study.

Conclusion

The educational program helped community-dwelling patients with hypertension improve their clinical outcomes and self-efficacy. This program can be incorporated into current hypertension management practice. The good retention rate and satisfaction rates indicate that it may be feasible to test the effectiveness of the program in a future larger-scale study.

Author contribution

Contributorship: HLT contributed to conceptualization, study design, data collection, data analysis, and writing of the article. EMLW and KC contributed to conceptualization, study design and critically revised the article. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Conflict of interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.06.001.

References

1. World Health Organization. Hypertension: World Health Organization. 2021 [cited 18 July 2022]. Available from: https://www.who.int/news-room/fact-sheets/detail/hypertension
2. Burnier M, Egan BM. Adherence in hypertension. Circ Res. 2019;124(7):1124–40. https://doi.org/10.1161/circresaha.118.313220
3. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223–49. https://doi.org/10.1016/s0140-6736(20)30752-2
4. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334–57. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026
5. Williams B, Mancia G, Spiering W, Agabiti RE, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021–104. https://doi.org/10.1093/eurheartj/ehy339
6. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71(19):e127–248. https://doi.org/10.1016/j.jacc.2017.11.006
7. Liu LS, Wu ZS, Wang JG, Wang W, Bao YJ, Cai J, et al. 2018 Chinese guidelines for prevention and treatment of hypertension-a report of the revision committee of Chinese guidelines for prevention and treatment of hypertension. J Geriatr Cardiol. 2019;16(3):182–241. http://www.jgc301.com/en/article/doi/10.11909/j.issn.1671-5411.2019.03.014
8. NCD Risk Factor Collaboration. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10304):957–80. https://doi.org/10.1016/s0140-6736(16)31919-5
9. Macau Health Bureau. Macao Health Survey 2016 [Chinese]. 2017 [cited 18 July 2022]. Available from: https://www.ssm.gov.mo/docs/13268/13268_0b02e64f509d4d5d8549486918157a2e_000.pdf
10. Carvalho AS, Santos P. Medication adherence in patients with arterial hypertension: the relationship with healthcare systems' organizational factors [review]. Patient Prefer Adherence. 2019;13:1761–74. https://doi.org/10.2147/PPA.S216091
11. Andualem A, Gelaye H, Damtie Y. Adherence to lifestyle modifications and associated factors among adult hypertensive patients attending chronic follow-up units of Dessie Referral Hospital, North East Ethiopia, 2020. Integr Blood Press Control. 2020;13:145–56. https://doi.org/10.2147/IBPC.S275575
12. Pan J, Wu L, Wang H, Lei T, Hu B, Xue X, et al. Determinants of hypertension treatment adherence among a Chinese population using the therapeutic adherence scale for hypertensive patients. Medicine (Baltim). 2019;98(27):e16116. https://doi.org/10.1097/MD.0000000000016116
13. Fang J, Moore L, Loustalot F, Yang Q, Ayala C. Reporting of adherence to healthy lifestyle behaviors among hypertensive adults in the 50 states and the District of Columbia, 2013. J Am Soc Hypertens. 2016;10(3):252–62.e3. https://doi.org/10.1016/j.jash.2016.01.008
14. Tam HL, Chair SY, Leung ISH, Leung LYL, Chan ASW. US adults practicing healthy lifestyles before and during COVID-19: comparative analysis of national surveys. JMIR Public Health Surveill. 2023;9:e45697. https://doi.org/10.2196/45697
15. Tam HL, Wong EML, Cheung K. Effectiveness of educational interventions on adherence to lifestyle modifications among hypertensive patients: an integrative review. Int J Environ Res Public Health. 2020;17(7):2513. https://doi.org/10.3390/ijerph17072513

16. Morrissey EC, Durand H, Nieuwlaat R, Navarro T, Haynes RB, Walsh JC, et al. Effectiveness and content analysis of interventions to enhance medication adherence and blood pressure control in hypertension: a systematic review and meta-analysis. Psychol Health. 2017;32(10):1195–232. https://doi.org/10.1080/08870446.2016.1273356
17. Xu R, Xie X, Li S, Chen X, Wang S, Hu C, et al. Interventions to improve medication adherence among Chinese patients with hypertension: a systematic review and meta-analysis of randomized controlled trails. Int J Pharm Pract. 2018;26(4):291–301. https://doi.org/10.1111/ijpp.12452
18. Foroumandi E, Kheirouri S, Alizadeh M. The potency of education programs for management of blood pressure through increasing self-efficacy of hypertensive patients: a systematic review and meta-analysis. Patient Educ Couns. 2020;103(3):451–61. https://doi.org/10.1016/j.pec.2019.09.018
19. Tam HL, Leung LYL, Wong EML, Cheung K, Chan ASW. Integration of text messaging interventions into hypertension management among older adults: a systematic review and meta-analysis. Worldviews Evid Based Nurs. 2022;19(1):16–27. https://doi.org/10.1111/wvn.12549
20. Conn VS, Ruppar TM. Medication adherence outcomes of 771 intervention trials: systematic review and meta-analysis. Prev Med. 2017;99:269–76. https://doi.org/10.1016/j.ypmed.2017.03.008
21. Conn VS, Ruppar TM, Chase JA, Enriquez M, Cooper PS. Interventions to improve medication adherence in hypertensive patients: systematic review and meta-analysis. Curr Hypertens Rep. 2015;17(12):94. https://doi.org/10.1007/s11906-015-0606-5
22. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061. https://doi.org/10.1136/bmj.n2061
23. Said MA, Eppinga RN, Lipsic E, Verweij N, van der Harst P. Relationship of arterial stiffness index and pulse pressure with cardiovascular disease and mortality. J Am Heart Assoc. 2018;7(2):e007621. https://doi.org/10.1161/JAHA.117.007621
24. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med. 2010;8(1):18. https://doi.org/10.1186/1741-7015-8-18
25. Song F, Cho MS. Geography of food consumption patterns between South and North China. Foods. 2017;6(5):34. https://doi.org/10.3390/foods6050034
26. Hertzog MA. Considerations in determining sample size for pilot studies. Res Nurs Health. 2008;31(2):180–91. https://doi.org/10.1002/nur.20247
27. Sakima A, Satonaka H, Nishida N, Yatsu K, Arima H. Optimal blood pressure targets for patients with hypertension: a systematic review and meta-analysis. Hypertens Res. 2019;42(4):483–95. https://doi.org/10.1038/s41440-018-0123-4
28. Flint AC, Conell C, Ren X, Banki NM, Chan SL, Rao VA, et al. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. N Engl J Med. 2019;381(3):243–51. https://doi.org/10.1056/NEJMoa1803180
29. Tam E, Gandesbery BT, Young L, Borson S, Gorodeski EZ. Graphical instructions for administration and scoring the Mini-Cog: results of a randomized clinical trial. J Am Geriatr Soc. 2018;66(5):987–91. https://doi.org/10.1111/jgs.15313
30. Pender N, Murdaugh C, Parsons MA. Health promotion in nursing practice. 7th ed. Upper Saddle River: Pearson Education; 2015.
31. World Health Organization. Noncommunicable disease education manual for primary health care professionals and patients. 2017 [cited 14 July 2022]. Available from: https://apps.who.int/iris/handle/10665/254746
32. Buis LR, Artinian NT, Schwiebert L, Yarandi H, Levy PD. Text messaging to improve hypertension medication adherence in African Americans: BPMED intervention development and study protocol. JMIR Res Protoc. 2015;4(1). https://doi.org/10.2196/resprot.4040. e1.
33. Varleta P, Acevedo M, Akel C, Salinas C, Navarrete C, Garcia A, et al. Mobile phone text messaging improves antihypertensive drug adherence in the community. J Clin Hypertens. 2017;19(12):1276–84. https://doi.org/10.1111/jch.13098
34. World Health Organization, International Telecommunications Union. Be Healthy, Be Mobile: a handbook on how to implement mHypertension 2020 [cited 14 December 2021]. Available from: https://www.who.int/publications/i/item/be-healthy-be-mobile-a-handbook-on-how-to-implement-mhypertension
35. Picone DS, Padwal R, Campbell NRC, Boutouyrie P, Brady TM, Olsen MH, et al. How to check whether a blood pressure monitor has been properly validated for accuracy. J Clin Hypertens. 2020;22(12):2167–74. https://doi.org/10.1111/jch.14065
36. Lorig KR, Sobel DS, Ritter PL, Laurent D, Hobbs M. Effect of a self-management program on patients with chronic disease. Eff Clin Pract. 2001;4(6):256–62.
37. Siu AM, Chan CC, Poon PK, Chui DY, Chan SC. Evaluation of the chronic disease self-management program in a Chinese population. Patient Educ Couns. 2007;65(1):42–50. https://doi.org/10.1016/j.pec.2006.04.013
38. Hu H, Li G, Arao T. Validation of a Chinese version of the Self-Efficacy for Managing Chronic Disease 6-Item Scale in patients with hypertension in primary care. ISRN Public Health. 2013;2013:298986. https://doi.org/10.1155/2013/298986
39. Chow SKY, Wong FKY. The reliability and validity of the Chinese version of the Short-form Chronic Disease Self-Efficacy Scales for older adults. J Clin Nurs. 2014;23(7-8):1095–104. https://doi.org/10.1111/jocn.12298
40. Ma C, Chen S, You L, Luo Z, Xing C. Development and psychometric evaluation of the Treatment Adherence Questionnaire for patients with hypertension. J Adv Nurs. 2012;68(6):1402–13. https://doi.org/10.1111/j.1365-2648.2011.05835.x
41. Ashe MC, Winters M, Hoppmann CA, Dawes MG, Gardiner PA, Giangregorio LM, et al. "Not just another walking program": Everyday Activity Supports You (EASY) model—a randomized pilot study for a parallel randomized controlled trial. Pilot Feasibility Stud. 2015;1:4. https://doi.org/10.1186/2055-5784-1-4
42. van Berckel MM, Bosma NH, Hageman MG, Ring D, Vranceanu AM. The correlation between a numerical rating scale of patient satisfaction with current management of an upper extremity disorder and a general measure of satisfaction with the medical visit. Hand (N Y). 2017;12(2):202–6. https://doi.org/10.1177/1558944716662019
43. Faraone SV. Interpreting estimates of treatment effects. P T. 2008;33(12):700–11.
44. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977;84(2):191–251.
45. Patil SJ, Ruppar T, Koopman RJ, Lindbloom EJ, Elliott SG, Mehr DR, et al. Effect of peer support interventions on cardiovascular disease risk factors in adults with diabetes: a systematic review and meta-analysis. BMC Public Health. 2018;18:398. https://doi.org/10.1186/s12889-018-5326-8
46. Wan LH, Zhang XP, You LM, Ruan HF, Chen SX. The efficacy of a comprehensive reminder system to improve health behaviors and blood pressure control in hypertensive ischemic stroke patients: a randomized controlled trial. J Cardiovasc Nurs. 2018;33(6):509–17. https://doi.org/10.1097/JCN.0000000000000496
47. Jahan Y, Rahman MM, Faruque ASG, Chisti MJ, Kazawa K, Matsuyama R, et al. Awareness development and usage of mobile health technology among individuals with hypertension in a rural community of Bangladesh: randomized controlled trial. J Med Internet Res. 2020;22(12):e19137. https://doi.org/10.2196/19137
48. Nolan RP, Feldman R, Dawes M, Kaczorowski J, Lynn H, Barr SI, et al. Randomized controlled trial of E-counseling for hypertension: REACH. Circ Cardiovasc Qual Outcomes. 2018;11(7):e004420. https://doi.org/10.1161/CIRCOUTCOMES.117.004420
49. Chen TY, Kao CW, Cheng SM, Chang YC. A web-based self-care program to promote healthy lifestyles and control blood pressure in patients with primary hypertension: a randomized controlled trial. J Nurs Scholarsh. 2022;54(6):678–91. https://doi.org/10.1111/jnu.12792
50. Pareek M, Vaduganathan M, Biering-Sorensen T, Byrne C, Qamar A, Almarzooq Z, et al. Pulse pressure, cardiovascular events, and intensive blood-pressure lowering in the Systolic Blood Pressure Intervention Trial (SPRINT). Am J Med. 2019;132(6):733–9. https://doi.org/10.1016/j.amjmed.2019.01.001
51. French DP, Olander EK, Chisholm A, Mc Sharry J. Which behaviour change techniques are most effective at increasing older adults' self-efficacy and physical activity behaviour? A systematic review. Ann Behav Med. 2014;48(2):225–34. https://doi.org/10.1007/s12160-014-9593-z
52. Gerrish K, Lacey A. The research process in nursing. 6th ed. Chichester, West Sussex: Wiley-Blackwell; 2010.
53. Nau T, Owen A, Mazza D, Smith BJ. Engaging primary care providers in a mobile health strategy to support lifestyle change and blood pressure management. Digit Health. 2021;7:20552076211066746. https://doi.org/10.1177/20552076211066746

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Research Article

Impact of Nursing Interventions on Hospital Readmissions in Patients With Pulmonary Tuberculosis: A Quasi-Experimental Study

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SUMMARY

Purpose: Our study aimed to evaluate the effectiveness of the nursing care program on the incidence and rate of 28-day hospital readmissions among pulmonary tuberculosis (TB) patients.
Methods: We conducted a quasi-experimental study using a historical control (usual care) group. Patients diagnosed with pulmonary TB who received nursing interventions between January 28, 2021, and May 31, 2021, were categorized as an intervention group, whereas historical controls were selected from January 1, 2020, to December 31, 2020. The primary outcomes were the incidence and rates of hospital readmissions within 28 days due to TB-related complications. The secondary outcome was the change in knowledge and self-care behavior scores at discharge and 28 days postdischarge. Cox models were used to assess the intervention's impact on the incidence of hospital readmission. Rates of readmission were compared by the Poisson model. Both Cox and Poisson models were adjusted for age, sex, sputum smears at diagnosis, serum albumin level, and diabetes mellitus at baseline.
Results: Among 104 pulmonary TB patients included in the analysis (68 were in a historical control group and 36 were in an intervention group), 20 patients were readmitted due to TB-related complications. We found that our nursing care program resulted in a significant reduction in the incidence (adjusted hazard ratio was 0.16 [95% CI 0.03, 0.87]) and the rate of hospital readmissions (adjusted incidence rate ratio was 0.22 [95% CI 0.06, 0.85]). Furthermore, nursing interventions significantly improved knowledge and self-care behavior scores with significant score retention at 28 days postdischarge.
Conclusions: The nursing care program can significantly decrease the incidence and rate of 28-day hospital readmission and improve knowledge and self-care behavior scores in pulmonary TB patients.

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Introduction

Pulmonary tuberculosis (TB) is a major health problem worldwide, especially in developing countries [1,2]. According to the World Health Organization (WHO), TB affects more than 10 million people so far, leading to 1.5 million deaths globally [1]. Thailand is among the countries where the TB burden is stretched. In 2021, the estimated incidence of TB in Thailand was 42.6 per 100,000 population [3].

Although TB is a curable disease, treatment failure is still challenging as patients need to strictly adhere to a long treatment duration (i.e., at least 6 months of a standard regimen). Therefore, to improve the treatment success, multimodalities of patient care from multidisciplinary healthcare professionals are required. These modalities include (1) Directly Observed Therapy (DOT) program, (2) home healthcare and nutritional supporting program, (3) pharmacist monitoring program, and (4) a nursing care program [4–9].

The nursing care program aims to enhance patients' and caregivers' knowledge and improve treatment adherence. The program also proactively monitors patients' responses and treatment-related adverse events. The previous study showed that nurses' discharge planning programs could improve TB patients' knowledge and self-care behavior scores [10]. However, it is unclear whether these improved scores could be maintained during the next follow-up visit. Moreover, a previous randomized controlled trial had shown that empowering patients through nursing care programs can decrease the readmission rate in heart failure patients [11]. Nevertheless, no study directly examines the impact of nursing intervention on TB outcomes.

We conducted a quasi-experimental study using a historical control to investigate the effectiveness of a nursing care program on the incidence and rates (i.e., frequency within a specific period) of hospital readmissions within 28 days after hospital discharge among pulmonary TB patients. We also examined the change and retention of TB patients' knowledge and self-care behavior scores after receiving nursing interventions.

Methods

The report of this study followed the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) statement (Supplementary Table S1) [12].

Study design

This study implemented a quasi-experimental design using a historical control group to assess the effectiveness of a recently initiated nursing care program at Phrae hospital, Thailand. All pulmonary TB patients diagnosed and admitted to the hospital from January 28, 2021, onward would receive a nursing care program during hospitalization, upon hospital discharge, and at 28 days postdischarge. These patients were then categorized as an intervention group and were followed for a month later. The data of a historical control group was collected from pulmonary TB patients who were initially diagnosed and admitted from January 1, 2020, to December 31, 2020 (the period before the nursing program was initiated). We only considered the first readmission episode after the TB diagnosis for individuals with several hospital admissions.

Setting and participants

This research was conducted on a general medicine ward at Phrae hospital, a 500-bed secondary hospital in northern Thailand. Eligible participants were inpatient pulmonary TB patients diagnosed by physicians using WHO's criteria [13], based on clinical manifestations, chest X-ray, and laboratory values. We excluded patients who were (1) aged $\leq$18 years old at the time of pulmonary TB diagnosis, (2) not able to fluently communicate in Thai, or (3) not able to cooperate with the investigation. Moreover, individuals who died within 28 days postdischarge, lost to follow-up, or had missing data in the electronic database were not included in the analysis.

