

Nonpharmacological interventions in the improvement of quality of life in children and adolescent cancer patients

Intervenções não farmacológicas na melhoria da qualidade de vida de crianças/adolescentes oncológicos
Intervenciones no farmacológicas en la mejora de la calidad de vida de niños/adolescentes oncológicos

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Abstract

Objective: To identify, in both the Brazilian and international literature, studies about the efficacy of nonpharmacological interventions oriented toward improving quality of life in children and adolescents with cancer.

Methods: Integrative review whose search process was carried out in September and October 2018 in the following databases: PsycINFO, Web of Science, Cumulative Index to Nursing and Allied Health Literature, Latin America and Caribbean Center on Health Sciences Information, *Índice Bibliográfico Español de Ciencias de la Salud*, *Banco de Dados em Enfermagem*, and MEDLINE®. The guiding question was "What are the nonpharmacological interventions available in the literature used to improve quality of life in children and adolescents with cancer?". Original articles published between 2013 and 2018 in English, Portuguese, or Spanish were included. Studies that focused on other subjects or adult population and review articles, dissertations, and theses were excluded.

Results: The sample was 22 articles, which were grouped, according to their similarities, into three categories. The described interventions consisted of: exclusive physical activity (6); physical activity combined with another intervention (8); and psychological interventions (8). Among these interventions, 13 showed significant differences in the improvement of quality of life.

Conclusion: The nonpharmacological interventions that applied physical exercise or were combined with another intervention were the most effective. The present review helps raising awareness of professionals of the importance of the subject and provides resources to plan strategic actions, in the context of pediatric nursing, that include nonpharmacological interventions, together with the standard treatment, to improve quality of life in children and adolescents with cancer. The results must be evaluated with caution, given that a variety of interventions, protocols, and number of participants was identified in the sample, which hinders the generalization of the findings.

Resumo

Objetivo: Identificar estudos na literatura nacional e internacional sobre a eficácia das intervenções não farmacológicas para melhoria da qualidade de vida de crianças e adolescentes com câncer.

Métodos: Revisão integrativa, cuja busca ocorreu nos meses de setembro e outubro de 2018, nas bases de dados PsycINFO, Web of Science, CINAHL, LILACS, IBECs, BDEFN e MEDLINE® para responder à questão norteadora: "Quais são as intervenções não farmacológicas disponíveis na literatura e utilizadas para melhorar

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a qualidade de vida de crianças e adolescentes com câncer?”. Foram incluídos artigos originais, publicados entre 2013 e 2018, nos idiomas inglês, português ou espanhol. Excluíram-se estudos que focavam outras temáticas, população adulta, artigos de revisão, dissertações e teses.

Resultados: A amostra foi constituída por 22 artigos, que foram agrupados, conforme suas similaridades, em três categorias. As intervenções utilizadas foram: atividade física exclusiva (6); atividade física conciliada à outra intervenção (8); e intervenções psicológicas (8). Destas intervenções, 13 apresentaram diferenças significativas na melhoria da qualidade de vida.

Conclusão: As intervenções não farmacológicas utilizando exercício físico exclusivo ou conciliado a outra intervenção foram as mais eficazes. Esta revisão auxilia na sensibilização dos profissionais sobre a importância da temática e fornece subsídios para o planejamento de ações estratégicas, no âmbito da enfermagem pediátrica, que incluam intervenções não farmacológicas, conciliadas ao tratamento padrão, para a melhoria da qualidade de vida de crianças e adolescentes com câncer. Os resultados devem ser avaliados com cautela, pois identificou-se uma diversidade de intervenções, protocolos e número de participantes – o que dificulta a generalização dos achados.

Resumen

Objetivo: Identificar estudios en la literatura nacional e internacional sobre la eficacia de las intervenciones no farmacológicas en la mejora de la calidad de vida de niños y adolescentes con cáncer.

Métodos: Revisión integradora, cuya búsqueda ocurrió en los meses de septiembre y octubre de 2018, en las bases de datos PsycINFO, Web of Science, CINAHL, LILACS, IBECS, BDEF y MEDLINE® para responder la pregunta orientadora: “¿Cuáles son las intervenciones no farmacológicas disponibles en la literatura y utilizadas para mejorar la calidad de vida de niños y adolescentes con cáncer?”. Se incluyeron artículos originales publicados entre 2013 y 2018 en los idiomas inglés, portugués y español. Se excluyeron estudios que se centraban en otras temáticas, como población adulta, artículos de revisión, tesis de maestría y doctorado.

Resultados: La muestra fue formada por 22 artículos, que fueron agrupados en tres categorías según sus similitudes. Las intervenciones utilizadas fueron: actividad física exclusiva (6), actividad física conciliada con otra intervención (8) e intervenciones psicológicas (8). De estas intervenciones, 13 presentaron diferencias significativas en la mejora de la calidad de vida.

