









## Effectiveness of complementary therapies for the management of symptom clusters in palliative care in pediatric oncology: a systematic review

Efetividade de terapias complementares para o manejo de *clusters* de sintomas em cuidados paliativos em oncopediatria: revisão sistemática

Efectividad de las terapias complementarias para el manejo de los grupos de síntomas en los cuidados paliativos en oncopediatria: revisión sistemática

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### ABSTRACT

**Objective:** To evaluate the effectiveness of complementary therapies in the management of symptom clusters in children and adolescents with cancer undergoing palliative care. **Method:** Systematic review guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, resorting to the databases MEDLINE, Web of Science, Central Cochrane, and PsycINFO. The identification, selection, inclusion, extraction, and methodological assessment were conducted by two independent reviewers. **Results:** Five quasi-experiments met the eligibility criteria. The heterogeneous characteristics of the studies made meta-analysis impossible. Two studies used therapeutic massage, one used Reiki, one used boswellic acid, and one used *Cannabis sativa*; three of them (therapeutic massage and Reiki) presented statistically significant results for the management of the cluster pain-anxiety-worry-dyspnea. Most studies presented a moderate risk of bias as per ROBINS-I tool. **Conclusion:** Therapeutic massage and Reiki may be effective for the symptom clusters management, especially the pain-anxiety-worry-dyspnea cluster in children and adolescents undergoing palliative care.

### DESCRIPTORS

Child; Adolescent; Palliative Care; Complementary Therapies; Oncology Nursing; Review.

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## INTRODUCTION

Rising to alarming levels, cancer is a contemporary worldwide public health problem and the second cause of mortality in several countries<sup>(1)</sup>. Particularly, cancer in children and adolescents (from 0 to 19 years old) corresponds to a group of many diseases that have in common the uncontrolled proliferation of abnormal cells and may occur in any part of the organism<sup>(2)</sup>. The global incidence of childhood cancer is increasing<sup>(3)</sup>. Estimates suggest 300 thousand new cases among children and adolescents up to 19 years old worldwide<sup>(4)</sup>. Pediatric tumors correspond to 1 to 4% of all malignant tumors in most populations<sup>(2)</sup>. In developing countries, where the population of children amounts to around 50%, this proportion corresponds to 3 to 10% of all neoplasms<sup>(3)</sup>. In Brazil, from 2020 to 2022, 4,310 new cases of cancer in children and teenagers are estimated for males, and 4,150 for females<sup>(5)</sup>.

Despite the progress in the diagnostic and therapeutic process in pediatric oncology, as well as the increase in survival for children and adolescents with cancer, part of these patients is not cured and benefit from palliative care as a fundamental focus of healthcare<sup>(6-8)</sup>. The objective of palliative care in children and adolescents is improving their quality of life, as well as of their families when they face life-limiting or deadly diseases. According to the World Health Organization (WHO), palliative care for this population comprises total active care of body, mind, and spirit, as well as providing family support<sup>(9)</sup>, which should start when the disease is diagnosed and continue regardless of treatment directed at the disease<sup>(10-11)</sup>.

When in its advanced form, cancer in children and adolescents evolves with the presence of symptom *clusters* which are hardly controllable and manageable, such as pain, nausea, vomit, anorexia, fatigue, depression, anxiety, and others<sup>(12-14)</sup>. The term *cluster* is defined as a group of symptoms which are related to one another and may be predicted<sup>(15)</sup>. A cluster of neuropsychological symptoms is defined as two or more emotional, behavioral, and physical symptoms which occur simultaneously and interrelatedly. The symptoms of a cluster have stronger relations with one another than with symptoms outside the cluster<sup>(15-16)</sup>. A cluster of neuropsychological symptoms was observed for the first time in laboratory animals submitted to induced infectious conditions (induced by gram-negative bacterial wall LPS - lipopolysaccharide) and the inoculation of pro-inflammatory cytokines. The result of these infectious and inflammatory conditions was a phenomenon known as sickness behavior<sup>(16)</sup>. The manifestations of *sickness behavior* may be related to tumor invasion, as well as adverse effects of treatment of some types of cancer, causing an intense discomfort to the patients and reducing their functional state, with a consequent reduction in quality of life<sup>(17-18)</sup>. Due to the high prevalence of cancer symptom clusters in palliative care in pediatric oncology, their management is crucial in pediatric oncology and one of the essential pillars of Nursing in Oncology<sup>(16,18-19)</sup>. Patients with cancer undergoing palliative care may benefit from the use of