Intervention: A nursing care program

The nursing care program consists of several proactive actions at three periods, including (1) during the hospital stay, (2) on hospital discharge day, and (3) at 28 days postdischarge. The multidisciplinary team, including registered nurses, infectious disease physicians, clinical pharmacists, and nutritionists, designed and developed this program. Details of the interventions given at each period are as follows:

During a hospital stay, the interventions included as follows:

1) Administering medications with the directly observed therapy (DOT) program by registered nurses.
2) Evaluating patients' treatment regimens and nutritional status by physicians, clinical pharmacists, and nutritionists.
3) Assessing baseline scores of patients' knowledge and self-care behaviors using two questionnaires (pulmonary TB knowledge questionnaire and self-care behaviors questionnaire) by registered nurses.

The details of the questionnaire used in our study have been described elsewhere [10]. In brief, this questionnaire is a set of questions designed to assess a patient's knowledge of the etiology, signs and symptoms, route of transmission, treatment, and prevention of TB infection. Responders were assigned one point for each correct answer or zero points if-else. The total score ranged from zero (i.e., no knowledge at all) to ten points (i.e., excellent knowledge) (Supplement TableS2). According to the previous study, the content validity index (CVI) and the Kuder & Richardson 20 (KR-20) of the knowledge questionnaire were 0.90 and 0.71, respectively [10].

The self-care behavior questionnaire contains twelve questions designed to address patients' hygienic habits to control the transmission of TB. Responders were given 5 (regular), 3 (occasional), and 0 (never) points for each question. Thus, the total score ranged from 0 (i.e., no hygienic habits at all) to 60 points (i.e., fully corporate with hygienic habits) (Supplement TableS3). Additionally, the self-care behavior questionnaire showed an excellent content validity (CVI of 1.00) and a good reliability (Crombach's α of 0.82) from the previous work [10].

4) Providing the information regarding the disease and the treatment to enhance patients' knowledge by registered nurses.
5) Contact tracing and monitoring potential adverse drug reactions due to anti-tuberculosis therapy (e.g., hepatotoxicity or an allergic reaction) by registered nurses and clinical pharmacists.

Upon hospital discharge, the interventions included as follows:

1) Assigning the home health care team to provide continuity of care and monitor patients at home.
2) Re-assessing patient's knowledge and self-care behavior by registered nurses.
3) Re-counseling patients about adverse drug reactions of anti-tuberculosis medications and emphasizing the importance of adherence to prescribed treatment.
4) Educating caregivers on the DOT program.

At 28 days postdischarge, the interventions included as follows:

1) Reassessing the patient's knowledge and self-care behavior through telehealth (conducted by registered nurses).
2) Monitoring patients' clinical status and potential adverse drug reactions by registered nurses at a primary care unit.
3) Reevaluating compliance to the DOT program at home by trained local village health volunteers.

Usual care

All pulmonary TB patients received usual care during admission on the general medicine wards. Using a multidisciplinary team consisting of physicians, clinical pharmacists, and registered nurses, all pulmonary TB patients received individualized antituberculosis therapy, followed by close monitoring for potential adverse drug reactions. Registered nurses were responsible for assuring standard isolation protocol for patients, updating physicians of laboratory results, administering medications (without DOT program), and periodically monitoring patients' vital signs.

Data collection and data source

The usual care group's demographic and clinical data were retrospectively obtained from electronic health records. In addition, data of the nursing intervention group were collected prospectively from medical records. Comorbidities were identified using the 10th revision of the international classification of disease (ICD-10). Included comorbidities in this study were anemia (i.e., D59.4), type 2 diabetes mellitus (i.e., E11.0-E11.9), cerebrovascular accident (i.e., I61.0-I61.9, I62.0-I62.9, and I63.0-I63.9), human immunodeficiency virus (i.e., B20.0-B20.9, B23.0-B23.8, and B24.0), chronic obstructive pulmonary disease (i.e., J44.0-J44.9), and respiratory failure (i.e., J96.0-J96.9).

Outcomes

Our primary outcomes were the incidence and rates of hospital readmissions from TB-related complications within 28 days after being discharged from the first TB treatment in a hospital. The incidence of hospital readmission was calculated as the number of patients readmitted to the hospital due to TB-related complications within 28 days after being discharged from initial TB treatment, divided by the total patient-time of follow-up (person-days). The ratio of the incidence rate (hazard rate) in the nursing care program and usual care groups gives us the hazard ratio of hospital readmission. Meanwhile, the rates of hospital readmissions were the frequency of hospital readmission within 28 days after discharge from the initial TB diagnosis and treatment. The ratio of the rates between groups gives us an incidence rate ratio. The TB-related complications were defined as hospital readmission due to treatment failure or reported adverse drug reactions. Reasons for hospital readmission were obtained from medical records. The secondary outcomes were the change in scores of knowledges and self-care behaviors at hospital discharge and 28 days thereafter, which were measured only in the nursing care program group. All patients were followed for 28 days after hospital discharge. Their outcome data were obtained from medical records (if they had a hospital visit in the next 28 days) or a phone call (if they had no hospital visit in the next 28 days).

Statistical analysis

Since we included all eligible participants in the analysis, the sample size was not estimated. Additionally, we planned to perform power calculation, providing that unadjusted results were nonsignificant. We described and compared patients' characteristics between groups using descriptive and inferential statistics as appropriate. To examine the impact of nursing intervention on hospital readmissions within 28 days, we used a Cox-proportional hazards model to assess the incidence of the first readmission. Poisson model was used to explore rates of readmission within 28 days.

In both models, we performed serial adjustment as follows: (1) unadjusted model, (2) a model adjusting for age and sex, and (3) age and sex-adjusted model with further adjustment for sputum smear results at diagnosis, baseline albumin levels, and diabetes mellitus, which are the proxy of TB severity, patient's nutritional status, and patient's comorbidity that can significantly affect treatment outcome [14,15] and prognosis [16,17]. We also controlled for the follow-up time of individuals in the Poisson model to satisfy models' assumptions.

To ensure the validity of the Cox model, we performed a Schoenfeld residuals test and created log-minus-log plots to examine the proportional-hazards assumption. We also tested a goodness-of-fit of the Poisson model in which nonsignificant p-values ($\geq$.05) from both deviance and Pearson statistics are required to ensure the appropriate use of Poisson regression with our data. Additionally, we analyzed each covariate's variance inflation factor (VIF) in fully adjusted models to test the multicollinearity.

Regarding the impact of the nursing care program on TB knowledge, patients receiving the nursing care program were asked to complete the questionnaire three times: at baseline (before teaching intervention), at hospital discharge (after teaching intervention), and at 28 days postdischarge. Scores at hospital discharge were then compared with baseline scores. We further compared scores retention as well. Paired t-test was used to analyze data since the distribution of mean differences was normally distributed. Moreover, to minimize the inflation of type-I error rate due to multiple comparisons, we used a Bonferroni adjusted significant p-value threshold at .008 (.05/6) and reported the corresponding 99.2% confidence interval [21].

All analyses were based on a complete-case approach with a two-sided alpha error of 5.0% using STATA version 16 (Stata Corp, LLC, College Station, Texas).

Ethical consideration

This quasi-experimental study was approved by Ethical Committee for Clinical Research at Phrae Hospital (No.34/2564). Inform consent was required for all patients who participated in the nursing care program group.

Results

Characteristics of participants

We identified 115 pulmonary TB patients from January 1, 2020, to May 31, 2021. Six of 115 patients expired before 28 days postdischarge, 3 had missing data, and 2 were lost to follow-up. Among 104 patients included for analysis, 68 were in the usual care group, and 36 were in the nursing care program group (Figure 1). Baseline characteristics are presented in Table 1. The majority of participants were female (58.7%) with a mean age of 56.24 years old and a mean body mass index of 18.65 kg/m^2. Of these, 40.4% had sputum smear-positive +1, 63.5% never smoked, and 65.4% denied alcohol drinking history. We also observed that anemia (16.4%) and diabetes mellitus (24.0%) were among the most prevalent comorbidities.

Most of the characteristics were not statistically different between groups except gender, smoking history, alcohol drinking status, sputum smear results, and baseline albumin levels. Patients receiving the nursing care program majority were male (p-

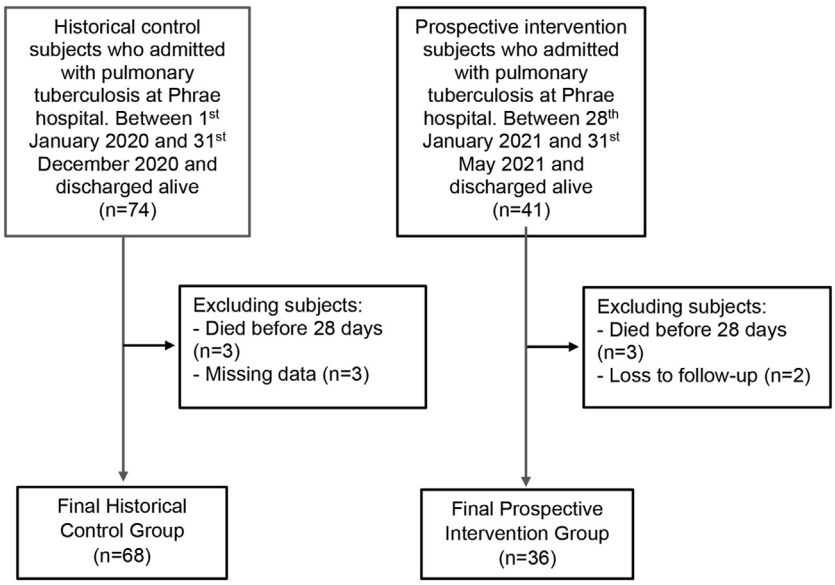

Figure 1. Patients Flow Diagram. Usual Care Group (left) and Nursing Care Program Group (right).

value<.001), ex- or current smokers (*p*-value<.001), ex- or current alcohol drinkers (*p*-value<.001) and had slightly lower albumin levels at diagnosis (*p*-value = .002), compared to those in the usual care group (Table 1).

Hospital readmissions due to pulmonary TB-related complications within 28 days

Twenty patients were readmitted due to pulmonary TB-related complications within 28 days postdischarge. Of these, 16 patients were readmitted due to treatment failure, whereas 4 were readmitted due to adverse drug reactions from anti-tuberculosis.

Patients receiving the nursing care program had a lower incidence of hospital readmission (HR, 0.19; 95% CI 0.04, 0.82). This finding remained consistent when adding age and sex to our analysis (HR, 0.18; 95% CI 0.04, 0.81) and even after combining age, sex, sputum smear at diagnosis, baseline albumin levels, and diabetes to the analysis (HR, 0.16; 95% CI 0.03, 0.87) (Table 2). Kaplan-Meier analysis confirmed that the nursing care program significantly lowered the incidence of hospital readmission due to pulmonary TB-related complications (Figure 2, *p*-value from log-rank

Table 1 *Characteristics of Included Participants.*

Characteristics	All participants (n = 104)	Usual care group (n = 68)	Nursing care group (n = 36)	*p*-value
Age, years (Mean ± SD)	56.24 ± 17.61	57.25 ± 17.17	54.33 ± 18.51	.424[a]
Female, numbers (%)	61 (58.7%)	51 (75.0%)	10 (27.8%)	<.001[b]
Weight, kg (Mean ± SD)	48.54 ± 10.46	49.78 ± 10.66	46.19 ± 9.79	.096[a]
Height, cm (Mean ± SD)	160.51 ± 8.80	161.16 ± 9.15	159.28 ± 8.08	.301[a]
BMI, kg/m^2 (Mean ± SD)	18.65 ± 3.94	18.85 ± 3.92	18.26 ± 3.99	.473[a]
Smoking status, numbers (%)				
Never	66 (63.5%)	58 (85.3%)	8 (22.2%)	<.001[b]
Ex-/Current-	38 (36.5%)	10 (14.7%)	28 (77.8%)	
Alcohol drinking, numbers (%)				
Never	68 (65.4%)	55 (80.9%)	13 (36.1%)	<.001[b]
Ex-/Current	36 (34.6%)	13 (19.1%)	23 (63.9%)	
Sputum smear results, numbers (%)				
+1	42 (40.4%)	30 (44.1%)	12 (33.3%)	.020[b]
+2	34 (32.7%)	16 (23.5%)	18 (50.0%)	.770[c]
+3	28 (26.9%)	22 (32.4%)	6 (16.7%)	
Albumin, g/dL (Mean ± SD)	2.49 ± 0.64	2.61 ± 0.73	2.28 ± 0.35	.002[d]
Intercurrent conditions, numbers (%)				
Anemia	17 (16.4%)	12 (17.7%)	5 (13.9%)	.622[b]
COPD	2 (1.9%)	1 (1.5%)	1 (2.8%)	1.000[e]
CVA	2 (1.9%)	1 (1.5%)	1 (2.8%)	1.000[e]
DM	25 (24.0%)	14 (20.6%)	11 (30.6%)	.258[b]
HIV	6 (5.8%)	5 (7.4%)	1 (2.8%)	.662[e]
Respiratory failure	5 (4.8%)	4 (5.9%)	1 (2.8%)	.657[e]

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; HIV, human immunodeficiency virus; SD, standard deviation; g/dL, gram per deciliter.

[a] Independent t-test with equal variance.
[b] Chi-squared test.
[c] *p*-value for trend.
[d] Independent t-test with unequal variance.
[e] Fisher's exact test.

Table 2 *Effectiveness of Nursing Care Programs on Hospital Readmission within 28 days (n = 104).*

Outcomes	Usual care group (n = 68)		Nursing care group (n = 36)		Effect size[a] (95% CI)
	Events	Event rate	Events	Event rate	
Incidence of 28-day hospital readmission					
Unadjusted model	18[b]	10.72 (6.75, 17.02)[d]	2[c]	2.04 (0.51, 8.15)[d]	0.19 (0.04, 0.82)
Age and sex adjusted model					0.18 (0.04, 0.81)
Fully adjusted model					0.16 (0.03, 0.87)
Rate (frequency) of 28-day hospital readmission					
Unadjusted model	21	0.31 ± 0.55[e]	3	0.08 ± 0.37[e]	0.27 (0.08, 0.89)
Age and sex-adjusted model					0.26 (0.08, 0.92)
Fully adjusted model					0.22 (0.06, 0.85)

Notes: Fully adjusted models were adjusted for age, sex, sputum smear-positive results at diagnosis, baseline albumin levels, and baseline comorbidity (i.e., diabetes mellitus).
Abbreviations: CI, confidence interval.
[a] Effect size was hazard ratio (HR) and incidence rate ratio (IRR) for incidence and rate of hospital readmission, respectively, in a nursing care group, compared to a usual group.
[b] 1,679 person-days of follow-up.
[c] 981 person-days of follow-up.
[d] Event rate per 1,000 person-days (95% CI).
[e] Total frequency divided by the number of participants ± standard deviation.

test = .012). Additionally, the number needed to treat (NNT) to prevent one hospital admission was 4.78 (95% CI 3.02, 18.42) over 28 days of follow-up.

In terms of rates of hospital readmissions within 28 days, compared to patients in the usual care group, those receiving the nursing care program had lower rates of hospital readmissions (IRR, 0.27; 95% CI 0.08, 0.89). After adding age and sex into consideration, we found that the readmission rate was still lower in the nursing care group than the usual care group (IRR, 0.26; 95% CI 0.08, 0.92). We also found similar findings after fully adjusting for potential confounders (IRR, 0.22; 95% CI 0.06, 0.85).

Knowledge and self-care behaviors

The knowledge and self-care behavior scores at baseline, upon hospital discharge, and 28 days postdischarge were shown in Table 3. We observed that nursing care programs significantly improved knowledge and self-care behavior scores at the time of hospital discharge compared with baseline (mean difference 2.22 [99.2% CI 1.21, 3.24], p-value<.001). Patients also showed good scores retention at 28 days postdischarge (mean difference 1.97 [99.2% CI 1.28, 2.67], p-value<.001) without significant drop of scores from time of hospital discharge to 28 days post-discharge (mean difference −0.25 [99.2% CI -0.96, 0.46], p-value = .330).

Furthermore, we observed a similar pattern of improvement in the self-care domain. The mean score was significantly increased by 11.67 points (99.2% CI 8.34, 15.00; p-value<.001) at the time of discharge and by 10.33 points (99.2% CI 6.69, 13.97; p-value<.001) at 28 days postdischarge compared with baseline. Patients were able to maintain the knowledge and self-care behavior scores between the time of discharge and 28 days later. No statistically significant difference of scores was found (−1.33 [99.2% CI -3.05, 0.38], p-value = .036).