Conclusión: Las intervenciones no farmacológicas utilizando ejercicio físico exclusivo o conciliado con otra intervención fueron las más eficaces. Esta revisión ayuda a sensibilizar a los profesionales sobre la importancia de esta temática y contribuye a la planificación de acciones estratégicas en el ámbito de la enfermería pediátrica, que incluyan intervenciones no farmacológicas, conciliadas con el tratamiento estándar, para la mejora de la calidad de vida de niños y adolescentes con cáncer. Los resultados deben analizarse con cautela, ya que se identificó una diversidad de intervenciones, protocolos y número de participantes, lo que dificulta la generalización de los descubrimientos.

Introduction

Cancer is a chronic condition considered a global public health issue. Its high prevalence, its relevance as a cause of death, the high expenditure of financial resources, and the psychosocial onus associated with it have mobilized efforts toward implementing actions and programs for its control and prevention.⁽¹⁾

Childhood cancer is defined as a set of different malignancies, with varying histopathology and clinical behavior.⁽¹⁾ In Brazil, cancer is the second cause of death among children, adolescents, and young adults, and the age group from 15 to 19 years is the one with the highest risk of having the disease. The measured percentage of neoplasms in the youth population is equal to 3%, and leukemias, lymphomas, and central nervous system tumors are the most frequent occurrences.⁽¹⁾

Developing cancer causes a great impact on the life of children, adolescents, and their relatives, meaning to live with signs and symptoms that come up suddenly and deal with frequent visits to hospitals, in addition to enduring significant changes in

their routines.^(2,3) During cancer treatment, patients are submitted to long hospital stays for tests and treatments involving chemotherapy, radiotherapy, surgery, and the use of several medications which, as a whole, originate physical and psychological limitations⁽⁴⁾. Furthermore, the regular exposition to pain and distress causes the interruption of their normal life, including school absence and social isolation, interfering with their quality of life.⁽⁴⁾

Currently, the negative impact of diseases has not been measured only by considering the mortality and survival rate endpoints. Significant importance has been given mostly to the impact on patients' quality of life, especially those with chronic diseases.⁽⁵⁾ Nonpharmacological measures have been extensively studied, with a focus on the improvement of quality of life. These measures are defined as “a varied set of systems, practices, and medical and health products that are not considered part of conventional medicine”.⁽⁶⁾ Among them, psychological therapies, such as music therapy, physical therapies, including exercises, and psychophysical therapies, such as yoga, stand out.⁽⁶⁾

Based on the consequences that cancer and its treatment originate in the youth population, it is considered suitable to identify and analyze non-pharmacological interventions oriented toward this public that can help health professionals to optimize quality of life in these patients. The objective of the present study was to identify, in the Brazilian and international literature, publications addressing nonpharmacological interventions used to improve quality of life in children and adolescents with cancer.

Methods

An integrative literature review was carried out.⁽⁷⁾ The following steps were established to develop the present study: identification of the subject and selection of the research question; definition of study inclusion and exclusion criteria; definition of the information to be extracted from the selected studies and categorization of the studies; evaluation of the studies included in the sample; interpretation of the results and presentation of the review; and synthesis of the knowledge.⁽⁸⁾

The delimited subject was the nonpharmacological interventions used to improve quality of life in children and adolescents with cancer, and the objective was to answer the following guiding question: “What are the nonpharmacological interventions available in the Brazilian and international literature used to improve quality of life in children and adolescents with cancer?”. The PICO strategy⁽⁹⁾ was applied to formulate a suitable question to solve the examined clinical issue. In this abbreviation, “P” stands for “population” (children and adolescents), “I” stands for “intervention” (nonpharmacological interventions), “C” stands for “comparison” (does not apply, because the present study is not comparative), and “O” stands for “outcome” (improvement in quality of life).

The following descriptors, identified on Health Sciences Descriptors, Medical Subject Headings, PsycINFO Thesaurus, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) Headings, were used: “*criança*” (“child”), “*adoles-*

cente” (“adolescent”), “*neoplasia*” (“neoplasms”), and “*qualidade de vida*” (“quality of life”). The keywords “*câncer*” (“cancer”) and “*intervenção*” (“intervention”) were also used. The search was carried out by applying different combinations of these words using the Boolean operator “and” in Portuguese and English, depending on the consulted database.

Data collection was performed between September and October 2018. The searched databases were MEDLINE® (PubMed®), PsycINFO, Web of Science, and CINAHL. An additional search was carried out on the Virtual Health Library (VHL) website, in the following health sciences databases: Latin America and Caribbean Center on Health Sciences Information (LILACS), *Índice Bibliográfico Español de Ciencias de la Salud* (IBECS), MEDLINE®, and *Banco de Dados em Enfermagem* (BDENF).

The sample included original articles whose subject answered the guiding question, published in English, Portuguese, or Spanish between 2013 and 2018. Studies that focused on other subjects or adult population, review articles, dissertations, and theses were excluded.