Complementary Therapies (CT), as a support to treatment, mainly for the management of cancer symptom clusters<sup>(20-22)</sup>.

The National Center for Complementary and Alternative Medicine (NCCAM) defines Complementary Alternative Medicine as a set of practices, medical and healthcare systems which are not considered part of conventional medicine<sup>(23)</sup>. The CT include techniques which aim at prevention, promotion, treatment, and recovery, to integrate the physical, mental, and spiritual dimensions of human beings<sup>(24)</sup>. There are many forms of classifying these therapies. The NCCAM classifies them mainly as use of natural products, practices of body and mind, and manipulation practices based on the body<sup>(23)</sup>.

Although there is robust scientific evidence of the effectiveness of the use of complementary therapies used for the management of specific symptoms in children and adolescents with cancer<sup>(7,25-30)</sup>, there is still a gap in the literature related to the effectiveness of complementary therapies in the management of symptom clusters, particularly in children and adolescents with cancer undergoing palliative care. Also, a search for registers of titles and protocols, as well as articles of systematic reviews, was carried out; however, no results were found regarding this specific theme. In this sense, the objective of this study was to evaluate the effectiveness of complementary therapies in the management of symptoms clusters in children and adolescents with cancer undergoing palliative care.

## METHOD

### DESIGN OF STUDY

This study is a systematic review which included writing a report following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>(31)</sup>. A protocol in the International Prospective Register of Systematic Reviews (PROSPERO/NHS) – Registry Number: CRD42020167468 was registered to guarantee the reliability of data and methodological transparency.

To formulate the objective and the research question for the review the strategy PICO<sup>(32)</sup> (P – Population or Patients; I – Intervention; C – Comparison; O – Outcomes) was employed, where P = Population (children and adolescents with cancer undergoing palliative care), I = Intervention (complementary therapies), C = Comparison (control group receiving no intervention or receiving standard/usual clinical care), O = Outcomes (improvement in cancer symptom clusters).

The definition of palliative care of the WHO was used in this systematic review to compose the element P (population in the PICO strategy) which determines palliative care as being an approach which enhances quality of life of patients and of families who face problems associated to diseases through prevention and suffering relief, early identification, correct evaluation, and pain treatment and of other problems of a physical, psychosocial, and spiritual nature<sup>(9)</sup>. The term cluster is defined as a set of symptoms related to one another and which may be predicted<sup>(15)</sup>. Such definitions and elements of the PICO strategy have facilitated the elaboration of the critical thinking on the theme and the formulation of the guiding question of this review: “What are the scientific evidence of the effectiveness of complementary therapies

in the management of cancer symptom clusters in children and adolescents with cancer undergoing palliative care”?

### SEARCH STRATEGY

The systematic search for primary studies was conducted in four electronic databases: MEDLINE - Medical Literature Analysis and Retrieval System Online (via PubMed), Cochrane Central Register of Controlled Trials (CENTRAL Cochrane), Web of Science, and PsycINFO (Psychology Information). The search strategy for these studies included a combination of controlled descriptors (indexing terms in each database) and keywords, following the indication offered in each electronic database. Thus, to search articles in MEDLINE, Medical Subject Headings (MeSH) controlled descriptors were used and PsycINFO Thesaurus was consulted for the PsycINFO database. The keywords were established after careful reading regarding the investigated theme. To widen the search strategy, a combination

of controlled descriptors and keywords was made through Boolean operators. The Boolean operators AND and OR were used to obtain restrictive and additive combinations, respectively<sup>(33)</sup>. Also, the search was conducted using identified descriptors and those with a broadened sense, with no use of filters to preserve significant samples and assure lower risks of loss.