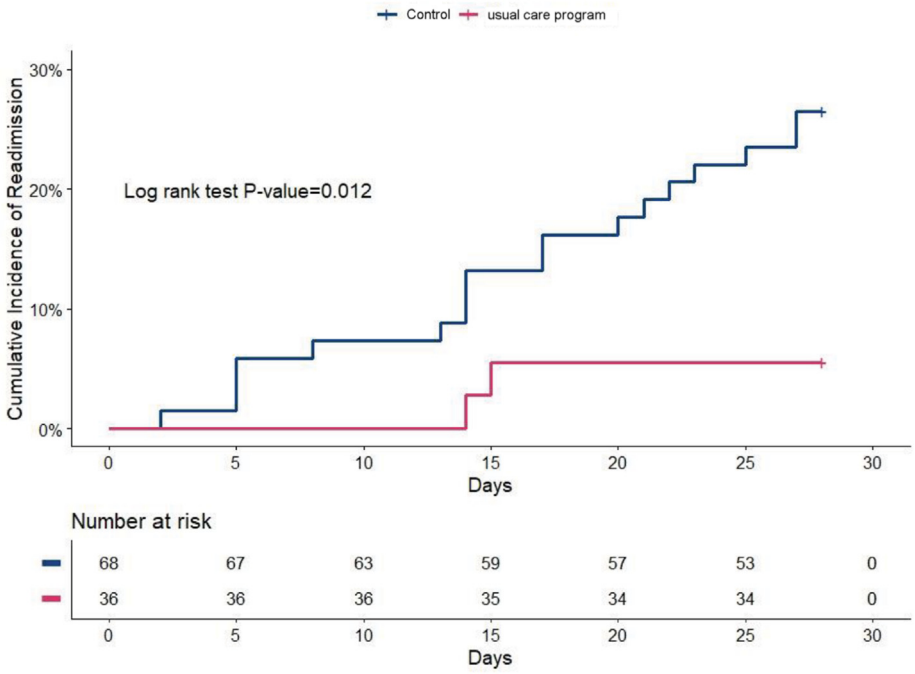

Figure 2. Kaplan-Meier Plot of the Cumulative Incidence of Hospital Readmission within 28 days.

Table 3 *Knowledge and Self-care Behavior Scores at Baseline (Pre-intervention) and After Discharge (Postintervention) in Patients Receiving a Nursing Care Program (n = 36).*

Testing domain	Baseline scores, Mean ± SD	Scores after receiving a nursing care program				Mean difference comparing between 28 days postdischarge and at hospital discharge (99.2% CI)[a]
		At hospital discharge, Mean ± SD	Mean difference (99.2% CI)[a]	At 28 days postdischarge, Mean ± SD	Mean difference (99.2% CI)[a]	
Knowledge	6.03 ± 1.68	8.25 ± 1.13	2.22 (1.21, 3.24)	8.00 ± 1.04	1.97 (1.28, 2.67)	−0.25 (−0.96, 0.46)
Self-care behaviors	44.25 ± 7.43	55.92 ± 2.30	11.67 (8.34, 15.00)	54.58 ± 3.14	10.33 (6.69, 13.97)	−1.33 (−3.05, 0.38)

Notes.
Abbreviations: CI, confidence interval; SD, standard deviation.
[a] Paired t-test compared postintervention scores with baseline scores unless specified otherwise.

Discussion

In this study, we evaluated the effectiveness of the nursing care program on hospital readmission, patient knowledge, and self-care behaviors among pulmonary TB patients. We showed that the nursing care program was significantly associated with the decrease in both incidence and rate of 28-day hospital readmission. Our patients in the nursing care program group showed significant improvement in knowledge and self-care behaviors with significant scores retention at 28 days postdischarge.

Compared to previous studies

After performing a systematic search from various databases (e.g., PubMed, Google Scholar, and Scopus), we could not find any studies examining nursing intervention's impact on clinical outcomes in pulmonary TB patients. Only a few studies have shown that educational intervention given to pulmonary TB patients can improve all aspects of knowledge, patients' satisfaction, and self-care behaviors [10,18]. Comparing with the previous study of 30 TB patients in Thailand [10], we observed a relatively similar degree of improvement in the knowledge domain at hospital discharge (2.22 vs. 3.13). In contrast to the previous study, our patients had higher scores of self-care behaviors at hospital discharge (55.92 vs. 21.36). This comparison has a limitation as it is difficult to compare the outcome solely based on scores. Participants in our study reportedly had high baseline scores (44.25). It would be beneficial to observe growth rate and retention scores. However, we cannot assess this as the other study did not report baseline scores that could have offered an opportunity for comparison.

Explanations

Our proposed nursing care program contributed to the significant decrease in the incidence of 28-day hospital readmission due to several explanations. First, our interventions primarily sought to empower patients to improve their self-care behaviors. A previous randomized controlled trial had shown that empowering patients positively impacted clinical outcomes in heart failure patients [11]. Furthermore, a meta-analysis of trials and observational studies also showed the importance of patient-centered modalities as a key to successful TB treatment [19]. Second, evidence has been demonstrated that DOT delivery in the community, which is a part of our intervention, led to better outcomes for TB treatment than DOT delivery at the clinic [19]. Third, improving patient TB knowledge has positively affected the treatment completion rate, cure rate, and adherence [19]. Lastly, evaluation of nutritional status was incorporated as a part of the intervention program during hospital admission. Previous studies had shown the association between poor nutritional status and mortality rates in TB patients [17,20].

Strengths and limitations

To the best of our knowledge, this study is among the first trial examining the clinical impact of nursing care programs in pulmonary TB patients in Thailand. We comprehensively investigated clinical (i.e., incidence and rates of hospital readmission due to TB-related complications within 28 days of admission) and surrogate endpoints (i.e., knowledge and self-care scores).

However, some limitations should be concerned. First, historical control might introduce bias due to changes in clinical practice over time, directly affecting hospital readmissions. It is worth noting that the guidelines for TB treatment in 2020 (usual care group) and 2021 (nursing care group) remained unchanged. Second, we did not randomize patients due to feasibility and ethical considerations. Nonetheless, as further protection against bias, the endpoints were adjusted for age, sex, sputum smears at diagnosis, baseline serum albumin levels, and diabetes mellitus. Importantly, due to the nature of the intervention, we cannot blind participants or investigators. This may lead to information bias and limit the causal inferences. Lastly, data collection was performed in only one setting. Thus, generalizability cannot be warranted.

Implications

Our study strongly supports the role of nurses as a key to improving clinical outcomes of pulmonary TB patients, and the nursing care program for pulmonary TB management should be widely adopted. Also, the impact of our proposed nursing care programs should be externally validated in other settings. Further study with a larger sample size may be needed to ensure the robustness of our findings.

Conclusion

Our nursing care program was significantly associated with the decrease in incidence and rate of 28-day hospital readmission due to pulmonary TB. In addition, patients receiving the nursing care program not only improved their knowledge and self-care behaviors but also continued to have knowledge retention over 28 days postdischarge. Therefore, we highly recommend implementing our nursing program in a clinical setting to improve the outcomes of pulmonary TB patients.

Abbreviations

DOT, Directly Observed Therapy; HR, hazard ratio; IRR, Incidence Rate Ratio; TB, Tuberculosis; VIF, Variance inflation factor; WHO, World Health Organization; CVI, Content Validity Index; KR-20, Kuder & Richardson 20

Ethical approval and consent to participate

All methods were performed in accordance with relevant guidelines and regulations. Our research received authorization from the Ethical Committee for Clinical Research of Phrae Hospital (No.34/2564). All patients in the intervention group have received the information about the study, and informed consent was obtained before study participation.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the study are available from the corresponding author upon reasonable request.

Author contributions

Chamlong Sunpapoa: Conceptualization, data curation, investigation, methodology, validation, writing-original draft, **Nat Na-Ek:** Conceptualization, formal analysis, methodology, writing-review and editing, **Areeya Sommai:** Conceptualization, writing-review and editing, **Kansak Boonpattharatthiti:** Data curation, **Nina S. Huynh:** Conceptualization, writing-review, editing and proofreading, **Sukrit Kanchanasurakit:** Conceptualization, data curation, formal analysis, methodology, validation, software, writing-original draft, writing-review and editing. All authors have read and approved the final manuscript.

Author statement

All authors meet the ICMJE authorship criteria.

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Conflict of interest

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.06.002.

References

1. World Health Organization. Global tuberculosis report 2020 [Internet]. Geneva: World Health Organization; 2020 [cited 2020 Dec 23]. Available from: https://www.who.int/publications/i/item/9789240013131
2. Cruz-Knight W, Blake-Gumbs L. Tuberculosis: an overview. Prim Care. 2013;40:743–56. https://doi.org/10.1016/j.pop.2013.06.003
3. Kamolwat P, Nateniyom S, Chaiprasert A, Disratthakit A, Mahasirimongkol S, Yamada N, et al. Prevalence and associated risk factors of drug-resistant tuberculosis in Thailand: results from the fifth national anti-tuberculosis drug resistance survey. Trop Med Int Health. 2021;26:45–53. https://doi.org/10.1111/tmi.13502
4. Clark PM, Karagoz T, Apikoglu-Rabus S, Izzettin FV. Effect of pharmacist-led patient education on adherence to tuberculosis treatment. Am J Heal Pharm. 2007;64:497–505. https://doi.org/10.2146/ajhp050543
5. Akande PA. The effect of an educational intervention to improve tuberculosis infection control among nurses in Ibadan, south-west Nigeria: a quasi-experimental study. BMC Nurs. 2020;19:81. https://doi.org/10.1186/s12912-020-00474-2
6. Riquelme-Miralles D, Palazón-Bru A, Sepehri A, Gil-Guillén VF. A systematic review of non-pharmacological interventions to improve therapeutic adherence in tuberculosis. Heart Lung. 2019;48:452–61. https://doi.org/10.1016/j.hrtlng.2019.05.001
7. Ngo CQ, Manabe T, Vu G Van, Chu HT, Vu TTT, Tran TT, et al. Difficulties in tuberculosis infection control in a general hospital of Vietnam: a knowledge, attitude, and practice survey and screening for latent tuberculosis infection among health professionals. BMC Infect Dis. 2019;19:951. https://doi.org/10.1186/s12879-019-4593-z
8. Akande PA. Knowledge and practices regarding tuberculosis infection control among nurses in Ibadan, south-west Nigeria: a cross-sectional study. BMC Health Serv Res. 2020;20:280. https://doi.org/10.1186/s12913-020-05156-y
9. Shrestha A, Bhattarai D, Thapa B, Basel P, Wagle RR. Health care workers' knowledge, attitudes and practices on tuberculosis infection control, Nepal. BMC Infect Dis. 2017;17:724. https://doi.org/10.1186/s12879-017-2828-4
10. Treenon P, Visudtibhan PJ, Siripitayakunkit A. Development of a discharge planning program for persons with pulmonary tuberculosis. Rama Nurs J. 2014;20:50–66 https://he02.tci-thaijo.org/index.php/RNJ/article/view/19196
11. Dianati M, Rezaei Asmaroud S, Shafaghi S, Naghashzadeh F. Effects of an empowerment program on self-care behaviors and readmission of patients with heart failure: a randomized clinical trial. Tanaffos. 2020;19:312–21.
12. Des Jarlais DC, Lyles C, Crepaz N. Improving the reporting quality of non-randomized evaluations of behavioral and public health interventions: the TREND statement. Am J Publ Health. 2004;94:361–6. https://doi.org/10.2105/AJPH.94.3.361
13. World Health Organization. WHO consolidated guidelines on tuberculosis Module 3: diagnosis - Rapid diagnostics for tuberculosis detection [Internet]. Geneva: World Health Organization; 2020 [cited 2021 Dec 23]. Available from: https://www.who.int/publications/i/item/9789240029415
14. Unsematham S, Kateruttanakul P. Factors predicting sputum smear conversion and treatment outcomes in new smear-positive pulmonary tuberculosis. J Med Assoc Thai. 2013;96:644–9.
15. Amante TD, Ahemed TA. Risk factors for unsuccessful tuberculosis treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia. Pan Afr Med J. 2015;20:247. https://doi.org/10.11604/pamj.2015.20.247.3345
16. Ukibe NR, Ndiuwem CK, Ogbu II , Ukibe SN, Ehiaghe FA, Ikimi CG. Prognostic value of some serum protein fractions as early index of clinical recovery in pulmonary tuberculosis subjects. Indian J Tubercul. 2020;67:167–71. https://doi.org/10.1016/j.ijtb.2019.08.015
17. Matos ED, Moreira Lemos AC. Association between serum albumin levels and in-hospital deaths due to tuberculosis. Int J Tubercul Lung Dis. 2006;10:1360–6.
18. Yousif K, Ei Maki M, Babikir RK, Abuaisha H. The effect of an educational intervention on awareness of various aspects of pulmonary tuberculosis in patients with the disease. East Mediterr Health J. 2021;27:287–92. https://doi.org/10.26719/emhj.20.102
19. Alipanah N, Jarlsberg L, Miller C, Linh NN, Falzon D, Jaramillo E, et al. Adherence interventions and outcomes of tuberculosis treatment: a systematic review and meta-analysis of trials and observational studies. PLoS Med. 2018;15:e1002595. https://doi.org/10.1371/journal.pmed.1002595
20. Okamura K, Nagata N, Wakamatsu K, Yonemoto K, Ikegame S, Kajiki A, et al. Hypoalbuminemia and lymphocytopenia are predictive risk factors for in-hospital mortality in patients with tuberculosis. Intern Med. 2013;52:439–44. https://doi.org/10.2169/internalmedicine.52.8158
21. Proschan MA, Waclawiw MA. Practical guidelines for multiplicity adjustment in clinical trials. Control Clin Trials. 2000;21:527–s39. https://doi.org/10.1016/s0197-2456(00)00106-9

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Research Article

Outcomes of Emergency Trauma Patients After the Implementation of Web Application Operating Systems

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SUMMARY

Purpose: Trauma has significant impacts on the livelihoods and well-being of patients. Prompt emergency, medical, and nursing care is the key to reducing mortality rates. Digital platforms have become important for patient care. This research aimed to evaluate patient outcomes after implementing a novel web application operating system in trauma care.

Methods: A descriptive comparative study was conducted on trauma patients. The patients were divided into two groups: those who used the developed application (n = 70) and those who did not (n = 70). The patients' characteristics, the time of the trauma team's arrival at the emergency department (ED) and the length of stay in the ED, and patients' outcomes were collected from electronic medical records and the application database. A statistical analysis was performed to evaluate this data. Sixty registered nurses who used the application completed the survey on the feasibility of the application.

Results: The activated trauma intervals for the non-application-used group and the application-used group were 5.0 ± 1.1 and 3.1 ± 0.4 minutes, respectively ($p = .010$). The length of stay in the ED for the non-application-used group and the application-used group were 30.1 ± 5.1 and 18.3 ± 6.2 minutes, respectively. A high level of agreement confirms the feasibility of the application.

Conclusions: This application improves patient outcomes in terms of length of stay. This mobile application can improve the cooperation and communication and efficacy of the trauma care team.

Introduction

Trauma injury is a major cause of death globally, especially in lower- and middle-income countries [1]. The primary cause of trauma is road traffic accidents [1]. Road traffic accidents are becoming an increasingly more severe global problem. In 2018, the World Health Organization stated that according to the most recently available data, the number of road traffic crashes that resulted in death had increased to 1.35 million people worldwide per year and accounted for an average of 3,700 people per day [2]. The death rate was mostly due to accidents involving cars (29.0%), followed by motorcycles (28.0%), bicycles and pedestrians (26.0%), and other road users (17.0%). In Thailand, the number of road deaths was ranked the ninth highest in the world and the overall first in Asia and the ASEAN region [2]. The estimation currently stands at 32.7 deaths per 100,000 population or an average of 22,491 deaths per year (60 daily) [3–5]. As the Office of Transport and Traffic Policy and Planning report in 2020 indicates, most accidents were caused by motorcycles (74.4%), followed by cars (12.3%), pedestrians (7.6%), cyclists (3.5%), and other road users (2.3%) [6]. Statistics information from the Strategy and Planning Division of the Office of the Permanent Secretary, the Ministry of Public Health 2018-2019 and the ThaiRSC Accident Information Center all confirm that road accident deaths increased steadily in 2020 [3–5]. Accidents have tremendous impacts on the physical, emotional, and overall state and quality of life. The major causes of death for trauma patients are excessive blood loss, airway obstruction or ineffective breathing, and severe brain injury [7]. The first hour is

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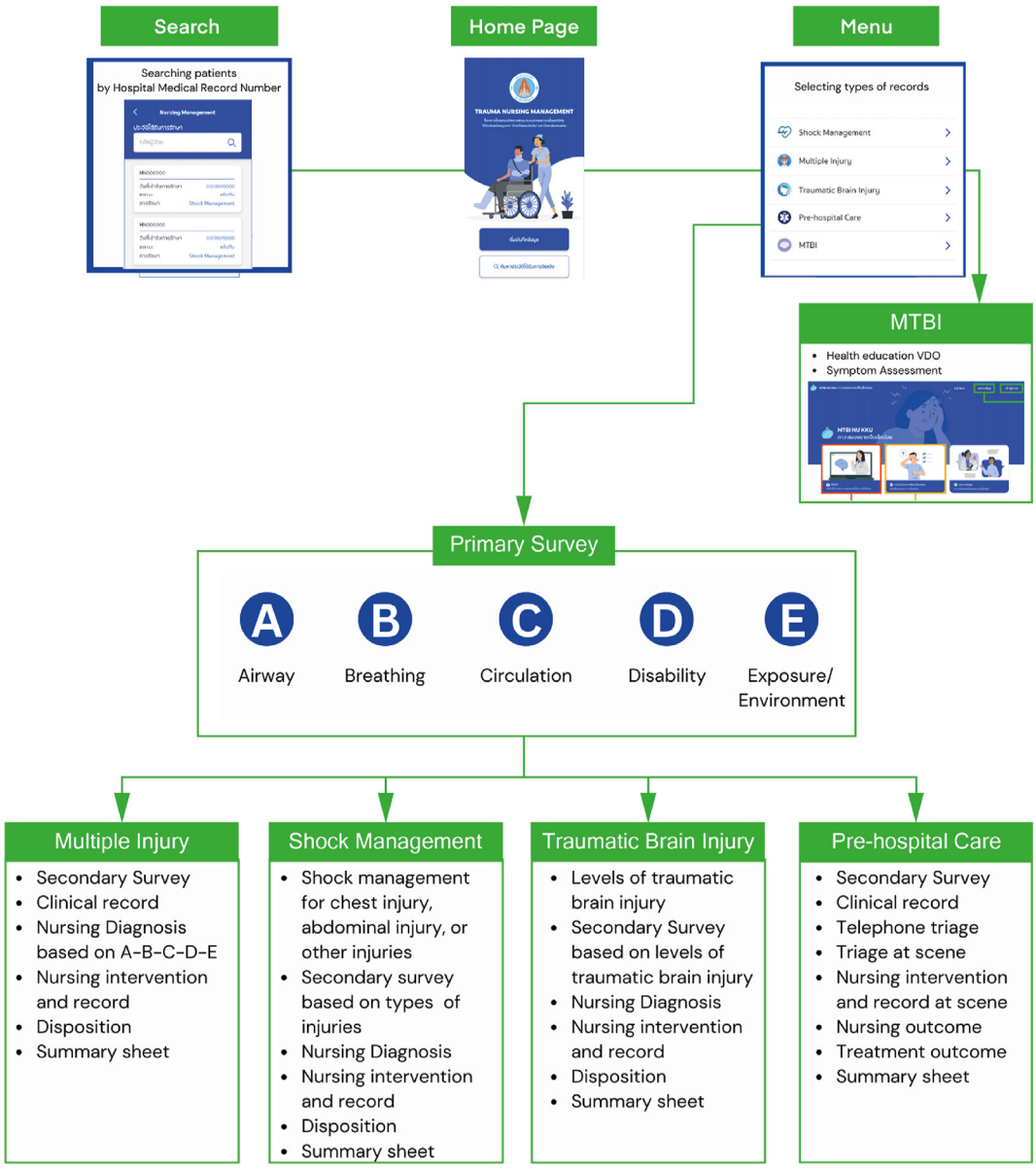

Figure 1. Web Application Operating Systems.

crucial in saving lives, and having a prompt emergency care system in place is essential [8].