A thorough reading of the titles and abstracts of the publications was carried out independently by two researchers to guarantee that the texts covered the guiding question of the present review and met the established inclusion criteria. In case of a doubt, whether the study should be selected, the researchers opted to initially include it in the sample and decide on its selection only after reading its full content.

Analysis of data used in the present integrative review was descriptive. A chart designed by the researchers was used to extract and summarize data from each primary study included in the sample, containing the following information: article title, origin country, authors’ area of activity, publication year, objectives, participants, used interventions, evaluation method of the intervention, study design, level of evidence, and main results and conclusions. This chart allowed to compare and organize data according to their differences, similarities, and the guiding question, which were analyzed critically and grouped into three categories.⁽¹⁰⁾

The level of evidence was identified based on the study design. According to this criterion, I designated systematic reviews and meta-analysis of randomized clinical trials, II indicated randomized clinical trials, III referred to non-randomized clinical trials, IV meant case-control or cohort studies, V symbolized systematic reviews of qualitative or descriptive studies, VI was assigned to qualitative or descriptive studies, and VII denoted authorities' and/or committees of experts' reports. This hierarchy classifies levels I and II as strong, III to V as moderate, and VI and VII as weak.⁽¹¹⁾

Results

The search in the consulted databases found 2,549 references, with 1,744 on MEDLINE® (PubMed®), 150 on CINAHL, 94 on PsycINFO, 513 on Web of Science, and 48 in the remaining databases (40 on MEDLINE® (VHL), 8 on LILACS, and none on IBECs and BDEFN). Exclusion covered 2,508

articles (Figure 1). After the exclusion of 19 duplicates, 22 studies were selected to be fully read, and all of them were included in the results of the present review.

The characterization of the selected publications according to the variables of interest is shown in Chart 1.

Regarding the countries where the studies were carried out, there was a predominance of the United States,^(16-18,26,27,30) with six studies, followed by Germany^(13,14,28) and Japan,^(19,20,22) with three publications each, and Canada^(23,31) and Netherlands,^(24,25) with two studies each. Countries such as China,⁽²¹⁾ Peru,⁽¹²⁾ Iran,⁽¹⁵⁾ Israel,⁽²⁹⁾ Brazil⁽³²⁾, and Sweden⁽³³⁾ contributed with one publication each, illustrating the limited number of studies addressing the subject.

Concerning the area of activity of the authors, most articles (eight) originated from multidisciplinary areas (six from the combination of medicine with psychology,^(18,23,24,25,26,33) one from the union of medicine and nursing,⁽²⁷⁾ and a study that encompassed three areas: medicine, nursing, and veteri-