There was no date or language restriction in the search strategy. In addition to the electronic databases, secondary searches were made on other diverse sources, such as Clinical Trial Registry websites, including ClinicalTrials.gov (National Institutes of Health, NIH, USA), The Brazilian Clinical Trials Registry (via ReBEC Platform), and Google Scholar. Also, the list of final references in the included primary studies was manually analyzed to find relevant studies to be added. Chart 1 presents the final search strategy processed in the respective databases, conducted on January 24th, 2020.

**Chart 1** – Search strategy in the consulted databases.

Database	Search strategy
MEDLINE* /PubMed 01/24/2020**	<p>#1 (“Child”[MeSH Terms]<sup>†</sup> OR “Children” OR “Child, Hospitalized”[MeSH Terms]<sup>†</sup> OR “Children, Hospitalized” OR “Hospitalized Children” OR “Hospitalized Child” OR “Pediatric Oncology” OR “Pediatric Cancer Patients” OR “Paediatric Oncology” OR “Adolescent”[MeSH Terms]<sup>†</sup> OR “Adolescents” OR “Teenagers” OR “Teenager” OR “Adolescent, Hospitalized”[MeSH Terms]<sup>†</sup> OR “Adolescents, Hospitalized” OR “Hospitalized Adolescent” OR “Hospitalized Adolescents” AND “Neoplasms”[MeSH Terms]<sup>†</sup> OR “Neoplasia” OR “Neoplasias” OR “Neoplasm” OR “Tumors” OR “Tumor” OR “Cancer” OR “Cancers” OR “Malignancy” OR “Malignancies” OR “Malignant Neoplasms” OR “Malignant Neoplasm” OR “Neoplasm, Malignant” OR “Neoplasms, Malignant” AND “Palliative Care”[MeSH Terms]<sup>†</sup> OR “Care, Palliative” OR “Palliative Treatment” OR “Palliative Treatments” OR “Treatment, Palliative” OR “Treatments, Palliative” OR “Therapy, Palliative” OR “Palliative Therapy” OR “Palliative Supportive Care” OR “Supportive Care, Palliative” OR “Supportive Cancer Care” OR “Palliative Medicine”[MeSH Terms]<sup>†</sup> OR “Palliative Care Medicine” OR “Medicine, Palliative Care” OR “Medicine, Palliative” OR “Hospices”[MeSH Terms]<sup>†</sup> OR “Hospice” OR “Hospice Care”[MeSH Terms]<sup>†</sup> OR “Care, Hospice”))</p> <p>#2 (“Complementary Therapies”[MeSH Terms]<sup>†</sup> OR “Therapies, Complementary” [All Fields] OR “Therapy, Complementary” [All Fields] OR “Complementary Medicine” [All Fields] OR “Medicine, Complementary” [All Fields] OR “Alternative Medicine” [All Fields] OR “Medicine, Alternative” [All Fields] OR “Alternative Therapies” OR “Therapies, Alternative” [All Fields] OR “Therapy, Alternative” [All Fields] OR “Non-pharmacological Intervention” [All Fields])</p> <p>#3 (“Symptom Cluster” [All Fields] OR “Cluster, Symptom” [All Fields] OR “Clusters, Symptom” [All Fields] OR “Symptom Clusters” [All Fields] OR “Cancer Symptom Clusters” [All Fields] OR “Psychoneurological Symptom Cluster” [All Fields] OR “Psychoneurological Symptom Clusters” [All Fields] OR “Symptom Management” [All Fields])</p> <p>#1 AND #2 AND #3</p>
CENTRAL Cochrane# 01/24/2020**	<p>#1 (“Child”[MeSH Terms]<sup>†</sup> OR “Children” OR “Child, Hospitalized”[MeSH Terms]<sup>†</sup> OR “Children, Hospitalized” OR “Hospitalized Children” OR “Hospitalized Child” OR “Pediatric Oncology” OR “Pediatric Cancer Patients” OR “Paediatric Oncology” OR “Adolescent”[MeSH Terms]<sup>†</sup> OR “Adolescents” OR “Teenagers” OR “Teenager” OR “Adolescent, Hospitalized”[MeSH Terms]<sup>†</sup> OR “Adolescents, Hospitalized” OR “Hospitalized Adolescent” OR “Hospitalized Adolescents” AND “Neoplasms”[MeSH Terms]<sup>†</sup> OR “Neoplasia” OR “Neoplasias” OR “Neoplasm” OR “Tumors” OR “Tumor” OR “Cancer” OR “Cancers” OR “Malignancy” OR “Malignancies” OR “Malignant Neoplasms” OR “Malignant Neoplasm” OR “Neoplasm, Malignant” OR “Neoplasms, Malignant” AND “Palliative Care”[MeSH Terms]<sup>†</sup> OR “Care, Palliative” OR “Palliative Treatment” OR “Palliative Treatments” OR “Treatment, Palliative” OR “Treatments, Palliative” OR “Therapy, Palliative” OR “Palliative Therapy” OR “Palliative Supportive Care” OR “Supportive Care, Palliative” OR “Supportive Cancer Care” OR “Palliative Medicine”[MeSH Terms]<sup>†</sup> OR “Palliative Care Medicine” OR “Medicine, Palliative Care” OR “Medicine, Palliative” OR “Hospices”[MeSH Terms]<sup>†</sup> OR “Hospice” OR “Hospice Care”[MeSH Terms]<sup>†</sup> OR “Care, Hospice”))</p> <p>#2 (“Complementary Therapies”[MeSH Terms]<sup>†</sup> OR “Therapies, Complementary” [All Fields] OR “Therapy, Complementary” [All Fields] OR “Complementary Medicine” [All Fields] OR “Medicine, Complementary” [All Fields] OR “Alternative Medicine” [All Fields] OR “Medicine, Alternative” [All Fields] OR “Alternative Therapies” OR “Therapies, Alternative” [All Fields] OR “Therapy, Alternative” [All Fields] OR “Non-pharmacological Intervention” [All Fields])</p> <p>#3 (“Symptom Cluster” [All Fields] OR “Cluster, Symptom” [All Fields] OR “Clusters, Symptom” [All Fields] OR “Symptom Clusters” [All Fields] OR “Cancer Symptom Clusters” [All Fields] OR “Psychoneurological Symptom Cluster” [All Fields] OR “Psychoneurological Symptom Clusters” [All Fields] OR “Symptom Management” [All Fields])</p> <p>#1 AND #2 AND #3</p>