The first and arguably the most important step in the response for injured patients is to screen and classify the injured patient rapidly and accurately to manage and deliver prehospital care, select a suitable hospital, and transfer important patient information to the destination hospital where the patient is transported to [9]. In practical situations, emergency medical service (EMS) providers use the radio to talk to command-and-control centers that pass along information to a healthcare provider at the emergency department (ED). However, there are a number of limitations to the strictly verbal communication used in EMS situations that often result in miscommunication. The impact of miscommunication between healthcare providers during treatment in time-sensitive emergencies may lead to delays and other negative patient outcomes. In the ED, the priority is to screen and provide care for injured patients promptly and accurately, especially in the first hour, known as the “Golden Hour” [10]. In many hospitals in Thailand, registered nurses work in both the EMS unit and the ED. Nurses have played an important role in initial assessment, monitoring, coordination, preparation of equipment, and nursing records. Thus, nurses’ competencies in rapid and accurate emergency response and nursing implementation are critical [11].

Currently, technology plays an important role in solving communication problems. The use of web applications has been demonstrated to reduce documentation time, improve patient outcomes, increase self-triage, and lead to a recommendation to call an emergency center [12,13]. Therefore, the development of web application tools for injured patients on mobile devices used by healthcare providers, particularly nurses, is needed on a larger scale. This application can provide lifesaving information about injured patients from EMS field crews and relay it to the hospital. This information will support healthcare provider decisions according to the pathological problems and will reduce the incidents of miscommunication. This platform can promptly provide the

trauma team before the patient's arrival at the ED and help the emergency healthcare providers better prepare for these patients.

The development of a web application needs to consider the characteristics of its end-user, including registered nurses in the targeted hospitals. The codesign concept is a creative and participatory process that involves a diverse group of stakeholders to explore, develop, and test an intervention for a shared challenge [14]. The greatest strength of applying the codesign process is that an app is likely to be acceptable by potential users and be technically feasible to implement in real-world settings [15]. Therefore, codesign and collaboration between healthcare professionals and app developers are recommended for developing all digital solutions.

The primary objective of this study was to compare the activated trauma team interval, length of stay, and clinical patient outcomes in the ED between before and after the web application has been implemented. This study also aimed to determine the feasibility of the web application in terms of user satisfaction.

Methods

Design and setting

This study was a descriptive comparative study conducted in trauma patients who received prehospital services from EMS teams at Khon Kaen province, Thailand during a six-month period from July to December 2021. This hospital is a level I trauma center in Northeastern Thailand, which has an average of roughly 800 to 1000 EMS operations of trauma patients per year.

Web application

The web application was developed to aid healthcare providers, especially nurses in the EMS unit and the ED, in providing care for trauma patients following the standard practice guideline. The initial content of the app was created by trauma and emergency care experts following the practice guidelines of the Advanced Trauma Life Support (ATLS) guidelines, 10th edition. An in-depth interview with five experts in trauma care, consisting of one emergency physician, two nursing instructors, and two emergency accident department nurses, was conducted to review the scientific content and accuracy of the context body. The content validity index (CVI) was verified to be 0.90. Afterward, the web application was developed by app developers using React Java Script Code for its ability to distribute the app on online platforms via smartphones and tablets. Subsequently, the content and design consistency of the web application prototype was reviewed by three experts in computer engineering. The CVI was 0.87.

The final web application operating system (Figure 1) contained the following key elements: a primary survey and a secondary survey for common traumatic problems, including prehospital care, multiple injuries, traumatic brain injury, and shock. This application allowed healthcare providers to record patients' vital signs, clinical conditions, and nursing care. Additionally, this application also displayed practices for patients with mild traumatic brain injury.

Study sample

This study focused on adult trauma patients during the stated period. Patients taken to other hospitals or dead-on-arrival were excluded. The patients were divided into two groups by EMS providers: patients in situations where this application was used and patients in situations where it was not used. The sample size was calculated using the G*Power software (Version 3.1.9.6) based on an α-value of 0.05, a power of 0.80, and an effect size of 0.5 for the independent t-test based on Cohen's recommendation [16]. The medium effect size was applied in this study due to the fact that there was no similar study in Thailand and a similar previous study showed a high effect size of 1.10 [23], resulting in a too-small calculated number of participants. The minimum predicted sample size was 64 patients per group. Concerning the missing data of around 10.0%, we recruited 70 patients per group.

The feasibility of this application was evaluated by 60 registered nurses who used the web application. Inclusion criteria were registered nurses having at least 1 year of working experience in the emergency department and willing to participate in the project.

Measurement

The interval for activating the trauma team was defined as the time from when EMS providers notified the trauma team of the case until the time when the trauma team arrived at the ED. The length of stay in the ED was defined as the time when patients arrived at the ED through the time when they were discharged from the ED. The time utilized for this study was determined by two synchronized clocks that were found within the command-and-control center and the ED. Patient outcomes included shock index (SI), Glasgow coma score (GCS), and oxygen saturation at the time before discharge from the ED. The SI is calculated by dividing the heart rate by the systolic blood pressure, with the accepted normal range of 0.5–0.9. A greater SI (>1.0) indicates a deteriorating hemodynamic state and shock [24]. The patients' characteristics consisted of gender, age, mechanism of injury, organ injury, the emergency severity index, and the area of injury.

The application utilized was defined as the nurses' perception of the possibility of using the web application. The questionnaire was adapted from previous research on surveys measuring satisfaction with smart phone applications [11]. The possibility of using the web application questionnaire consists of 10 Likert scale items that refer to the app's design, audio, visual quality, content, usefulness, and user-friendliness. The CVI was 0.92. The Cronbach's α of this the web application scale was 0.94. The mean score of each item was interpreted into five levels of agreement: least agreed (1.00–1.50), slightly agreed (1.51–2.50), moderately agreed (2.51–3.50), highly agreed (3.51–4.50), and extremely highly agreed (4.51–5.00) [17].

Ethical considerations

This study was carried out in compliance with the Declaration of Helsinki's principles and Good Clinical Practice recommendations. The study was approved by the Khon Kaen University Ethics Committee for Human Research (HE642124). Requirement for informed consent from the patients was waived since all identifiers were removed from the obtained data to ensure confidentiality. Written informed consent was obtained from all registered nurses.

Data collection

The data consisting of characteristics of patients, the time of trauma team arrival at the ED, the time of patients receiving nursing care, and the length of stay in the ED were all acquired from electronic medical records and the database from the application. The data were extracted and put into Microsoft Excel, and the duplicate data entry was completed by two independent investigators who were not associated with the treatment team. At the end of the six-month trial period, we distributed the survey to users to assess the feasibility of this web application and explore the direction to further improvements.

Data analysis

All data were recorded in Microsoft Excel 2016, and statistical analyses were performed using IBM SPSS 2017 for Windows, version 28.0. Descriptive statistics for the approximately normally distributed numerical variables were presented as mean (standard deviation) and N (percent) for categorical variables. Independent sample t-tests were used to compare the two groups' differences in terms of activated trauma interval and length of stay in the ED. Chi-square test was applied to compare the categorical variables, including SI, GCS, oxygen saturation, and patients' characteristics. A p value of <.05 was considered statistically significant, and all tests were two-tailed. The results of the user's perception survey were summarized as descriptive statistics.

Results

Data from 140 participants were collected. The characteristics of patients in both groups were familiar. More than a half of participants in this study were male. Most of them were aged between 18 and 60 years. The most common mechanism of injuries was traffic accidents. Most severity assessments according to the Emergency Severity Index were in level 2, as shown in Table 1.

The activated trauma interval for the non-application-used group and the application-used group were 5.0 ± 1.1 minutes and 3.1 ± 0.4 minutes ($p = .010$), respectively (Table 2). Lengths of stay in ED for the non-application-used group and the application-used group were 30.1 ± 5.1 minutes and 18.3 ± 6.2 minutes, respectively.

The number of EMS providers using this application was 60 participants. Users' perception of the possibility of using the web application of the nursing practice guidelines in the ED settings was demonstrated in Table 3.

Discussion

The web application was developed to facilitate emergency staff communication for trauma patients. This study aimed to evaluate the outcome of patients after implementing these applications in the nursing care system. The results of this study show that implementing this new application could considerably reduce patient care time.

In regards to the time the trauma team took to arrive at the ED after notification from the EMS (the activated trauma interval), our study found that patients who applied this application took less time than the group that did not. This is consistent with previous studies [9,15,17] which demonstrated that smartphone applications improve teamwork and communication and enhanced the safety and efficiency of trauma care delivery. The reason may be due to the fact that EMS providers who use this application can transfer real-time patient information to the ED staff and trauma team without obstacles resulting from verbal miscommunication. Not only was there a time reduction, but a previous study also demonstrated that the electronic documentation captured more data elements, especially the time of team activation, the primary assessment, and the arrival time of the attending physician, than the paper documentation [18].

Our study demonstrated that patients' length of stay in the ED was shorter in the group that implemented this application. This may be due to one of the parts of this application containing trauma nursing care guidelines that can help EMS providers, ED staff, and trauma teams to evaluate and manage patients early and provide accurate emergency nursing care following ATLS guidelines. However, this study did not explore any details in the diagnosis or ED disposition delay. The next step should be to particularize the impact of this web application on each step of care. Furthermore, the use of portable devices allows nurses to record patient care assessments and nursing practice in real-time rather than on paper, which may reduce the time required for nursing documentation

Table 1 *Patients' Characteristics (N = 140) in Both Groups.*

Category	Non-application-used n = 70(%)	Application-used *n* = 70(%)	*p*-value
Gender			.620
Men	38 (54.3)	37 (52.9)	
Women	32 (45.7)	33 (47.1)	
Age (years)			.582
18–60	56 (80.0)	58 (82.9)	
>60	14 (20.0)	12 (17.1)	
Mechanism of injury			.510
Traffic accident	56 (80.0)	58 (82.9)	
Falls, slips, trips	10 (14.2)	7 (10.0)	
Assaults	2 (2.9)	3 (4.2)	
Struck by objects	2 (2.9)	2 (2.9)	
Emergency severity index			.486
Level 1	32 (45.7)	30 (42.9)	
Level 2	38 (54.3)	40 (57.1)	
Area of injury			.512
Head	39 (55.7)	37 (52.9)	
Abdomen	38 (54.3)	37 (52.9)	
Chest	34 (48.6)	32 (45.7)	
Extremities	22 (31.4)	20 (28.6)	

Table 2 *Comparing Patient Outcomes between Each Group (N = 140).*

Patient outcomes	Non-application-used *n* = 70(%)	Application-used *n* = 70(%)	*p-value*
Activate trauma interval, Mean (SD) (min)	5.02 (1.07)	3.10 (0.42)	.010
Length of stay in the ED, mean (SD) (min)	30.10 (5.10)	18.31 (6.20)	.012
Shock Index			.262
<1.0	48 (68.6)	54 (77.1)	
1.00–1.09	7 (10.0)	4 (5.7)	
1.10–1.49	10 (14.3)	8 (11.4)	
>1.49	5 (7.1)	4 (5.7)	
Oxygen saturation			<.001
>94	44 (62.9)	64 (91.4)	
≤94	26 (37.1)	6 (8.6)	
Glasgow coma score			.624
13–15	47 (67.1)	48 (68.6)	
9–12	9 (12.9)	8 (11.4)	
<9	14 (20.0)	14 (20.0)	

ED = Emergency department; SD = Standard deviation.

Table 3 *Users' Perception of the Possibility of Using the Web Application (N = 60).*

Possibility	Mean	SD	Level of agreement
1. The web application can be used to record the nursing care of trauma patients	4.25	0.72	High
2. The process of the web application is clear and reliable	4.21	0.69	High
3. The web application uses plain language and is easy to understand	3.98	0.74	High
4. The web application is easy and convenient to use	4.03	0.71	High
5. Using a web application reduces nursing recording information time	4.06	0.86	High
6. The web application can help in caring for injured patients	4.15	0.70	High
7. The web application is suitable for use in practical work	3.98	0.74	High
8. Using a web application is more cost-effective	4.01	0.74	High
9. The use of web applications will be effective for patients	4.08	0.71	High
10. The use of web applications satisfies my colleagues and me	4.13	0.79	High
Overall mean score	**4.09**	**0.74**	**High**

SD = Standard deviation.

[19]. Our findings were consistent with those of a prior study conducted in Greece, which found that using electronic documentation decreased the time between admission and completion of planned care, the total length of stay in the ED, and the time between completion of care and discharge from the ED [20].

In terms of patient outcomes, our study found that patients in the application group had more clinical improvement than patients in the comparison group, especially in the case of oxygen saturation because both EMS providers and the ED team could deliver oxygen to patients faster by performing nursing care following the guideline in this application. However, the SI and GCS did not improve in this group. A study in Thailand partially supported these findings that using the multisystem trauma care guideline for nurses improved clinical outcomes, particularly the SI and oxygen saturation [21]. This may be due to the nature of trauma patients' conditions that needed more advanced care, especially where surgery was required. This was consistent with previous studies [22,23,25–27], which demonstrated the utility of medical applications in smartphones that are widely used in health care and show improvement in the overall clinical practice.

Users who participated in the project expressed their opinions on the web application used to record patient data in accordance with the conceptual framework of the nursing process, which is comparable to following the guidelines of nursing care for emergency trauma patients. It was found that the mean score was very high, indicating that the web application could actually be used and was reliable, particularly to closely monitor changes in injured patients and provide timely care and assistance. The assessment of nursing practices in trauma patients was analyzed to adjust for nursing diagnosis to be appropriate for the injured patient continuously. This is consistent with the study of Zhang et al. [28], which established a guideline to assist injured persons in the framework of ATLS for the assessment of life-threatening symptoms in trauma patients in the first phase (Primary Assessment) and Phase II (Secondary Assessment), thus, enabling patients to receive standardized care and deliver the patient outcomes in a positive direction [29–33]. In addition, the recording of nursing activities in the operating system web application also helps to systematically build and store the database. Nurses can use the data to analyze for continuous improvement and can print out documents as evidence of nursing records that save time as opposed to writing redundant records [19]. However, users can record more important patient information that is specific to each patient.

Limitations

The study's limitations were (1) data collection from a single EMS team and single level of EMS personnel, who may have a different perspective on the studied population compared to other organizations. As a result, the generalizability of the study's findings is limited. Future research with a larger number of participants, across multi-centered settings, should be implemented to address these issues. (2) This study did not demonstrate the patient outcomes related to patient mortality or intensive care admissions. Moreover, this study did not analyze the severity of trauma patients that may interfere with the results of this study. To address this concern, the evaluation of the web application in improving other clinical patient outcomes is needed in the future. (3) The unstable quality of the internet signal may cause delays in some cases and should be concerned during using the web application.

Conclusions

Developing nursing practice guidelines for emergency trauma patients on the platform of a web application is useful for EMS providers and staff members who work in the emergency department. The results reflect that this application has a high likelihood of improving the trauma patient care processes, especially in the areas of communication, knowledge, and coordination between teams. Additionally, the nurse's perception supported the possibility of using the web application in the ED settings. This web application should be introduced to targeted hospitals and be implemented in several clinical settings.

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Author contributions

Conceptualization: CP, PW, WP, AJ. Data curation: CP, WP. Formal analysis: CP, WP. Funding acquisition: CP. Methodology: CP, PW, WP, KA, AJ. Project administration: CP. Visualization: PW, WP, KL. Writing - original draft: CP, PW, KL. Writing - review & editing: PW, CP, WP. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that there are no conflicts of interest.