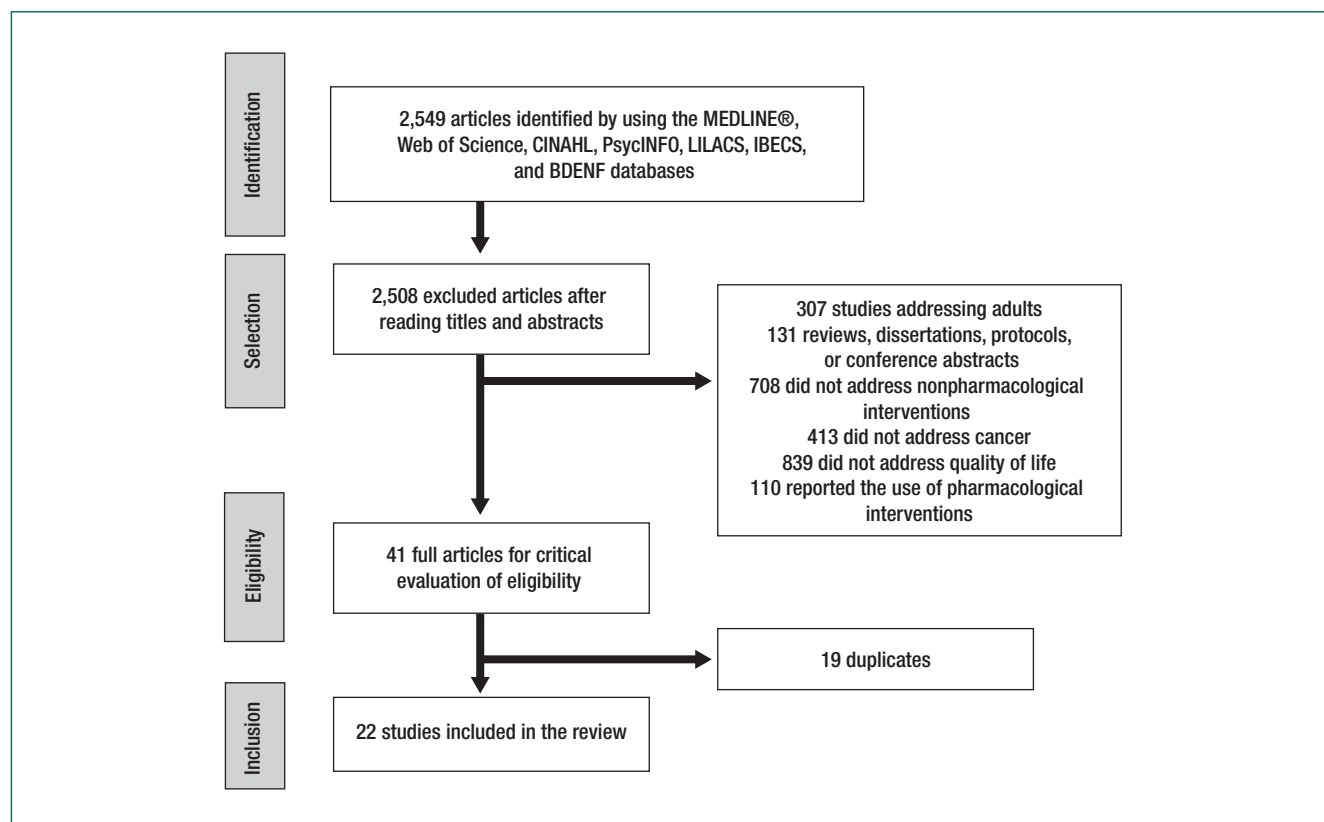


Figure 1. Flow chart.

Chart 1. Characterization of the selected studies according to the variables of interest.

Citation/Year/ Country/ Area of activity	Participants	Methods	Main results	Level of evidence
Interventions based exclusively on physical activity				
Tanir; Kuguoglu ⁽¹²⁾ 2013 Peru Nursing	40 children between 8 and 12 years old with ALL	Randomized clinical trial Intervention group (n=19) Intervention: physical activity, such as walking and climbing Control group (n=21) Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	Pain scores, injuries, nausea, and anxiety related to the procedure did not show significant differences when the intervention and control groups were compared. However, the group that participated in the intervention experienced a significant increase in these scores.	II
Beulertz et al. ⁽¹³⁾ 2016 Germany Medicine	33 children between 4 and 17 years old with cancer under outpatient treatment	Randomized clinical trial Intervention group (n=20) Intervention: physical activity over six months, once a week, for 60 minutes Control group (n=13) Instrument: KINDL® questionnaire	Significant differences were found in the physical and emotional well-being when the groups were compared. Additionally, there was a significant difference in the emotional well-being since the beginning of the intervention until the post-intervention period, favoring those who practiced the exercises.	II
Müller et al. ⁽¹⁴⁾ 2016 Germany Medicine	150 children between 4 and 18 years old after treatment for leukemia, lymphoma, brain tumor, or sarcoma	Non-randomized controlled trial (quasi-experiment) Intervention: physical activity over four weeks Instrument: KINDL® questionnaire	Immediate and persistent effects on HRQL were identified in children and adolescents with different types of cancer. However, patients with sarcoma reported higher global and physical well-being scores in comparison with patients with leukemia and lymphoma.	III
Khodashenas et al. ⁽¹⁵⁾ 2017 Iran Medicine	20 children between 5 and 12 years old with cancer	Randomized clinical trial Intervention group (n=10) Intervention: aerobic physical activity Control group (n=10) Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	Improvement in the well-being of children with cancer, demonstrated in the improvement in the pain and injury subscale, in addition to a better performance at school according to the parents' report.	II
Mendoza et al. ⁽¹⁶⁾ 2017 United States Medicine	59 adolescents between 14 and 18 years old with a post-cancer treatment period longer than 1 year	Randomized clinical trial Intervention: physical activity (walking) over ten weeks using a tracking device (Fitbit Flex) and a virtual support group based on a Facebook group Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	Significant decrease in social functioning and absence of alterations in the other scale domains. There was good acceptability and an increase in the motivation for the intervention.	II
Sparrow et al. ⁽¹⁷⁾ 2017 United States Medicine	9 children between 2 and 12 years old diagnosed with brain tumor and hemiplegia after the end of the therapy	Non-randomized controlled trial (quasi-experiment) Intervention: physical activity (movement therapy), with 15 therapy sessions, each lasting three hours Instruments: PedsQL SF15 and PedsQL 4.0 Generic Core (parents' report)	Despite the higher HRQL scores obtained after the intervention, the difference was not significant.	III
Howell et al. ⁽¹⁸⁾ 2018 United States Psychology and medicine	78 children between 11 and 15 years old with cancer	Randomized clinical trial Intervention group (n=53) Intervention: physical activity; the group received educational materials, a device to monitor the activities, and access to an interactive website designed to encourage physical activity by providing rewards Control group (n=25) Instrument: PedsQL 4.0 Generic Core	Groups that performed physical activity showed better general HRQL results and better scores in the physical performance subscale.	II
Interventions based on physical and educational activities				
Li et al. ⁽¹⁹⁾ 2013 Japan Nursing	71 children between 9 and 16 years old who survived cancer	Randomized clinical trial Experimental group (n=34) Intervention: four-day training integrated program based on adventure and health education Control group (n=37) Instrument: PedsQL 4.0 Generic Core	There was no statistically significant change in the children's quality of life.	II
Chung et al. ⁽²⁰⁾ 2015 Japan Nursing	69 survivors with an average age of 12.6 years	Non-randomized controlled trial (quasi-experiment) Intervention group (n=33) Intervention: physical activity and health education Control group (n=36) Regular medical care Instrument: PedsQL 4.0 Generic Core	Improvement in HRQL, especially in the physical and emotional functioning.	III
Lam et al. ⁽²¹⁾ 2018 China Nursing	70 children between 9 and 18 years old with cancer	Randomized clinical trial Intervention group (n = 37) Intervention: 15 minutes of health education and physical activity Control group (n = 33) 15 minutes of health education and playing cards or chess, in addition to receiving health advice on how to prevent the flu and the importance of a healthy diet Instrument: PedsQL 3.0 Cancer Module	Participants in the intervention group showed a better quality of life when compared with participants in the control group over the nine-month follow-up.	II
Li et al. ⁽²²⁾ 2018 Japan Nursing	222 children between 9 and 16 years old who survived cancer	Randomized controlled trial Intervention group (n=117) Intervention: physical activity (based on adventures), four times a week, over 12 months Control group (n=105) Leisure activity, four times a week, over six months Instrument: PedsQL 4.0 Generic Core	The participants in the intervention group reported a better quality of life than those in the control group.	II