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Database	Search strategy
Web of Science 01/24/2020**	(TS <sup>  </sup> =(“Child” OR “Children” OR “Child, Hospitalized” OR “Children, Hospitalized” OR “Hospitalized Children” OR “Hospitalized Child” OR “Pediatric Oncology” OR “Pediatric Cancer Patients” OR “Paediatric Oncology” OR “Adolescent” OR “Adolescents” OR “Teenagers” OR “Teenager” OR “Adolescent, Hospitalized” OR “Adolescents, Hospitalized” OR “Hospitalized Adolescent” OR “Hospitalized Adolescents” AND “Neoplasms” OR “Neoplasia” OR “Neoplasm” OR “Tumors” OR “Tumor” OR “Cancer” OR “Cancers” OR “Malignancy” OR “Malignancies” OR “Malignant Neoplasms” OR “Malignant Neoplasm” OR “Neoplasm, Malignant” OR “Neoplasms, Malignant” AND “Palliative Care” OR “Care, Palliative” OR “Palliative Treatment” OR “Palliative Treatments” OR “Treatment, Palliative” OR “Treatments, Palliative” OR “Therapy, Palliative” OR “Palliative Therapy” OR “Palliative Supportive Care” OR “Supportive Care, Palliative” OR “Supportive Cancer Care” OR “Palliative Medicine” OR “Palliative Care Medicine” OR “Medicine, Palliative Care” OR “Medicine, Palliative” OR “Hospices” OR “Hospice” OR “Hospice Care” OR “Care, Hospice”) AND TS=(“Complementary Therapies” OR “Therapies, Complementary” OR “Therapy, Complementary” OR “Complementary Medicine” OR “Medicine, Complementary” OR “Alternative Medicine” OR “Medicine, Alternative” OR “Alternative Therapies” OR “Therapies, Alternative” OR “Therapy, Alternative” OR “Non-pharmacological Intervention”) AND TS=(“Symptom Cluster” OR “Cluster, Symptom” OR “Clusters, Symptom” OR “Symptom Clusters” OR “Cancer Symptom Clusters” OR “Psychoneurological Symptom Cluster” OR “Psychoneurological Symptom Clusters” OR “Symptom Management”))
PsycINFO§ 01/24/2020**	((“Child Care” [Thesaurus] OR “Pediatrics” [Thesaurus] OR “Adolescent Health” [Thesaurus] AND “Neoplasms” [Thesaurus] OR “Terminal Cancer” [Thesaurus] OR “Oncology” [Thesaurus] AND “Palliative Care” [Thesaurus] OR “Terminally Ill Patients” [Thesaurus] OR “Hospice” [Thesaurus] AND “Alternative Medicine” [Thesaurus] OR “Complementary Therapies” [Thesaurus] OR “Non-pharmacological interventions” [Thesaurus] OR “Mind Body Therapy” [Thesaurus] OR “Meditation” [Thesaurus] OR “Medicinal Herbs and Plants” [Thesaurus] OR “Massage” [Thesaurus] OR “Hypnotherapy” [Thesaurus] OR “Holistic Health” [Thesaurus] OR “Dietary Supplements” [Thesaurus] OR “Acupuncture” [Thesaurus] OR “Aromatherapy” [Thesaurus] OR “Faith Healing” [Thesaurus] AND “Symptoms” [Thesaurus] OR “Symptoms Based Treatment”))