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References

1. Mwandri M, Hardcastle TC, Sawe H, Sakita F, Mfinanga J, Urassa S, et al. Trauma burden, patient demographics and care-process in major hospitals in Tanzania: a needs assessment for improving healthcare resource management. Afr J Emerg Med. 2020;10(3):111–7.
2. World Health Organization. Death on the roads. Based on the WHO global status report on road safety. 2018 [cited 2022 Jun 10]. Available from: https://extranet.who.int/roadsafety/death-on-the-roads/#ticker/all_road_users
3. Ward JL, Kieling CC, Viner RM. Global, regional, and national mortality among young people aged 10–24 years, 1950–2019: a systematic analysis for the global burden of disease study 2019. Lancet. 2021;398(10311):1593–618. https://doi.org/10.1016/S0140-6736(21)01546-4
4. Hakkenbrak NAG, Mikdad SY, Zuidema WP, Halm JA, Schoonmade LJ, Reijnders UJL, et al. Preventable death in trauma: a systematic review on definition and classification. Injury. 2021;52(10):2768–77. https://doi.org/10.1016/j.injury.2021.07.040
5. Surlin V. Emergency and trauma surgery. Chirurgia (Bucur). 2021;116(6):643–4 https://doi: 10.21614/chirurgia.116.6.643
6. Samuthtai W, Patumanond J, Samutrtai P, Charernboon T, Jearwattanakanok K, Khorana J. Clinical prediction scoring scheme for 24 h mortality in major traumatic adult patients. Healthcare (Basel). 2022;10(3):577. https://doi.org/10.3390/healthcare10030577
7. Frink M, Lechler P, Debus F, Ruchholtz S. Multiple trauma and emergency room management. Dtsch Arztebl Int. 2017;114(29-30):497–503 https://doi: 10.3238/arztebl.2017.0497
8. Mitchnik IY, Rivkind AI. Succeeding in continuing trauma education during a pandemic. World J Surg. 2022;46(5):977–81. https://doi.org/10.1007/s00268-022-06462-8
9. Martin TJ, Stephen AH, Adams CA, Lueckel SN, Kheirbek T. Impact of direct transport vs. transfer on out-of-hospital traumatic cardiac arrest. R I Med J. 2021;104(10):31–5.
10. American College of Surgeons. Advanced trauma life support. 2018. Retrieved December 30, 2021, from https://www.emergencymedicinekenya.org/wp-content/uploads/2021/09/ATLS-10th-Edition.pdf

11. Tsuru S, Tamamoto T, Furuya H, Nakao A, Fukuyama M, Tanizaki K, et al. Nursing record innovations aimed at harmonizing structured clinical knowledge among doctors and nurses. Stud Health Technol Inf. 2020;270:638–42.
12. Phaken C, Pearkao C, Potisopha Angkasith P. Evaluation of a web application for nursing records of multiple trauma patients in an emergency department. J Emerg Trauma Shock. 2022;15(4):167–72. https://doi.org/10.4103/jets.jets_87_22
13. Galmiche S, Rahbe E, Fontanet A, Dinh A, Bénézit F, Lescure FX, et al. Implementation of a self-triage web application for suspected COVID-19 and its impact on emergency call centers: observational study. J Med Internet Res. 2020;22(11):e22924. https://doi.org/10.2196/22924
14. Blomkamp E. The promise of co-design for public policy. Aust J Publ Adm. 2018;77(4):729–43. https://doi.org/10.1111/1467-8500.12310
15. Matthew-Maich N, Harris L, Ploeg J, Markle-Reid M, Valaitis R, Ibrahim S, et al. Designing, implementing, and evaluating mobile health technologies for managing chronic conditions in older adults: a scoping review. JMIR Mhealth Uhealth. 2016;4(2):e29. https://doi.org/10.2196/mhealth.5127
16. Cohen J. Statistical power analysis. Curr Dir Psychol Sci. 1992;1(3):98–101.
17. Pearkao C, Thaweekhoon R. The development of smart phone application for symptomatic observation of neurological system in mild traumatic brain injury patients. J Nurs Sci Health. 2019;43:31–40.
18. Ghaffarzad A, Ghalandarzadeh A, Rahmani F, Rajaei Ghafouri R, Dorosti F, Morteza-Bagi HR. Helicopter emergency medical services in East Azerbaijan province: assessment of patients' outcome. Ulus Travma Acil Cerrahi Derg. 2021;27(4):427–33. https://doi.org/10.14744/tjtes.2020.04788
19. Teng CY, Davis BS, Rosengart MR, Carley KM, Kahn JM. Assessment of hospital characteristics and interhospital transfer patterns of adults with emergency general surgery conditions. JAMA Netw Open. 2021;4(9):e2123389. https://doi.org/10.1001/jamanetworkopen.2021.23389
20. Coffey C, Wurster LA, Groner J, Hoffman J, Hendren V, Nuss K, et al. A comparison of paper documentation to electronic documentation for trauma resuscitations at a level I pediatric trauma center. J Emerg Nurs. 2015;41(1):52–6.
21. Sumritrin S, Wunsupong S, Palaree P, Jirawatchotikan P, Techa-atik P, Tangpaisarn T. Implementation of clinical nursing practice guideline for treatment of multiple injury patients admitted to emergency department. J Med Assoc Thai. 2021;104:49–53.
22. Schachner MB, Sommer JA, González ZA, Luna DR, Benítez SE. Evaluating the feasibility of using mobile devices for nurse documentation. Stud Health Technol Inf. 2016;225:495–9.
23. Zikos D, Diomidous M, Mpletsa V. The effect of an electronic documentation system on the trauma patient's length of stay in an emergency department. J Emerg Nurs. 2014;40(5):469–75.
24. Koch E, Lovett S, Nghiem T, Riggs RA, Rech MA. Shock index in the emergency department: utility and limitations. Open Access Emerg Med. 2019;11:179–99. https://doi.org/10.2147/OAEM.S178358. PMID: 31616192; PMCID: PMC6698590.
25. Książczyk M, Dębska-Kozłowska A, Warchoł I, Lubiński A. Enhancing healthcare access-smartphone apps in arrhythmia screening: viewpoint. JMIR Mhealth Uhealth. 2021;9(8):e23425. https://doi.org/10.2196/23425
26. Hunt B, Ruiz A, Pogue B. Smartphone-based imaging systems for medical applications: a critical review. J Biomed Opt. 2021;26(4):040902. https://doi.org/10.1117/1.JBO.26.4.040902
27. Bairapareddy KC, Alaparthi GK, Jitendra RS, Prathiksha, Rao PP, Shetty V, et al. "We are so close; yet too far": perceived barriers to smartphone-based telerehabilitation among healthcare providers and patients with chronic obstructive pulmonary disease in India. Heliyon. 2021;7(8):e07857. https://doi.org/10.1016/j.heliyon.2021.e07857
28. Zhang GX, Chen KJ, Zhu HT, Lin AL, Liu ZH, Liu LC, et al. Preventable deaths in multiple trauma patients: the importance of auditing and continuous quality improvement. World J Surg. 2020;44(6):1835–43.
29. Li G, Jin C, Zhao B, Wu B. Smartphone use, technology affordance for healthcare and elders' life satisfaction. Front Public Health. 2022;10:861897. https://doi.org/10.3389/fpubh.2022.861897
30. Bentvelsen RG, Holten E, Chavannes NH, Veldkamp KE. eHealth for the prevention of healthcare-associated infections: a scoping review. J Hosp Infect. 2021;113:96–103. https://doi.org/10.1016/j.jhin.2021.04.029
31. Alharbi RJ, Shrestha S, Lewis V, Miller C. The effectiveness of trauma care systems at different stages of development in reducing mortality: a systematic review and meta-analysis. World J Emerg Surg. 2021;16(1):38. https://doi.org/10.1186/s13017-021-00381-0
32. Binks F, Wallis LA, Stassen W. The development of consensus-based descriptors for low-acuity emergency medical services cases for the South African setting. Prehospital Disaster Med. 2021;36(3):287–94. https://doi.org/10.1017/S1049023X21000169
33. Gamberini L, Picoco C, Del Giudice D, Zenesini C, Tartaglione M, Coniglio C, et al. Improving the appropriateness of advanced life support teams' dispatch: a before-after study. Prehospital Disaster Med. 2021;36(2):195–201. https://doi.org/10.1017/S1049023X21000030

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Research Article

A Theory-Based, Technology-Assisted Intervention in a Hybrid Cardiac Rehabilitation Program for Patients with Coronary Heart Disease: A Feasibility Study

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SUMMARY

Purpose: To assess the feasibility of a technology-assisted intervention in a hybrid cardiac rehabilitation program among patients with coronary heart disease.
Methods: This study was a two-arm parallel randomized controlled trial. Twenty-eight patients with coronary heart disease were randomly assigned to either the intervention group, receiving a 12-week technology-assisted intervention ($n = 14$), or the control group ($n = 14$), receiving usual care. Guided by the Health Belief Model, the intervention group received three center-based, supervised exercise training sessions, a fitness watch that served as a cue to action, six educational videos, and a weekly video call. The Self-efficacy for Exercise, exercise capacity, and Health Promoting Lifestyle Profile II were assessed at baseline and immediately post-intervention (12-weeks).
Results: Among the 28 patients who participated in this study, 85.7% completed the program, with a relatively low attrition rate (14.3%). The number of exercise training sessions accomplished by the participants in the intervention group was 51.27 ± 19.41 out of 60 sessions (85.5%) compared to 36.46 ± 23.05 (60.8%) in the control group. No cardiac adverse events or hospitalizations were reported throughout the study. Participants in the intervention group showed greater improvement in health-promoting behaviors when compared with the control group at 12 weeks. Within-group effects demonstrated improvement in exercise self-efficacy and exercise capacity among participants in the intervention group. A participant satisfaction survey conducted immediately post-intervention revealed that participants were “very satisfied” (23.1%) and “satisfied” (76.9%) with the technology-assisted intervention.
Conclusions: The findings demonstrated that technology-assisted intervention in a hybrid cardiac rehabilitation program was feasible and suggested to be beneficial in improving exercise self-efficacy, exercise capacity, and health promoting behavior among patients with coronary heart disease. A full-scale study is needed to determine its effectiveness in the long term.
Trial and protocol registration: ClinicalTrials.gov NCT04862351.
https://clinicaltrials.gov/ct2/show/NCT04862351.

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of global mortality, with approximately 18 million people dying of CVDs each year, contributing to 32% of all deaths [1]. Cardiac rehabilitation (CR) is a comprehensive care model that includes structured exercise training, psychological support, and health education for patients with CVD such as coronary heart disease (CHD), heart failure, and those who underwent coronary revascularization [2]. According to the European Society of Cardiology, CR is

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classified as a class 1A recommendation [3]. Besides reducing long-term hospital readmissions by 52%, CR is associated with a 78% lower risk of death from all causes [4]. Patients who participated in CR reported significantly improved exercise capacity, blood lipid profile, psychological outcomes, and quality of life [5]. Despite the benefits of CR, participation and adherence rates are relatively low, ranging between 31% and 43% and 36.7% and 84.6%, respectively [6]. A previous retrospective cohort study reported a dropout rate of 24% [7]. Based on a narrative review, the CR dropout rates were even higher in the middle-income countries, which could be up to 82% [8]. Several traditional barriers to CR have been identified in previous studies, including a lack of self-efficacy and perceived benefits of CR, access (distance and transportation), and travel or work conflicts [9,10]. Given there is a need to improve the participation and adherence to CR, it is time to develop an alternative approach using technologies to deliver CR especially in the midst of the COVID-19 pandemic, and investigate its feasibility in the real-world settings.

The COVID-19 pandemic has further reduced CR attendance and completion due to patients' fear of face-to-face attendance at health services and limited service access. In the early days of the pandemic, ambulatory and nonessential services were temporarily closed while CR programs were reduced or stopped, and recruitment of new patients was halted [11]. This phenomenon reinforced the urgent need to provide alternatives to conventional, center-based CR, such as home-based or hybrid (a combination of center-based and home-based) CR. A global survey suggested the need to support alternative models that provide CR programs outside of major institutions to reach a vast number of eligible patients [12]. There are several terminologies of technology-assisted interventions in CR including eHealth, telehealth/telemedicine, and mobile health (mHealth) [13]. The utilization of technology for CR delivery has been proliferating, and in recent years, previous studies have examined a web-based educational support intervention [14] and an exercise-based telerehabilitation program [15]. Both studies demonstrated positive patient outcomes. Hence, this is the time to focus more on CR delivery using technologies to boost utilization and promote its availability and accessibility to eligible patients. A previous mixed-methods study reported that the majority of patients with chronic diseases preferred combined in-person visits and telerehabilitation [16] Nevertheless, there is a lack of literature on hybrid CR programs. It would be interesting to examine the feasibility of a hybrid CR program, particularly during the COVID-19 pandemic, which may pose additional challenges to patients.

Although findings from the aforementioned studies that delivered technology-assisted interventions have shown promising results in the improvement of patient outcomes, they lacked interactive approaches (synchronous communication) and follow-up interventions (e.g., a weekly video/telephone call). Also, the feasibility of implementation in Southeast Asia, especially in a multicultural, high- middle-income country, is uncertain, and limited evidence is available on cardiac rehabilitation. This study aimed to explore the feasibility of a technology-assisted intervention in a hybrid cardiac rehabilitation (TecHCR) program among patients with CHD based on four key areas; implementation, practicality, limited-efficacy testing, and acceptability [17].

Methods

Study design

This was a single site, two-arm, parallel randomized controlled trial (RCT).

Study setting

This study was conducted in an outpatient CR clinic of the largest teaching hospital in Malaysia. On average, 25 patients with CHD were referred to the phase II CR program per month. The study recruitment was conducted from March to May 2021 with a 12-week post-intervention assessment, and registered with the U.S. National Library of Medicine, ClinicalTrials.gov (Registration Number: NCT04862351).

Participants and sample

A consecutive sampling method was used to recruit participants for this study. A list of eligible patients was obtained from the outpatient CR clinic on a weekly basis. The eligible patients were approached at the Non-invasive Cardiology Clinic after their exercise stress test. Study inclusion criteria were: 1) adults $\geq$18 years old; 2) clinically diagnosed coronary heart disease; 3) treated with thrombolytic therapy or percutaneous coronary intervention (PCI) or revascularization surgery; 4) stratified into low or moderate risk for cardiac events by a rehabilitation medicine physician based on clinical assessments and exercise stress tests as per American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) guidelines; 5) own a smartphone with Internet access; 6) literate; 7) understand English or Malay language; 8) return home for living after hospital discharge; and 9) medically stable, referred to the CR program and able to give informed consent to participate in this study. Exclusion criteria included: 1) participating in other studies; 2) comorbidities such as dementia, impaired hearing or vision, or psychiatric illness that might affect their ability to participate in the CR program; and 3) pre-existing mobility problems that prevent them from exercising.

As suggested by Julious et al. [18], a sample size of 12 participants per group in a 2-arm parallel trial is adequate to preliminarily estimate effect sizes for the size planning of a full-scale trial. Further allowing for some attrition, we aimed to recruit a total of 28 participants (14 participants per study group).

Randomization, allocation and blinding

Consented participants were randomly allocated to either the intervention group (TecHCR, $n = 14$) or control group (usual care, $n = 14$) in a 1:1 ratio based on computer-generated random codes. Allocation was concealed by using sequentially numbered, opaque, and sealed envelopes. Due to the nature of the study, participants were unable to be blinded to the group allocation but were strongly advised against disclosing the group assignment to other patients. The outcome assessor was blinded to group allocation and study hypotheses.

Theoretical framework

A theoretical framework may guide the design of interventions and increase the probability of successful outcomes [19]. Only about one-third of the included studies in a recent systematic review used behavior change theory, with a lack of description of the theoretical framework integrated into the intervention components [13]. A review by Timlin et al. [20] mentioned that poor theory application to intervention design and fidelity might explain the inconclusive effectiveness of an intervention.

The Health Belief Model (HBM) was chosen in this study as this model has yielded significant results in research, and the six constructs (perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy) are suitable to be included in a framework for developing short-term

and long-term behavioral change interventions [21]. A scoping review identified that both perceived barriers and perceived benefits were the strongest predictors of health behaviors [22]. HBM has been used as a framework in previous CR studies to guide the implementation of an educational support intervention through a web link [14] and examine the motivation and barriers to attending a CR maintenance program [23]. The primary concepts of HBM include accepting the diagnosis, believing that the condition may have serious consequences, and believing that the susceptibility or severity of the condition may be reduced by a course of action [24]. To make a change in behavior, an individual must have a change in belief; they need to recognize the risks and consequences of a condition, as knowledge alone is inadequate to make behavioral changes [25]. Once an individual has made behavior changes, motivation is maintained through self-efficacy, which provides self-regulation of behavior [26]. Evidence suggests that HBM constructs could be applicable in the development of behavioral change interventions. Therefore, HBM may be suitable to underpin the intervention design to promote behavioral changes in a hybrid CR program that provides a transition from face-to-face, center-based CR to home-based CR. Table 1 presents the details of the development of the TecHCR intervention based on the HBM constructs.