Continue...

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Continuation.

Citation/Year/ Country/ Area of activity	Participants	Methods	Main results	Level of evidence
Interventions based on physical and psychological activities				
Wurz et al. ⁽²³⁾ 2014 Canada Psychology and medicine	8 children between 5 and 17 years old with cancer	Non-randomized controlled trial (quasi-experiment) Intervention: supervised yoga sessions, twice a week, over 12 weeks Instrument: PedsQL 4.0 Generic Core	Significant improvement in the total HRQL score and the psychosocial subscale, in addition to an improvement in the physical functioning and the performance at school according to the parents' report.	III
Van Dijk-Lokkart et al. ⁽²⁴⁾ 2015 Netherlands Psychology and medicine	68 children between 8 and 18 years old with cancer	Randomized clinical trial Intervention group (n=30) Intervention: physical exercises (45 minutes over 12 weeks) and psychosocial intervention Control group (n=38) Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	No effect on HRQL was identified in the children's self-report. However, the parents' report revealed a significant improvement in the score in the pain subscale, less anxiety in the short term, and less nausea in the long term.	II
Van Dijk-Lokkart et al. ⁽²⁵⁾ 2015 Netherlands Psychology and medicine	61 children between 8 and 18 years old with cancer	Randomized clinical trial Intervention: physical and psychosocial intervention program Instrument: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	The results did not show the efficacy of the intervention in improving HRQL in children and adolescents with cancer.	II
Orsey et al. ⁽²⁶⁾ 2017 United States Psychology and medicine	20 children and adolescents between 8 and 18 years old under cancer treatment and their parents	Non-randomized controlled trial (quasi-experiment) Intervention: yoga over eight weeks Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	It identified a significant increase in the emotional and social function and an improvement in HRQL.	III
Exclusively psychological interventions				
Akard et al. ⁽²⁷⁾ 2015 United States Nursing and medicine	28 children between 7 and 17 years old with cancer	Randomized clinical trial Intervention group (n=15) Intervention: legacy-making; individual interviews with children with advanced cancer addressing what they would like their relatives and friends to remember about them. The children wrote some words or made something special to give to somebody significant to them Control group (n=13) Instrument: PedsQL 4.0 Generic Core	There was not a significant difference in HRQL scores, although the parents perceived that the intervention facilitated the communication between them and their children. It was a coping strategy and it helped the children deal with the disease and feel better emotionally, socially, physically, and spiritually.	II
Malboeuf- Hurtubise et al. ⁽²⁸⁾ 2016 Germany Psychology	14 adolescents between 11 and 18 years old with cancer	Non-randomized controlled trial (quasi-experiment) Intervention: mindfulness Instrument: PedsQL 3.0 Cancer Module	All the participants reported that they liked the group. There was a reduction in stress before the treatments, ease to fall asleep more quickly, and no report of sadness or depression. However, the differences between pre- and post-intervention were not significant regarding QL.	III
Shoshani et al. ⁽²⁹⁾ 2016 Israel Psychology	66 children between 5 and 12 years old with cancer and showing risk of death	Randomized controlled trial Intervention group (n=32) Intervention: Make-a-Wish; evoking hope and joy to cope with the disease, indulging the children's greatest wish Control group (n=34) Instrument: PedsQL 4.0 Generic Core	Children in the intervention group showed a significant reduction in general distress, depression, and anxiety symptoms, in addition to improved HRQL and greater hope and positive affection.	II
McCullough et al. ⁽³⁰⁾ 2017 United States Nursing, medicine and veterinary medicine	106 children between 3 and 17 years old newly diagnosed with cancer	Randomized clinical trial Intervention group (n=60) Intervention: animal-assisted therapy Control group (n=46) Instruments: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	There were no significant differences between the groups over time.	II
Barrera et al. ⁽³¹⁾ 2018 Canada Psychology	91 children between 8 and 16 years old with brain/spinal tumor	Randomized clinical trial Intervention group (n=43) Intervention: social skills (friendship, cooperation, management of teasing and bullying, conflict resolution, empathy, and affirmation) Control group (n=48) Instrument: PedsQL 4.0 Generic Core	There was no significant difference in quality of life.	II
Silva; Osório ⁽³²⁾ 2018 Brazil Medicine	24 children between 6 and 12 years old with a solid tumor or ALL	Non-randomized controlled trial (quasi-experiment) Intervention: animal-assisted therapy Instrument: Quality of Life Evaluation Scale	There was no significant difference in the quality of life scores.	III
Ugglä et al. ⁽³³⁾ 2018 Sweden Psychology and medicine	29 children between 0 and 17 years old submitted to a hematopoietic stem cell transplantation	Randomized clinical trial Intervention group (n=14) Intervention: music therapy Control group (n=15) Instrument: PedsQL 4.0 Generic Core and PedsQL 3.0 Cancer Module	Significant improvement in all the domains of the generic scale, except the school one, and significant improvement in the subscales related to anxiety associated with the treatment, concerns, cognitive problems, and communication in the cancer module.	II