\*MEDLINE - Medical Literature Analysis and Retrieval System Online; †MeSH - Medical Subject Headings; ‡CENTRAL - Cochrane Central Register of Controlled Trials; §PsycINFO - Psychology Information. ||TS - Topic. \*\*01/24/2020 - Date on which the search strategy was conducted.

## ELIGIBILITY CRITERIA

The included studies had a quantitative approach (observational studies and experimental studies) conducted with children and adolescents with cancer undergoing palliative care, from 0 to 19 years old, of both sexes, with a diagnosis of any type of malignant neoplasm; studies encompassing the effectiveness of any complementary therapy classified by The National Center for Complementary and Alternative Medicine (National Institutes of Health, USA), which categorizes them mainly as: use of natural products, practices of body and mind, and manipulation practices based on the body<sup>(23)</sup> and whose primary outcome was the improvement of cancer symptom clusters. There was no date or language restriction in the search strategy. Excluded studies were qualitative, observational (cross-sectional, ecological, cohort, case-control – since these designs do not test the effectiveness of interventions), as well as all gray literature.

This part of the review used the reference manager EndNote™ to store, organize, and exclude duplicates to assure a systematic, comprehensive, and manageable search. The studies retrieved from each database and exported to EndNote™ were later imported to the Rayyan™ app, developed by the Qatar Computing Research Institute<sup>(34)</sup> – a tool to help selecting articles, especially in the phase of study eligibility and inclusion. The sample was selected by two independent reviewers blindly at the end of January 2020. After this selection, a third reviewer was responsible for analyzing and deciding (with the others) on the inclusion or exclusion of each article, especially regarding those with a conflicting decision, using the Rayyan™ App.