Control group

Participants randomized to center-based CR (CCR) had the usual care for 6 or 8 sessions at the outpatient clinic depending on their stratified risk category (6 sessions for low risk and 8 sessions for moderate risk) as per hospital policy during the pandemic, including 1-hour individualized exercise training and 1-hour occupational therapy. Each exercise training session consisted of a 10-minute warm-up, 30 minutes of moderate-intensity exercise and a 10-minute cool down supervised by a physiotherapist. End-of-session education [e.g., symptoms to watch out for during exercise, Rating of Perceived Exertion (RPE) scale] and feedback were provided by the physiotherapist. The exercise prescription was based on age, stress test results, and exercise tolerance, with each participant having an individualized target heart rate while exercising at home. All participants were encouraged to exercise for $\geq$30 minutes at least five days/week (150 minutes/week) of moderate intensity, following the guidelines from the World Health Organization [27]. For the occupational therapy, participants received education on topics including stress and anxiety management, time management, sleep hygiene, and relaxation techniques, and relaxation sessions. Both participants in the control and intervention groups received a daily log (checklist with exercise and dietary practices) to balance the psychological effect.

Intervention group

The principal investigator (an experienced nurse) would demonstrate how to use a wearable technology (a fitness watch), upload the exercise data, and sign in to the video call application with each recruited participant, followed by a return demonstration. Participants received three sessions of usual care at the outpatient clinic scheduled for Week 1, Week 3, and Week 12. Each session consisted of 1 hour of individualized exercise training and 1 hour of occupational therapy. The first two (Week 1 and Week 3) supervised exercise training sessions were intended to prepare the participants to be able to exercise in a home environment, allowing the transition of exercise training from the center to home. The third session (the last session, Week 12) was to recap the previous sessions and act as a closure of the exercise training sessions for phase II CR before entering maintenance phase III CR.

Participants were asked to wear the fitness watch to record their heart rate, exercise frequency, and duration during the exercise training at home. The exercise training data were synced to the Zepp App by each participant. Simultaneously, the data were automatically pulled into the UMFit website, allowing the principal investigator to review the exercise data on a weekly basis. Over 12 weeks, participants received a weekly video call that lasted for approximately 30 minutes each for the following purposes: 1) to strengthen participants' self-efficacy in recommended health behaviors, 2) to improve perceived benefits, 3) to enhance problem-solving skills (i.e., how to improve perceived barriers), and 4) to provide reinforcement for positive changes 4). From Week 1 to Week 6, participants received a weekly audio-visual educational video via a messaging application (a total of six videos).

Technical support was provided to the participants in the TecHCR group. First, the principal investigator ensured the participants knew how to use the technologies by assessing their demonstrations. If participants encountered any technological issues, they were able to get support via telephone call, text messaging, or video call.

Measurements

1. Implementation

The implementation was assessed by examining the recruitment process within a specified period with data such as the number of eligible patients for screening, the number of patients randomized into the intervention and control groups, reasons for declining participation, and the number of follow-ups. To determine whether the study protocol could be executed as planned, the attrition rate and treatment adherence were assessed. Treatment adherence was defined as a percentage of the total exercise sessions accomplished by the participants [28]. In total, each participant should have 60 exercise training units, considering a recommended exercise schedule of 5 days/week $\times$ 12 weeks. For participants in the CCR, the number of supervised exercise training sessions at the outpatient clinic was recorded, and daily log exercise entries were counted. The exercise data for each participant in TecHCR was extracted from the UMFit website, and daily log exercise entries were counted.

2. Practicality

One of the outcomes of interest in practicality is to explore the adverse effects on the target participants [17]. Based on a nationwide survey by Saito et al. [29], adverse events associated with CR were defined as incidents (e.g., unstable angina, acute myocardial infarction, cardiac arrest, mortality, stroke, and severe musculoskeletal injury) that happened during exercise or within 24 hours after an exercise session. In this study, participants were required to report any adverse events throughout the program. Data related to adverse events (i.e., reasons for outpatient visits or hospital admissions) were also collected from the patient's electronic medical record.

3. Limited-efficacy testing

An intervention in a feasibility study will be tested in a limited way, including with limited statistical power or a shorter duration of follow-up [17]. In this study, limited-efficacy testing was performed on the following outcomes; exercise self-efficacy, exercise capacity, and health-promoting behavior, specifically looking at the intended effects and effect size estimation at 12-week follow-up.

Table 1 *Integration of Health Belief Model into a Technology-assisted Intervention in a Hybrid Cardiac Rehabilitation.*

Health Belief Model construct	Objectives	Content	Delivery mode	Component	Technological devices and software used
Perceived susceptibility and severity	To provide educational support with accurate information about cardiovascular risk factors, the consequences of the disease, and recommended action.	• Educational content includes: 1) Heart disease 2) Cardiovascular risk factors 3) Effects of a poor diet 4) Effects of stress 5) Effects of smoking	Asynchronous	Electronic learning	Smartphone and instant messaging app (WhatsApp)
Perceived benefit	To provide information on the benefits of a recommended healthy lifestyle and diet.	• Educational content includes: 1) Benefits of exercise for the heart 2) Benefits of a healthy diet 3) Benefits of quitting smoking 4) Benefits of stress management	Asynchronous	Electronic learning	Smartphone and instant messaging app (WhatsApp)
	To provide positive reinforcement to portray the positive benefits of adopting health behavior changes	• Congratulate the participant on his/her achievement (e.g., achieved target heart rate, reduced intake of sugar) • Check with the participant on his/her perception of adopting health behavior changes (e.g., "So far, how you feel after starting to exercise regularly?" "Did you notice the changes in your body with health diet and regular exercise?" • Affirm the positive feedback from the participant.	Synchronous	Telecoaching	Smartphone/laptop, and video communication service app (Google Meet).
Perceived barrier	To facilitate problem-solving strategies in patients to overcome barriers to adopting health behavior changes	• Assess the potential barriers and facilitators in adopting health behavior change (e.g., "What could be the factors prevented you from achieving the exercise frequency?") • Facilitate the participants to think of the possible ways of overcoming the barriers (e.g., "Now, let's think of some alternatives. What do you think about indoor exercises?")	Asynchronous	Electronic learning	Smartphone/laptop, and video communication service app (Google Meet).
Cues to action	The heart rate and exercise duration data on the fitness watch act as the biofeedback strategy that will be used as an external trigger.	• The fitness watch provides synchronous exercise data on the watch and Zepp App, allowing participants to monitor their exercise. • The fitness watch vibrates once the participant achieves certain goals such as 10000 steps.	Synchronous and Asynchronous	Wearable technology Telemonitoring	Commercial fitness watch and health monitor app (Zepp App) Note: participants have to sync the exercise data onto the health monitor app and researchers will receive the data on the UMFit website.
	To provide feedback and advice as external cues for participants to activate the recommended health actions	• Review the exercise data for the past 7 days. • Recap the goals set for the past 7 days. • Remind the participant the importance of achieving the recommended health actions.	Synchronous	Telecoaching	Smartphone/laptop, and video communication service app (Google Meet).
Self-efficacy	To build participant's beliefs about his/her ability to adopt health behavioral changes by using incremental goal setting strategies	• Assess the confidence level of the participant in making changes to his/her lifestyle (e.g., how would you describe your confidence level in making your diet healthier in the past one week? • Review the participant's progress for the past 7 days. • Validate the participant's efforts to make progress. • Focus on incremental goals (e.g., You have made a great effort in exercising for 100 minutes for the past 7 days, what about	Synchronous	Telecoaching	Smartphone/laptop, and video communication service app (Google Meet).

(*continued on next page*)

Table 1 (*continued*)

Health Belief Model construct	Objectives	Content	Delivery mode	Component	Technological devices and software used
		increasing the duration to 120 minutes this week? Let's say 4 days a week and 30 minutes each time?			

The primary outcome for this study was exercise self-efficacy, which significantly predicted the initiation of exercise and its maintenance [30]. The secondary outcomes were exercise capacity and health-promoting behavior.

Exercise self-efficacy was measured by Bandura's 18-item exercise self-efficacy scale (ESE) to assess the perceived self-efficacy to get oneself to perform an exercise routine regularly [31]. For the English version, each item is rated from 0 representing "cannot do at all" to 100 representing "highly certain can do", with a higher score indicating a higher level of self-efficacy. It has a high internal consistency, with a Cronbach's α of 0.95 in a CR setting [32]. The Malay version of ESE has a significant factor loading of more than 0.40 and an intra-class correlation of 0.99 [33]. For this study, we quantified the response of each item following the Malay version, a 5-point response scale from 1 "not at all confident" to 5 "extremely confident". The current study showed good reliability of ESE with a Cronbach's α of 0.98.

The exercise capacity was assessed by the metabolic equivalent of task (MET), determined by an exercise stress test with modified Bruce Protocol, conducted at the non-invasive cardiology laboratory by a rehabilitation medicine physician and a trained technician. One MET equals 3.5 ml of oxygen/kg (body weight)/minute, the consumption of oxygen while sitting at rest [34]. In our study, a treadmill (T-2100, GE Case Stress System V6.73) was used for the exercise stress test with a modified Bruce Protocol. According to the guidelines by the American College of Sports Medicine [35], Stage 1 to Stage 3 (3 minutes for each interval) of the protocol has a constant speed of 1.7 mph and the grade (inclination) increases by 5%; from Stage 4 onwards, both speed and grade increase every 3 minutes and the test will be terminated when the patient reaches volitional exhaustion. During the test, participants had continuous real-time 12-lead ECG and heart rate monitoring. The participant's blood pressure was measured before, at the last 45 seconds of each stage, immediately post-exercise stress test, and every 2 minutes thereafter [35]. The MET was automatically recorded by the treadmill controller based on its speed and grade [36]. Higher METs indicate higher exercise capacity.

The Health Promoting Lifestyle Profile II (HPLP II) was used to measure participants health-promoting behaviors. It consists of six subscales: health responsibility, self-actualization, physical activity, interpersonal relationships, nutrition, and stress management, with a 4-point response scale of 1 (never), 2 (sometimes), 3 (often), and 4 (routinely) [37]. The mean shall be used as the overall score for the 52-item scale as well as the mean of each subscale to maintain the 1–4 metric of item responses. Both the English and Malay versions of HPLP II have shown high internal consistency, with the α coefficients for the subscales ranging from 0.793 to 0.872 [37] and 0.737 to 0.878 [38], respectively. A CR-related study used this instrument to measure one of its outcomes [39]. The current study demonstrated good reliability with a α coefficient of 0.97.

4. Acceptability

Acceptability of the program focused on the perceived satisfaction among targeted participants related to the intervention. A self-reported program satisfaction survey by Chiang [40] was adopted and used to determine the acceptability of the TecHCR intervention among the participants. It consists of five statements on participant perceptions of TecHCR intervention, including TecHCR design, program duration, relevance of the educational information, performance of the intervener, and overall satisfaction with TecHCR. This instrument is based on a 5-point Likert scale, from a scale of 1 = "very unsatisfied", 2 = "unsatisfied", 3 = "neutral", 4 = "satisfied", and 5 = "very satisfied".

Procedure

Assessments were conducted at two time points: [baseline (T0) and 12-week, immediate post-intervention (T1)]. All participants completed the sociodemographic and clinical data questionnaires on, exercise self-efficacy, exercise capacity, and health-promoting behaviors at T0 before randomization. The sociodemographic and clinical data of the participants, including age, gender, marital status, educational level, employment status, monthly household income, smoking status, comorbidities, current medications, distance from home to the CR center (kilometer), transportation mode, were obtained from the electronic medical record and a self-reported structured questionnaire. After 12 weeks (T1), data were collected during the post-intervention exercise stress test appointment, including exercise self-efficacy, exercise capacity, health promoting behavior, treatment adherence, adverse events, and a program satisfaction survey.

Data analysis

IBM SPSS 25 (IBM Crop. Armonk, NY) was used to perform the statistical analyses. As this feasibility study had a relatively small sample size and a 12-week follow-up, there was no missing data detected, but those who dropped out were not included in the final analysis. Skewness and Q-Q plots were assessed to check the normality assumption. The baseline sociodemographic and clinical characteristics were described using mean and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Homogeneity of baseline characteristics between the TecHCR and control groups was assessed using the Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Statistical comparisons were performed within and between groups to describe the outcome variables across time points (T0 to T1) using the Wilcoxon signed rank test and Mann-Whitney test, respectively. The change in each outcome (T1 − T0) was compared between groups and used for effect size estimation. Following the recommendation by Tijssen and Kolm [41] for pilot studies with small sample sizes, the main focus of the outcome analysis was effect size estimations rather than their significance multiplicity correction was therefore not performed. Hedges' g effect sizes and their 95% confidence intervals for the outcomes were calculated using the online calculator: https://www.psychometrica.de/effect_size.html. All the statistical tests involved were two-sided with level of significance set at 0.05.

Ethical considerations

Ethical approvals were obtained from the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (Reference Number: 2020.621) and University of Malaya Medical Centre-Medical Research Ethics Committee (Reference No. 202117-9674). Prior to randomization, written informed consent was sought from each participant. Assurance was provided to participants that their identity and personal data would be kept confidential. Participants were informed that they had the right to withdraw from the study at any time without affecting their treatment in the study setting. If the findings demonstrate effective intervention outcomes, the TecHCR may be provided to participants in the control group after the completion of the main study.

Results

Table 2 summarizes the baseline characteristics of the participants. The mean age of participants was 54.6 ± 12.6 vs. 58.4 ± 13.6 years (range 35–74) and predominantly male (96.4%) with only one female participant. Most of them were married (92.9%), with more than half of the participants having secondary school education (57.1%) and self-driving from home to the CR center (64.3%), with a distance between 5 and 40 kilometers. Four participants were stratified into moderate-risk groups (1 participant vs. 3 participants). The majority of the participants were diagnosed with hypertension (78.6%) and dyslipidemia (89.3%). Out of 28 participants, 67.9% had PCI. Over half (64.3%) of the participants in TecHCR had a family history of CHD. TecHCR and control groups were generally homogeneous regarding baseline characteristics, except that the latter had a low proportion of participants using beta-blockers. In view of the small sample size, no further adjustment was made to the statistical analysis.

1. Implementation

Among the 67 patients screened for eligibility, 35 were excluded as they did not fulfill the inclusion criteria. Out of the 32 patients who were invited to participate in the study, four declined due to a lack of interest in participating. Twenty-eight patients (87.5%) agreed and consented, with 14 participants in each arm of the study. Among the participants ($N = 28$) who completed the baseline assessment (T0), a total of four were lost to follow-up during the 12-week program. Three participants from the TecHCR dropped out due to fear of attending face-to-face supervised exercise training during high daily COVID-19 cases ($n = 1$), were diagnosed with COVID-19 ($n = 1$), and left to work abroad ($n = 1$), and one participant from the CCR dropped out due to fear of attending the outpatient, center-based CR appointments ($n = 1$), representing an attrition rate of 14.3%. At 12-weeks, a total of 24 participants completed the study, with 11 and 13 participants in the TecHCR and CCR, respectively (Figure 1).

The treatment adherence of participants is shown in Table 3. Participants from TecHCR who completed the post-intervention assessment ($n = 11$) accomplished 51.27 ± 25.22 exercise training sessions (85.5%), in the range between 12 and 84 exercise training sessions within the 12 weeks of intervention. However, only 9 out of 11 participants (81.8%) in the TecHCR group performed at least 150 minutes of exercise each week. Two participants who were unable to perform the targeted duration of exercise per week provided reasons, including 1) the unavailability of a conducive environment for exercise due to the closure of parks and 2) a lack of time due to work commitments. Completers in the TecHCR attended all video call sessions except for one participant who had to be contacted five times using telephone calls due to work. Thirteen participants from CCR who completed the post-intervention assessment performed 36.46 ± 25.03 exercise training sessions (60.5%), in the range between 10 and 84 exercise training sessions. Seven out of 13 participants (53.8%) in the control group performed at least 150 minutes of exercise per week. Reasons for failing to achieve exercise duration in a week were similar to those in the intervention group, including a lack of motivation.

Table 2 *Baseline Sociodemographic and Clinical Characteristics of the Study Sample (N = 28).*

Characteristics	Intervention ($n = 14$) *n* (%)	Control ($n = 14$) *n* (%)	*p*
Age (years)[a] [range: 35–74]	54.6 (12.6)	58.4 (13.6)	.608[b]
Gender			
Men	13 (92.9)	14 (100.0)	.999[c]
Women	1 (7.1)	0 (0)	
Ethnicity			.999[c]
Malay	8 (57.1)	8 (57.1)	
Chinese	4 (25.0)	3 (21.4)	
Indian	2 (14.3)	3 (21.4)	
Occupation			.454[c]
Employed	4 (28.6)	7 (50.0)	
Unemployed	3 (21.4)	1 (7.1)	
Home maker	1 (7.1)	0 (0)	
Retired	6 (42.9)	6 (42.9)	
Monthly household income (RM)			.999[c]
<5000 (<US$ 1220)	9 (64.3)	10 (71.4)	
≥5000 (≥US$ 1220)	5 (35.7)	4 (28.6)	
Marital status			.481[c]
Married	14 (100.0)	12 (85.7)	
Single/divorced/married	0 (0)	2 (14.3)	
Education			.999[c]
Primary	0 (0)	1 (7.1)	
Secondary	8 (57.1)	8 (57.1)	
Tertiary	6 (42.9)	5 (35.7)	
Driving to cardiac rehabilitation center	11 (78.6)	7 (50.0)	.423[c]
Distance from home to rehabilitation center (kilometres)[a] [range: 5–40]`	19.0 (12.3)	16.8 (8.6)	.361[b]
Coronary family history	9 (64.3)	5 (35.7)	.257[c]
Smoking status			
Never	7 (50.0)	4 (28.6)	.239[c]
Former smoker	7 (50.0)	7 (50.0)	
Current smoker	0 (0)	3 (21.4)	
AACVPR risk category			.596[c]
Low	13 (92.9)	11 (78.6)	
Moderate	1 (7.1)	3 (21.4)	
Hypertension	13 (92.9)	9 (64.3)	.165[c]
Dyslipidemia	12 (85.7)	13 (92.9)	.999[c]
Diabetes	7 (50.0)	6 (53.8)	.999[c]
Percutaneous coronary intervention	10 (71.4)	9 (64.3)	.999[c]
Coronary artery bypass graft surgery	4 (28.6)	4 (28.6)	.999[c]
Medication			
Antiplatelet	14 (100.0)	14 (100.0)	–
Nitrates	3 (21.4)	1 (7.1)	.596[c]
Beta-blocker	14 (100.0)	7 (50.0)	.006[c]
ACE inhibitors/Angiotensin receptor blocker	8 (57.1)	8 (57.1)	.999[c]
Calcium channel blocker	9 (64.3)	3 (21.4)	.678[c]
Statin	14 (100.0)	14 (100.0)	–

Note. AACVPR = American Association of Cardiovascular and Pulmonary Rehabilitation.
[a] Mean (standard deviation), others are presented as frequency (%).
[b] Mann-Whitney test.
[c] Fisher's exact test.