nary medicine).⁽³⁰⁾ Six publications were carried out by authors from the medical field,^(13-17,32) followed by five studies in the nursing area,^(12,19-22) and three in the psychology one.^(28,29,31)

The instruments applied to evaluate quality of life were the Pediatric Quality of Life Inventory™ (PedsQL™), 4.0 Generic Core^(12,15-20,22-27,29,30-33) and PedsQL 3.0 Cancer Module,^(12,16,21,24-26,30,32) the KINDL® questionnaire,^(13,14) and the Quality of Life Evaluation Scale.⁽³²⁾ It is important to stress that some studies used more than one instrument to assess quality of life.

Regarding study design, 15 articles described randomized clinical trials,^(12,13,15,16,18,19,21,22,24,25,27,29-31,33) which were classified as level of evidence II studies, and seven publications reported non-randomized controlled trials (quasi-experiments),^(14,17,20,23,28,26,32) whose level of evidence was categorized as III.

Among the 22 studies in the sample, seven applied physical activity exclusively,⁽¹²⁻¹⁸⁾ with five reporting significant results in the improvement of quality of life.^(12-15,18) Eight had a protocol that combined physical activity and another intervention⁽¹⁹⁻²⁶⁾, among which four implemented health education⁽¹⁹⁻²²⁾ and four explored psychological activities,⁽²³⁻²⁶⁾ with six describing significant improvements in quality of life.^(20-24,26) Seven studies applied psychological interventions: animal-assisted therapy was used in two studies^(30,32) and music therapy,⁽³³⁾ full-attention practice (mindfulness),⁽²⁸⁾ development of social skills,⁽³¹⁾ an activity related to wishes,⁽²⁹⁾ and another one addressing the legacy the children would like to leave⁽²⁷⁾ contributed with one article each, with two studies demonstrating significant improvement in quality of life.^(29,33)

The studies were grouped empirically, based on the nonpharmacological interventions performed to improve quality of life in children and adolescents with cancer. Three categories were defined: physical interventions, physical interventions combined with educational or psychological actions, and psychological interventions.

Category 1. Physical interventions

Seven studies resorted to physical exercises as the only intervention,⁽¹²⁻¹⁸⁾ among which five (71.4%)

described a significant improvement in quality of life.^(12-15,18)

The first study in the sample applied walking as physical activity. In this investigation, 59 adolescents between 14 and 18 years old who survived cancer had their steps counted by a tracking device (Fitbit Flex™). The results pointed to a better health-related quality of life in the social functioning of PedsQL™ Generic Core in the control group. The other scale domains did not show significant changes, although they had good acceptability and were associated with an increase in motivation.⁽¹⁶⁾

The second study used simple rehabilitation exercises by applying games and practices of daily life in children between 2 and 12 years old with brain tumor and hemiplegia. Nine parents participated in the study and reported that health-related quality of life scores increased or remained stable over the study period, but no significant difference was found.⁽¹⁷⁾