## DATA EXTRACTION

The data were extracted using pre-established tools<sup>(35-39)</sup> and included four domains: a) study identification, with data

on the article's title, the journal's impact factor, country of the study's authors, year of publication, host institution of the study (hospital, university, research center, multicentric study or study in a single institution); conflicts of interest, funding; b) methodological characteristics (study design, study objective or research question or hypotheses, sample characteristics), e.g., sample size, age, baseline characteristics of experimental and control groups, recruitment method, dropouts, duration of follow-up, statistical analyses; c) main findings and implication for clinical practice and d) conclusions. For data extraction, two tables were elaborated in Microsoft Word® by two researchers independently to synthesize all data of the included studies. After this phase, the tables were compiled into one to carry on with the syntheses.

## METHODOLOGICAL ASSESSMENT

Initially, the evidence level was identified based on the study design. Thus, I was attributed to systematic reviews and meta-analyses of randomized clinical trials; II to randomized clinical trials; III to non-randomized controlled trials; IV to case-control, cohort, or cross-sectional studies; V to systematic reviews of qualitative or descriptive studies; VI to qualitative or descriptive studies, and VII to opinion by authorities and/or expert committee reports. This hierarchy classifies the levels I and II as strong, III to V as moderate, and VI to VII as weak<sup>(40)</sup>.

The evaluation of the methodological quality of the studies was defined as an essential process to establish internal validity, verifying possible biases and reliability of the identified evidence. In this systematic review, the methodological quality of the included studies was evaluated by two independent reviewers, using the tool Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I). The tool ROBINS-I was developed recently and is particularly useful for the methodological

evaluation of non-randomized clinical trials of interventions<sup>(41)</sup>. This tool is guided by seven domains of bias chronologically organized in three dimensions (pre-intervention, intervention, and post-intervention) and the interpretations of the domain level and general risk of biased judgement in ROBINS-I are classified into low, moderate, serious, or critical risk of bias<sup>(41)</sup>.

## DATA SYNTHESIS AND ANALYSIS

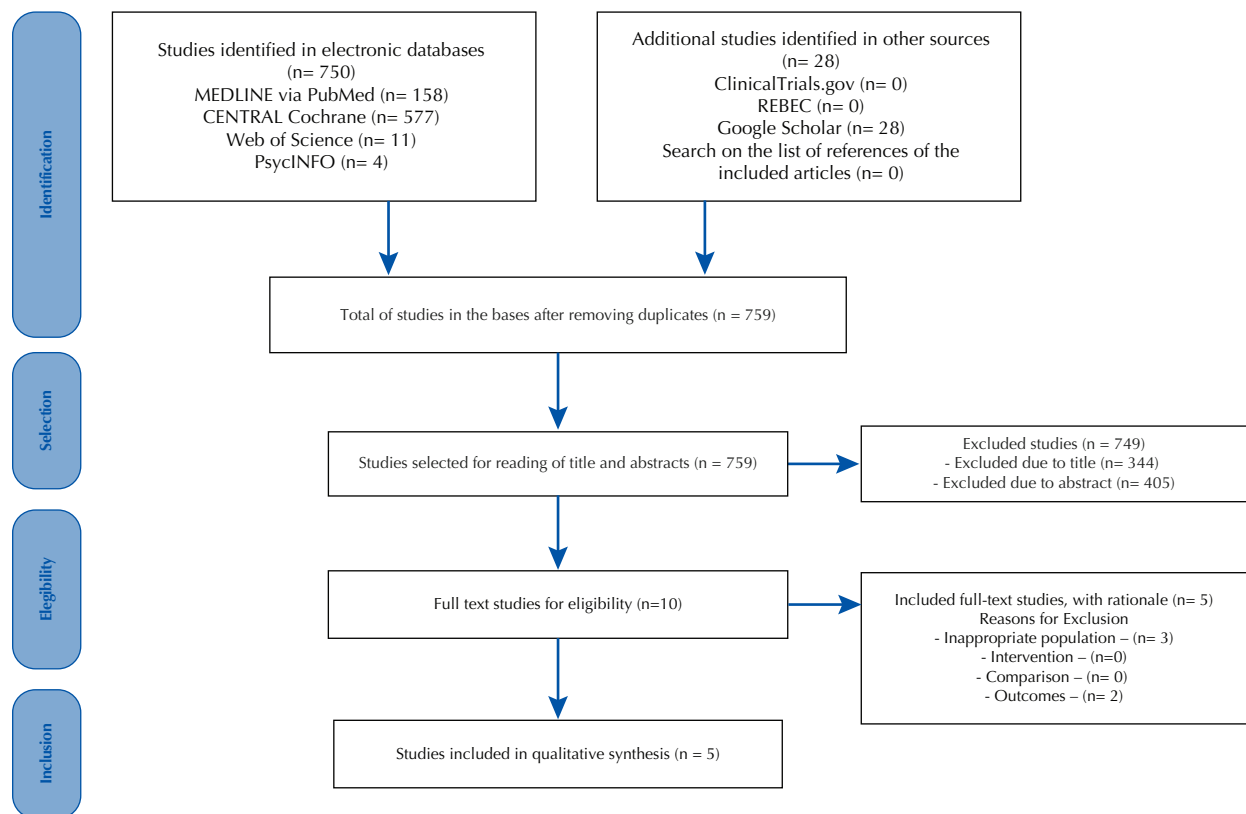
The global judgement of ROBINS-I is systematized and attributed as follows: a) Low risk of bias, in which the study is comparable to a well-designed randomized trial (the study is considered as low risk of bias for all domains); b) Moderate risk of bias – the study is consistent with a non-randomized clinical trial design, but cannot be considered comparable to a well-designed randomized study (in this case, the study is considered as low or moderate risk of bias for all domains); c) Serious risk of bias – the study has some important problems (the study is considered as low or moderate risk of bias for most domains, but presents serious risk of bias in at least one of the domains); d) Critical risk of bias – the study is too problematic to provide any evidence (the study is considered as critical risk of bias in at least one domain); e) No information – when no information is available to provide grounds