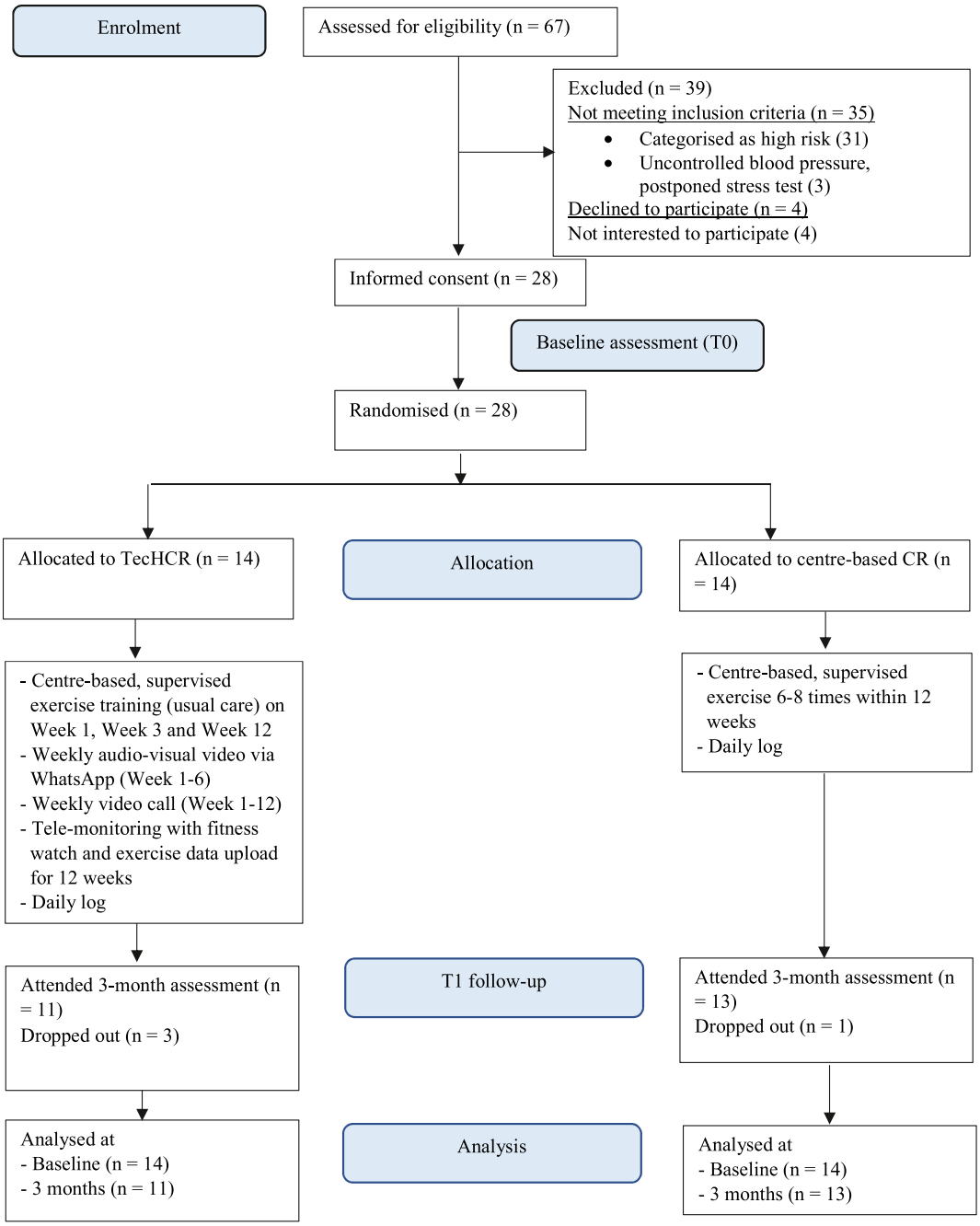

Figure 1. Study Design and Recruitment Flow Diagram.

2. Practicality

No adverse events were reported by the participants or found in the patient's electronic medical record. Unrelated to the interventions, one of the participants in the TecHCR group was diagnosed with COVID-19 positivity in the midst of the program and chose to discontinue the program while serving home quarantine.

3. Limited-efficacy testing of TecHCR on exercise self-efficacy, exercise capacity, and health-promoting behavior.

Table 4 presents the results of limited-efficacy testing in the study. The results of the Wilcoxon signed rank test indicated that TecHCR had a significant within-group effect over the 12-week course of study in exercise self-efficacy, exercise capacity, and health-promoting behavior. In addition, the Mann-Whitney test showed a significant improvement in health-promoting behavior in TecHCR when compared with CCR (Hedges' g effect size = 1.04, 95% CI: 0.19 to 1.90, $p = 0.007$). However, no differences on exercise self-efficacy (Hedges' g effect size = 0.47, 95% CI: −0.35 to 1.28, $p = 0.323$) or exercise capacity (Hedges' g effect size = 0.17, 95% CI: −0.64 to 0.97, $p = 0.132$) were detected between groups.

4. Acceptability

Table 5 shows that the majority of the participants (69.2%) were very satisfied, and the remaining (30.8%) were also satisfied (30.8%)

Table 3 *Treatment Adherence of the Control and Intervention Groups.*

Treatment adherence	Control ($n = 13$)		Intervention ($n = 11$)	
	Mean (SD)	(%)	Mean (SD)	(%)
Exercise training sessions (range: 0 −60)	36.46 (25.03)	60.5	51.27 (25.22)	85.5
Exercise duration (minutes/week) (achieved ≥150 minutes/week)	7[a]	53.8	9[b]	81.8

[a] Frequency − 7 out of 13 participants in the control group performed ≥150 minutes of exercise per week.
[b] Frequency − 9 out of 11 participants in the intervention group performed ≥150 minutes of exercise per week.

Table 5 *Participant Satisfaction of TecHCR Program (N = 11).*

	Very satisfied	Satisfied	Neutral	Unsatisfied	Very unsatisfied
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Intervention design	9 (69.2)	4 (30.8)	0 (0)	0 (0)	0 (0)
Duration	3 (23.1)	7 (53.8)	3 (23.1)	0 (0)	0 (0)
Relevance of information	7 (53.8)	6 (46.2)	0 (0)	0 (0)	0 (0)
Performance of intervener	8 (61.5)	5 (38.5)	0 (0)	0 (0)	0 (0)
Overall satisfaction of the program	3 (23.1)	10 (76.9)	0 (0)	0 (0)	0 (0)

Note. TecHCR = Technology-assisted intervention in a hybrid cardiac rehabilitation data are presented in frequency (%).

with the intervention design. Participants were either very satisfied (23.1%) or satisfied (53.8%) with the duration of the program, but 23.1% reported being neutral. More than half of the participants (53.8%) were very satisfied with the relevance of the educational information, and 61.5% were very satisfied with the performance of the intervener. Overall, the participants were very satisfied (23.1%) and satisfied (76.9%) with the TecHCR program.

Discussion

Our findings suggest that technology-assisted intervention, including supervised exercise training sessions (three times at the center), a wearable technology (a fitness watch), educational videos, and telecoaching (a weekly video call), is feasible. Given the fact that this study was conducted during the COVID-19 pandemic and the non-invasive cardiology clinic only conducts the exercise stress test for patients referred to CR once a week, recruitment proceeded smoothly, with only four out of 32 eligible patients rejecting participation. In recent years, much attention has been paid to improving CR among underrepresented groups, especially women, with meta-analyses reporting significantly lower referral rates among women when compared with men [42]. Despite our study setting providing automatic referral to CR for all eligible patients, the number of females with CVD in Malaysia was lower than the males; amongst the individuals who had undergone PCI, only 17% of them were females [43]. Therefore, it was not surprising that there were only two female, eligible patients during our recruitment period; one female participant consented while another female declined our invitation to participate in the study due to a lack of interest in participating in a trial.

Overall, the completion rate of our study was a notable 85.7%. This is comparable to the results of a recent RCT by Batalik et al. [28], which demonstrated a completion rate of 91% in a 12-week home-based telerehabilitation. With respect to treatment adherence, our TecHCR group showed greater exercise training adherence when compared to the center-based CR program (85.5% versus 60.5%). A recently published systematic review revealed that nine out of 14 included studies demonstrated greater treatment adherence among patients who had digital interventions compared to conventional CR [44]. In contrast, a meta-analysis by Chong et al. [13] reported that no significant differences in treatment adherence were found between home-based/hybrid CR and center-based CR. These previous results were rather inconclusive. A possible explanation of our desirable findings is that the HMB constructs of "external cues to action" and "self-efficacy," which were delivered through wearable technology (a fitness watch) and telecoaching (weekly video call), may in part account for the treatment adherence. Indeed, Odnoletkova et al. [45] reported that nurse-led telecoaching promotes health behavior changes that are aligned with the goals set by the patients.

Regarding practicality, we found no adverse effects reported by both groups in our study, suggesting TecHCR can be safely implemented among non-high-risk cardiac patients, even in elderly patients. A recent study on smartphone-based telemonitored exercise showed no occurrence of serious complications or adverse events throughout the study period [46]. According to Sanchis-Gomar et al. [47], there may be potential adverse events related to exercise training triggered by exercise intensity and physiological demands in certain individuals. In our study, precautions during exercise (i.e., measuring the intensity of physical activity with RPE and when to seek immediate medical attention) were emphasized

Table 4 *Outcomes Across Time Points between the Control and Intervention Groups.*

Outcome variables	Control			Intervention			Between group comparisons	
	Baseline measurement (T0) ($n = 14$)	Immediate post intervention (T1) ($n = 13$)	*p* (within-group comparison)[a]	Baseline measurement (T0) ($n = 14$)	Immediate post intervention (T1) ($n = 11$)	*p* (within-group comparison)[a]	Hedges' g effect size (95% CI)[b]	*p* (between-group comparison)[a]
Exercise self-efficacy (ESE)	38.1 (12.1)	45.5 (11.0)	.003	47.5 (20.6)	59.5 (15.9)	.012	0.47 (−0.35, 1.28)	.323
Exercise capacity (MET)	7.3 (2.3)	8.6 (2.7)	.058	8.6 (2.1)	10.0 (2.3)	.008	0.17 (−0.64, 0.97)	.132
Health promoting behavior (HPLP II)	132.9 (28.5)	140.9 (28.0)	.001	130.3 (23.9)	150.5 (19.8)	.004	1.04 (0.19, 1.90)	.007

Note. MET = metabolic equivalent of task; ESE = Exercise Self-Efficacy; HPLP = Health-Promoting Lifestyle Profile II.
Data are presented as mean (standard deviation).
[a] Only those participants with both baseline and post intervention data were involved in within-group and between-group comparisons (i.e. $n = 13$ in control group and $n = 11$ in intervention group).
[b] Hedges'g effect size which corresponds to the standardized mean difference of the change score at T1 with respect to T0 between the intervention and control group.

to the participants in both groups. Hannan et al. [48] highlighted the lack of data collection on adverse events in CR studies with a specific protocol. Heindl et al. [49] suggested that future research should look into detailed reporting on patient assessment and home inspection before the commencement of exercise training in the home environment. This creates opportunities to identify the gaps in home-based exercise and improve measures to minimize the risks of adverse events before translating the evidence into clinical practice.

In this present study, results on the limited-efficacy testing were desirable. We observed a significant improvement in health-promoting behavior with a large effect size ($g = 1.04$) following the intervention. Similarly, a recent RCT that delivered the eHealth approach in CR also demonstrated significantly improved the health-promoting behavior at 12-week post-intervention [39]. Zafari Nobari et al. [50] reported that a healthy lifestyle empowerment program significantly improved the health-promoting behavior of patients with coronary bypass graft surgery. From the viewpoint of promoting a healthy lifestyle, TecHCR provided educational videos on topics related to physical activity and exercise, a healthy diet, stress management, and smoking cessation. Together with these videos, our telecoaching was intended to motivate participants to adopt healthy behavioral changes. These components of TecHCR might have contributed to improving perceived health promoting behavior among the participants. Although there was no statistical evidence in favor of TecHCR on exercise self-efficacy and exercise capacity, both showed relatively greater improvement than those of CCR. Smarz et al. [51] suggested that other than exercise dose, intensity, and adherence, the improvement of exercise capacity is also influenced by several potential, factors such as both cardiac and non-cardiac-related factors and comorbidities. Future research may examine exercise capacity based on stratification by comorbidity. Also, as the present study is a pilot study with a relatively small sample size, a larger sample size may be required to statistically detect significant differences in both exercise self-efficacy and exercise capacity.

Successful implementation of an intervention in a real-world, clinical setting requires acceptability. Our study highlights the acceptability of TecHCR among participants from a wide range of ages, including older adults aged 60 years and above. All the participants in the TecHCR group were satisfied with the overall program, with three participants rating the program as “very satisfied” and 10 participants rating it as “satisfied”. We believe that this could be due to the fact that our participants were able to use the technologies throughout the program. A national survey by the Department of Statistics Malaysia [52] showed the vast majority of individuals had access to the Internet (96.8%) and mobile phone (98.7%), which allows additional options for patients other than the usual center-based CR. Of note, several barriers to adopting technology in CR among older adults include physical barriers such as visual and fine motor skills and technological anxiety [53]. In order to minimize the technical challenges during the present study, we assisted participants in the TecHCR group to install the apps upon recruitment and ensured they knew how to operate the fitness watch and apps by return demonstration. Taking into consideration of possible barriers among the older adults, our intervention was carefully planned to reduce complexity of the integrated technologies. We included a fitness watch that has a simple, user-friendly interface, educational videos that were sent to participants' messaging apps, and a weekly video call using Google Meet with a secured password. More than half of the participants were satisfied with the duration of the program. As of now, there is no identified optimal duration for a CR program, and it varies across countries. An explanation might be that the duration of 12 weeks might allow participants to achieve their optimal outcomes (i.e., physical function) as reported by Morrin et al. [54], and this could enhance their satisfaction. The majority of the participants in the current study reported being very satisfied with the relevance of the educational information. Gomez-Perez et al. [55] recommended contents that are useful, easy to understand, eye-catching, and well-designed. In our opinion, the audio-visual educational videos in the study were not only attention-grabbing with the use of colors and voice-over for the contents, but they also enabled participants to know more about CR, their disease, and other important components of CR, including exercise, diet, smoking cessation, and stress management. To the best of our knowledge, no previous studies have reported patient satisfaction with a nurse-led CR program as an outcome. Nonetheless, previous studies reported high levels of satisfaction among patients with primary care provided by nurse practitioners [56,57]. One possible explanation of our findings could be due to the nurse-patient rapport. We indirectly built the rapport through the weekly video call over 12 weeks. Communication is the cornerstone of patient-centered care, and effective communication skills are associated with improved patient satisfaction [58].

According to Bowen et al. [17], feasibility studies allow researchers to determine the applicability of the interventions and whether adjustments are needed to make them more applicable in practice, as these issues have to be solved before actual implementation. Crucially, our findings provide invaluable insights, showing that TecHCR can be potentially implemented in future research with a larger sample size. Despite a small sample size, the TecHCR was well accepted, creating potential equitable access to hybrid CR in the future. This innovation may be an alternative to facilitate the sustainability of the CR program in the midst of the pandemic. Besides, the integration of HBM in the intervention development may aid in the successful implementation of the intervention and improve patient outcomes.

Our study has several strengths and limitations. This study had substantially high completion and treatment adherence rates in the TecHCR group, with strategies such as proactive and timely technical support and video calls to enhance participant engagement through frequent positive reinforcement and problem-solving. Our participants aged between 35 and 74 years old, suggesting that the feasibility of TecHCR is not limited to younger participants who are deemed to be more technology savvy. However, this study was underpowered to detect statistical significance; a large-scale trial with a longer duration of follow-up is required to examine the effectiveness of the TecHCR on the outcome variables. Although the exercise capacity was objective data, other self-reported outcomes might be subject to social desirability bias. To the best of our knowledge, there is no available data on the reliability of MET measured by the treadmill used, which could be one of the limitations of the study. Another limitation included the lack of qualitative data on participant experience that could provide rich descriptions. Future research may consider an open-ended interview to yield in-depth responses from participants on their experiences and opinions about the program. Also, several internet connection problems caused disruptions in video call sessions. An assessment of the types of internet connections needs to be taken into consideration. Due to the nature of this study, participants in the intervention group were expected to have basic Internet skills to use the fitness watch and mobile applications. The findings might not be generalizable to patients who are not able to use the technologies independently.