The third article described the use of aerobic exercises (walking, running, and playing games) in 20 children between 5 and 12 years old with cancer. The programmed exercise, which spanned 12 weeks, could increase the well-being of the children. The improvement in health-related quality of life was demonstrated in the pain and injuries subscale of the PedsQL™ Cancer Module, and the increase in the performance at school was shown by the parents' report in the PedsQL™ Generic Core.⁽¹⁵⁾

Another study verified the efficacy of exercises (running, long jump, and side jump) in 33 children between 4 and 17 years old with cancer who were under outpatient care. Significant differences in quality of life and physical and emotional well-being were found when the groups were compared. A significant increase in the emotional well-being was detected since the beginning of the intervention and remained in the post-intervention period, favoring those who practiced physical exercise.⁽¹³⁾

The study carried out with 40 children between 8 and 12 years old who had acute lymphoid leukemia reported that the patients participated in a three-month exercise program, including active amplitude of movement, muscle strengthening in the legs, and aerobic exercises. The results revealed that pain scores

and injuries, nausea, and anxiety related to the procedure did not show significant differences when the intervention and control groups were compared. However, there was a significant increase in the group that participated in the intervention.⁽¹²⁾

The sixth study implemented a rehabilitation program in 150 children, whose age ranged from 4 to 18 years, after completion of the treatment for leukemia, lymphoma, brain tumor, or sarcoma. Immediate and persistent effects on health-related quality of life in the examined children and adolescents were observed for the different types of cancer. However, patients with sarcoma obtained higher global and physical well-being scores in comparison with patients who had leukemia and lymphoma.⁽¹⁴⁾

The seventh article described the assessment of the encouragement to physical activity in 78 children between 11 and 15 years old who survived cancer. There was an improvement in health-related quality of life in the general score and in the physical performance subscale.⁽¹⁸⁾

Category 2. Physical interventions combined with educational or psychological actions

Eight articles made up this category,⁽¹⁹⁻²⁶⁾ with 75% of them indicating improvement in quality of life.^(20-24,26)

Four studies applied physical exercises and educational actions.⁽¹⁹⁻²²⁾ Among them, two applied physical exercises based on adventure activities together with educational activities and identified an improvement in health-related quality of life in the intervention group. The sample of one of them had 69 survivors with an average age of 12 years,⁽²⁰⁾ and the other examined 22 children between 9 and 16 years old.⁽²²⁾ However, a similar investigation carried out with 71 children from 9 to 16 years old who survived cancer which developed a health education action in combination with adventure-based training (climbing, mini olympic games, and running) did not find a statistically significant effect on the quality of life of children.⁽¹⁹⁾

In the fourth study, 70 children and adolescents with cancer who were under treatment attended a lecture on the importance of physical exercises; after that, the experimental group went through physical training with coaching. The members of the exper-

imental group reported significantly better levels of quality of life compared with those in the control group over the nine-month follow-up.⁽²¹⁾

The other four articles in this category described the use of physical exercises combined with psychological activities.⁽²³⁻²⁶⁾ Two studies joined physical exercises performed twice a week at a physical therapy center and a psychosocial training developed over six sessions, once every six weeks, in over 60 children between 8 and 18 years old with cancer. However, one of them did not show any efficacy in improving quality of life,⁽²⁵⁾ whereas the other identified a significant improvement in the scores of the pain subscale, as well as in anxiety in the short term and nausea in the long term according to the parents' report.⁽²⁴⁾

The two remaining studies applied the practice of yoga. One of them, developed with children and adolescents between 8 and 18 years old, indicated a significant increase in the emotional, social, and total function in the general health-related quality of life scale according to the children's report.⁽²⁶⁾ The results of the other investigation, carried out with patients whose ages ranged from 5 to 17 years, showed significant improvements in the total and psychosocial health-related quality of life scores, in addition to a better physical functioning and a higher performance at school according to the parents' report.⁽²³⁾

Category 3. Psychological interventions

Seven studies in the sample applied psychological interventions,⁽²⁷⁻³³⁾ and only two of them (28.6%) reported effectiveness in the procedures.^(29,33)

The first one used adapted full-attention practices (mindfulness) in 14 adolescents between 11 and 18 years old with a cancer diagnosis. All the participants reported that they enjoyed the group and the opportunity to talk about their emotions openly. The adolescents mentioned the decrease in stress before the treatments, the ease to fall asleep, and the absence of sadness or depression after the conversations about the cancer experience as positive points. However, the quantitative differences between the pre- and post-intervention groups were not significant regarding quality of life, mood, and sleep.⁽²⁸⁾

The second study used the encouragement to the practice and development of social skills (friendship, cooperation, management of teasing or bullying, conflict resolution, empathy, and affirmation) as its intervention in 91 children between 8 and 16 years old diagnosed with a brain tumor. The results did not point to a significant difference in either quality of life or the report of caregivers or teachers.⁽³¹⁾