Contemporary CR programs that included patient education and exercise training were established in developed countries as early as the 1970s [59]. The COVID-19 pandemic has pushed forward the implementation of alternative models such as hybrid or home-based CR. However, limited literature is available on the CR

situation in developing countries or Southeast Asia. Due to limited resources, the pilot study was conducted in a country situated in Southeast Asia which might not be able to represent the whole region. Nonetheless, the findings of the current study will be able to provide insights to policymakers and health care providers in supporting the development of CR programs, particularly in developing countries.

Conclusion

The findings of this study demonstrate that theory-based TecHCR is feasible among the low- to moderate-risk cardiac patients referred to phase II CR. A high overall satisfaction rating for the program further supports the idea that TecHCR was acceptable among participants in the intervention group. The results of limited-efficacy testing demonstrated positive improvements in exercise self-efficacy, exercise capacity, and health-promoting behavior among patients in the TecHCR group. A full-scale RCT with a longer follow-up is warranted to provide more conclusive estimates of the benefits of TecHCR.

Ethical approvals

Ethical approvals were obtained from the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (Reference Number: 2020.621) on and University of Malaya Medical Centre-Medical Research Ethics Committee (Reference No. 202117-9674).

Author contributions

CMS, JSWH and CSY contributed to the concept and design of this pilot study. CMS provided the intervention and AS contributed in the recruitment and supervision of intervention. CMS and CKC completed the analysis and interpreted the results. CMS, JSWH, CKC, AS and CSY drafted and revised manuscript. All authors read and approved the final version of manuscript.

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Conflict of interest

None declared.

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References

1. World Health Organization. Cardiovascular diseases: key facts [Internet]. Geneva. 2021 June [cited 2022 April 10]. Available from https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Supervia M, Turk-Adawi K, Lopez-Jimenez F, Pesah E, Ding R, Britto RR, et al. Nature of cardiac rehabilitation around the globe. EClinicalMedicine. 2019;13:46–56. https://doi.org/10.1016/j.eclinm.2019.06.006
3. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227–337. https://doi.org/10.1093/eurheartj/ehab484
4. Graham HL, Lac A, Lee H, Benton MJ. Predicting long-term mortality, morbidity, and survival outcomes following a cardiac event: a cardiac rehabilitation study. Rehabil Process Outcome. 2019;8:1179572719827610. https://doi.org/10.1177/1179572719827610
5. Chair SY, Chan SW, Thompson DR, Leung KP, Ng SK. Effect of motivational interviewing on the clinical and psychological outcomes and health-related quality of life of cardiac rehabilitation patients with poor motivation. Hong Kong Med J. 2014;20(3 Suppl 3):15–9.
6. Resurrección DM, Moreno-Peral P, Gómez-Herranz M, Rubio-Valera M, Pastor L, Caldas de Almeida JM, et al. Factors associated with non-participation in and dropout from cardiac rehabilitation programmes: a systematic review of prospective cohort studies. Eur J Cardiovasc Nurs. 2019;18(1):38–47. https://doi.org/10.1177/1474515118783157
7. Brouwers RWM, Houben VJG, Kraal JJ, Spee RF, Kemps HMC. Predictors of cardiac rehabilitation referral, enrolment and completion after acute myocardial infarction: an exploratory study. Neth Heart J. 2021 Mar;29(3):151–7. https://doi.org/10.1007/s12471-020-01492-0
8. Turk-Adawi KI, Grace SL. Narrative review comparing the benefits of and participation in cardiac rehabilitation in high-, middle- and low-income countries. Heart Lung Circ. 2015;24(5):510–20. https://doi.org/10.1016/j.hlc.2014.11.013
9. Foster EJ, Munoz SA, Crabtree D, Leslie SJ, Gorely T. Barriers and facilitators to participating in cardiac rehabilitation and physical activity in a remote and rural population: a cross-sectional survey. Cardiol J. 2021;28(5):697–706. https://doi.org/10.5603/CJ.a2019.0091
10. Sérvio TC, Britto RR, de Melo Ghisi GL, da Silva LP, Silva LDN, Lima MMO, et al. Barriers to cardiac rehabilitation delivery in a low-resource setting from the perspective of healthcare administrators, rehabilitation providers, and cardiac patients. BMC Health Serv Res. 2019;615(1):19. https://doi.org/10.1186/s12913-019-4463-9
11. Vigorito C, Faggiano P, Mureddu GF. COVID-19 pandemic: what consequences for cardiac rehabilitation? Monaldi Arch Chest Dis. 2020;90(1). https://doi.org/10.4081/monaldi.2020.1315
12. Turk-Adawi K, Supervia M, Lopez-Jimenez F, Pesah E, Ding R, Britto RR, et al. Cardiac rehabilitation availability and density around the globe. EClinicalMedicine. 2019;13:31–45. https://doi.org/10.1016/j.eclinm.2019.06.007
13. Chong MS, Sit JWH, Karthikesu K, Chair SY. Effectiveness of technology-assisted cardiac rehabilitation: a systematic review and meta-analysis. Int J Nurs Stud. 2021;104087:124. https://doi.org/10.1016/j.ijnurstu.2021.104087
14. Wong EML, Leung DYP, Chair SY, Sit JWH. Effects of a web-based educational support intervention on total exercise and cardiovascular risk markers in adults with coronary heart disease. Worldviews Evid Based Nurs. 2020;17(4):283–92. https://doi.org/10.1111/wvn.12456
15. Maddison R, Rawstorn JC, Stewart RAH, Benatar J, Whittaker R, Rolleston A, et al. Effects and costs of real-time cardiac telerehabilitation: randomised controlled non-inferiority trial. Heart. 2019;105(2):122–9. https://doi.org/10.1136/heartjnl-2018-313189
16. Hwang R, Mandrusiak A, Morris NR, Peters R, Korczyk D, Bruning J, et al. Exploring patient experiences and perspectives of a heart failure telerehabilitation program: a mixed methods approach. Heart Lung. 2017;46(4):320–7. https://doi.org/10.1016/j.hrtlng.2017.03.004
17. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. Am J Prev Med. 2009;36(5):452–7. https://doi.org/10.1016/j.amepre.2009.02.002
18. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharm Stat. 2005;4(4):287–91. https://doi.org/10.1002/pst.185
19. Graham H, Prue-Owens K, Kirby J, Ramesh M. Systematic review of interventions designed to maintain or increase physical activity post-cardiac rehabilitation phase ii. Rehabil Process Outcome. 2020;9:1179572720941833. https://doi.org/10.1177/1179572720941833
20. Timlin D, McCormack JM, Kerr M, Keaver L, Simpson EEA. Are dietary interventions with a behaviour change theoretical framework effective in changing dietary patterns? A systematic review. BMC Public Health. 2020;1857(1):20. https://doi.org/10.1186/s12889-020-09985-8
21. Parandeh L, Shafaie FS, Malakouti J, Mirghafourvand M, Asghari-Jafarabadi M. The effect of educational text message based on health belief model on osteoporosis preventive behaviors in women: a randomized controlled clinical trial. Women Health. 2019;59(10):1128–40. https://doi.org/10.1080/03630242.2019.1590495
22. Sulat JS, Prabandari YS, Sanusi R, Hapsari ED, Santoso B. The validity of health belief model variables in predicting behavioral change: a scoping review. Health Educ. 2018;116(8):499–512.
23. Horwood H, Williams MJ, Mandic S. Examining motivations and barriers for attending maintenance community-based cardiac rehabilitation using the health-belief model. Heart Lung Circ. 2015 Oct;24(10):980–7. https://doi.org/10.1016/j.hlc.2015.03.023
24. Champion VL, Skinner CS. The health belief model. In: Glanz K, Rimer BK, Viswanath K K, editors. Health behavior and health education: theory, research and practice. San Francisco, CA: Jossey-Bass; 2008.
25. Rise MB, Pellerud A, Rygg LØ, Steinsbekk A. Making and maintaining lifestyle changes after participating in group based type 2 diabetes self-management educations: a qualitative study. PLoS One. 2013;8(5):e64009. https://doi.org/10.1371/journal.pone.0064009
26. Terbraak M, Verweij L, Jepma P, Buurman B, Jørstad H, Scholte Op Reimer W, et al. Feasibility of home-based cardiac rehabilitation in frail older patients: a clinical perspective. Physiother Theory Pract. 2022:1–16. https://doi.org/10.1080/09593985.2022.2025549

27. World Health Organization. Global Recommendations on Physical Activity for Health [Internet]. Geneva. 2010 Jan [cited 2022 April 10]. Available from: https://www.who.int/publications/i/item/9789241599979
28. Batalik L, Dosbaba F, Hartman M, Batalikova K, Spinar J. Benefits and effectiveness of using a wrist heart rate monitor as a telerehabilitation device in cardiac patients: a randomized controlled trial. Medicine (Baltimore). 2020;99(11):e19556. https://doi.org/10.1097/MD.0000000000019556
29. Saito M, Ueshima K, Saito M, Iwasaka T, Daida H, Kohzuki M, et al. Safety of exercise-based cardiac rehabilitation and exercise testing for cardiac patients in Japan: a nationwide survey. Circ J. 2014;78(7):1646–53. https://doi.org/10.1253/circj.cj-13-1590
30. Ha FJ, Hare DL, Cameron JD, Toukhsati SR. Heart failure and exercise: a narrative review of the role of self-efficacy. Heart Lung Circ. 2018;27(1):22–7. https://doi.org/10.1016/j.hlc.2017.08.012
31. Bandura A. Guide for constructing self-efficacy scales. In: Pajares F, Urdan T, editors. Self-efficacy beliefs of adolescents. Greenwich, CT: Information Age Publishing; 2006. p. 307–37.
32. Everett B, Salamonson Y, Davidson PM. Bandura's exercise self-efficacy scale: validation in an Australian cardiac rehabilitation setting. Int J Nurs Stud. 2009;46(6):824–9. https://doi.org/10.1016/j.ijnurstu.2009.01.016
33. Sabo A, Kueh YC, Kuan G. Psychometric properties of the Malay version of the self-efficacy for exercise scale. PLoS One. 2019;14(5):e0215698. https://doi.org/10.1371/journal.pone.0215698
34. Franklin BA, Brinks J, Berra K, Lavie CJ, Gordon NF, Sperling LS. Using metabolic equivalents in clinical practice. Am J Cardiol. 2018;121(3):382–7. https://doi.org/10.1016/j.amjcard.2017.10.033
35. Ligouri G. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. 11th ed. Philadelphia: Lippincott Williams & Wilkins; 2021.
36. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. Philadelphia: Lippincott Williams & Wilkins; 2013.
37. Walker SN, Hill-Polerecky DM. Psychometric evaluation of the Health Promoting Lifestyle Profile II. Unpublished manuscript. University of Nebraska Medical Center; 1996. p. 120–6.
38. Kuan G, Kueh YC, Abdullah N, Tai ELM. Psychometric properties of the health-promoting lifestyle profile II: cross-cultural validation of the Malay language version. BMC Public Health. 2019;751:19. https://doi.org/10.1186/s12889-019-7109-2
39. Su JJ, Yu DS. Effects of a nurse-led eHealth cardiac rehabilitation programme on health outcomes of patients with coronary heart disease: a randomised controlled trial. Int J Nurs Stud. 2021;104040:122. https://doi.org/10.1016/j.ijnurstu.2021.104040
40. Chiang CY. Effectiveness of nurse-led person-centered behavioral risk modification on secondary prevention of coronary heart disease [dissertation]. [Hong Kong]: The Chinese University of Hong Kong; 2016. p. 390.
41. Tijssen JG, Kolm P. Demystifying the new statistical recommendations: the use and reporting of p values. J Am Coll Cardiol. 2016;68(2):231–3. https://doi.org/10.1016/j.jacc.2016.05.026
42. Colella TJ, Gravely S, Marzolini S, Grace SL, Francis JA, Oh P, et al. Sex bias in referral of women to outpatient cardiac rehabilitation? a meta-analysis. Eur J Prev Cardiol. 2015;22(4):423–41. https://doi.org/10.1177/2047487314520783
43. Wan Ahmad WA. Annual report of the Malaysian NCVD-ACS Registry, Year 2017-2018. National cardiovascular disease database [Internet]. Malaysia; 2021 September [cited 2022 January 20]. Available from:. 2021 https://www.malaysianheart.org/files/614484cd4fa75.pdf
44. Wongvibulsin S, Habeos EE, Huynh PP, Xun H, Shan R, Porosnicu Rodriguez KA, et al. Digital health interventions for cardiac rehabilitation: systematic literature review. J Med Internet Res. 2021;23(2):e18773. https://doi.org/10.2196/18773
45. Odnoletkova I, Buysse H, Nobels F, Goderis G, Aertgeerts B, Annemans L, et al. Patient and provider acceptance of telecoaching in type 2 diabetes: a mixed-method study embedded in a randomised clinical trial. BMC Med Inform Decis Mak. 2016;142(1):16. https://doi.org/10.1186/s12911-016-0383-3
46. Song Y, Ren C, Liu P, Tao L, Zhao W, Gao W. Effect of smartphone-based telemonitored exercise rehabilitation among patients with coronary heart disease. J Cardiovasc Transl Res. 2020;13(4):659–67. https://doi.org/10.1007/s12265-019-09938-6
47. Sanchis-Gomar F, Lavie CJ, Marín J, Perez-Quilis C, Eijsvogels TMH, O'Keefe JH, et al. Exercise effects on cardiovascular disease: from basic aspects to clinical evidence. Cardiovasc Res. 2022;118(10):2253–66. https://doi.org/10.1093/cvr/cvab272
48. Hannan AL, Hing W, Simas V, Climstein M, Coombes JS, Jayasinghe R, et al. High-intensity interval training versus moderate-intensity continuous training within cardiac rehabilitation: a systematic review and meta-analysis. Open Access J Sports Med. 2018;9:1–17. https://doi.org/10.2147/OAJSM.S150596
49. Heindl B, Ramirez L, Joseph L, Clarkson S, Thomas R, Bittner V. Hybrid cardiac rehabilitation – the state of the science and the way forward. Prog Cardiovasc Dis. 2022;70:175–82. https://doi.org/10.1016/j.pcad.2021.12.004
50. Zafari Nobari S, Vasli P, Hosseini M, Nasiri M. Improving health-related quality of life and adherence to health-promoting behaviors among coronary artery bypass graft patients: a non-randomized controlled trial study. Qual Life Res. 2021;30(3):769–80. https://doi.org/10.1007/s11136-020-02675-3
51. Smarz K, Jaxa-Chamiec T, Zaborska B, Tysarowski M, Budaj A. Mechanisms of exercise capacity improvement after cardiac rehabilitation following myocardial infarction assessed with combined stress echocardiography and cardiopulmonary exercise testing. J Clin Med. 2021;10(18):4083. https://doi.org/10.3390/jcm10184083
52. Department of Statistics Malaysia. ICT use and access by individuals and households survey report, Malaysia 2021 [Internet]. Malaysia [cited 2022 April 1]. Available from: https://www.dosm.gov.my/v1/index.php?r=column/cthemeByCat&cat=395&bul_id=OWUvVnV5SHI2WFU2VFhnQ2ZjTm1Bdz09&menu_id=amVoWU54Utl0a21NW mdhMjFMMWcyZz09; 2021 April 12
53. Searcy RP, Summapund J, Estrin D, Pollack JP, Schoenthaler A, Troxel AB, et al. Mobile health technologies for older adults with cardiovascular disease: current evidence and future directions. Curr Geriatr Rep. 2019;8:31–42. https://doi.org/10.1007/s13670-019-0270-8
54. Morrin L, Black S, Reid R. Impact of duration in a cardiac rehabilitation program on coronary risk profile and health-related quality of life outcomes. J Cardiopulm Rehabil. 2000;20(2):115–21. https://doi.org/10.1097/00008483-200003000-00005
55. Gómez-Pérez D, Seron P, Oliveros MJ, Morales G, Arancibia MJ, Grace SL. Evaluation of counselling materials for hybrid cardiac rehabilitation in a low-resource setting: perceptions of patients and providers. Patient Educ Couns. 2023;107772. https://doi.org/10.1016/j.pec.2023.107772
56. Kippenbrock T, Emory J, Lee P, Odell E, Buron B, Morrison B. A national survey of nurse practitioners' patient satisfaction outcomes. Nurs Outlook. 2019;67(6):707–12. https://doi.org/10.1016/j.outlook.2019.04.010
57. Rickards T, Hamilton S. Patient experiences of primary care provided by nurse practitioners in New Brunswick, Canada. J Nurse Pract. 2020;16(4):299–304. https://doi.org/10.1016/j.nurpra.2019.12.027
58. Lofti M, Zamanzadeh V, Valizadeh L, Khajehgoodari M. Assessment of nurse-patient communication and patient satisfaction from nursing care. Nurs Open. 2019;6(3):1189–96. https://doi.org/10.1002/nop2.316
59. Zohman LR. Cardiac rehabilitation: its role in evaluation and management of the patient with coronary heart disease. Am Heart J. 1973;85(5):706–10. https://doi.org/10.1016/0002-8703(73)90179-8