In an activity about legacy, 28 children and adolescents at the end of their lives communicated what they would like their family and friends to remember about them and wrote some words or made something special to give someone. Although the parents' perception was that the intervention facilitated the communication between them and their children, the intervention was a coping strategy and helped children deal with the disease and feel better emotionally, socially, physically, and spiritually. A significant difference in health-related quality of life scores was not obtained.⁽²⁷⁾

The fourth and fifth studies applied animal-assisted therapy as the intervention in 24 children between 6 and 12 years old⁽³²⁾ and in 106 children from 3 to 17 years old, respectively.⁽³⁰⁾ Despite finding a significant improvement in pain, irritation, and stress levels, depression symptoms, and anxiety, none of the studies identified significant differences in health-related quality of life.^(24,32)

The sixth investigation applied music therapy in children between 0 and 17 years old during and after the period of a hematopoietic stem cell transplantation. The results were a higher total score in generic quality of life and a significant improvement in all the scale domains, except the school one. In the cancer module, the scores were higher for the intervention group, with a more significant improvement in the following items: treatment-related anxiety, concerns, cognitive problems, and communication. The parents' report provided similar results, with a functioning improvement in three out of the four domains in the generic module and all the items in the cancer module, indicating a better quality of life in children who received music therapy.⁽³³⁾

The last study used the Make-a-Wish® activity, which is part of an international foundation that

indulges children between 5 and 12 years old with severe health problems with wishes. The objective of this intervention is to fulfill children's greatest wish, supported by the idea that hope and joy will potentially give children more strength to deal with cancer. The results showed a significant reduction in general distress, depression, and anxiety symptoms, in addition to an improvement in health-related quality of life, hope, and positive affection.⁽²⁹⁾

Discussion

The results reported in the selected articles point out to an increasing research interest in the application of nonpharmacological strategies to manage symptoms and obtain an improved quality of life. Most of the studies used the PedsQL™ instrument to assess quality of life. The choice of this instrument may have been favored by the fact that it has been translated and adapted to several languages.⁽³⁴⁾

Nursing occupied the third rank in the classification showing the number of publications in each area of activity of the authors. Taking into account all the consequences of cancer in children's life, awareness and training are indispensable for nursing professionals who use interventions oriented toward handling symptoms and improving quality of life.⁽²⁾ The authors of the present review emphasize the need for more studies on the subject to provide resources to qualify the provided care.

Most of the publications described the application of physical exercises, either exclusive or combined with other nonpharmacological strategies, to improve quality of life. It is understandable that the interventions that resorted to physical exercises were the most successful ones. The use of physical training has been extensively studied in cancer scenarios to be included as a part of prevention or rehabilitation strategies.⁽³⁵⁾ Physical exercises increase the levels of the brain-derived neurotrophic factor, a substance associated with cognitive improvement and relief of depression and anxiety.⁽³⁶⁾ The molecular and systemic changes in the infiltration of immune cells and inflammatory cytokines originated by physical exercises may directly affect the tumor's specific outcomes,

controlling its initiation and progression through the regulation of immune and inflammatory functions, indicating that physical activity can be used as an antineoplastic treatment if incorporated into standard cancer therapies.^(37,38) Additionally, recent evidence suggests that physical exercises reduce the risk of developing 17 out of 27 cancer types.⁽³⁹⁾

Exercises combined with educational or psychological actions represented the strategies that showed the highest number of studies reporting a significant improvement in quality of life. Integration of physical activity and health education strengthens the positive effect of the exercises, because this union promotes awareness of the participants of the importance of physical exercises, corrects misconceptions, increases self-efficacy, and leads to a better adaptation to the new life.⁽¹⁹⁾ Other reviews have shown that both physical and psychological interventions help improve symptoms such as fatigue and stress and quality of life in children and adolescents with cancer.⁽⁴⁰⁻⁴²⁾ Psychological interventions combined with physical exercises can also favor well-being and the practice of physical activities, improving patients' quality of life; however, more studies are necessary to reinforce this tendency.

Despite the considerable number of studies with a good level of evidence, the present review has some limitations that must be stressed. Its results must be evaluated with caution because the risk of bias in all the selected studies is high, taking into account the diversity of types of interventions and protocols, the varied number of participants, and the lack of a control group and randomization in most of the studies. These characteristics hinder the generalization of the findings.

Conclusion

Interventions using physical exercises exclusively or in combination with another strategy were prevalent in the studies examined in the present review, and were also those associated with higher efficacy in improving quality of life in children and adolescents with cancer. Studies that applied psychological interventions were also found. Among the implications for

the practice, the compiled evidence raise professionals' awareness of the importance of the subject and emphasize the relevance of using nonpharmacological interventions together with standard treatments. These interventions can be useful in supporting clinical practices, aiming to qualify care in the planning of strategical actions in the pediatric nursing context, and consequently, improve quality of life in children and adolescents with cancer.

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