to any judgment of risk of bias (missing information on one or more domains)<sup>(41)</sup>. Since most of the evaluated studies presented significant methodological differences, a qualitative synthesis of the data was opted for this systematic review.

## RESULTS

### STUDY SELECTION

The searches on four electronic databases, as well as manual search on other sources, led to 778 studies. Out of these, 19 studies were duplicated in the databases and were removed in the reference manager EndNote™. The studies which made it to the selection phase amounted to 759; these proceeded to the process of screening by title and abstract. In this step, conducted in Rayyan™ App, 749 studies were excluded for not meeting the pre-established inclusion criteria. Exclusion due to title or abstract resulted in the selection of 10 studies, which proceeded to complete reading. After the step of exhaustive complete reading of the studies, other five studies were excluded, resulting thus in five articles to be included for qualitative synthesis and analysis, as shown in Figure 1.



**Figure 1** – PRISMA Flowchart<sup>(31)</sup> for study selection.

### STUDY CHARACTERIZATION

Regarding the characteristics of the five included studies, the date of publication was verified to range from 2000 to 2020<sup>(42-46)</sup>, all of them were published in English in four

different countries (Germany, Canada, United States, and Israel), and had a quasi-experimental design. Chart 2 synthesizes chronologically the main characteristics of the studies included in the qualitative synthesis.

**Chart 2** – Characteristics of quasi-experimental studies included in the systematic review.

Reference/ Country	Objective	Sample	Complementary therapy / Intervention protocol	Clinical outcomes/ Symptom clusters	Instruments	Main results
Janben <i>et al.</i> 2000 <sup>(42)</sup> Germany	To evaluate the effects of boswellic acid (H15*) administered to children with progressive or recurrent brain tumors receiving palliative care	19 patients (11 boys and 8 girls) Age: 6 months to 18 years (mean age: 8.4 years old)	Use of boswellic acid (H15*) / The oral dose of H15 was of 40±126 (median= 77) mg / kg weight/day administered in 3 doses during 1±26 (median= 9) months. Fourteen patients received H15* as monotherapy, whereas 5 patients received H15* with additional conventional therapy	- Clinical outcomes: muscular strength, hemiparesis, ataxia, and weight gain - Symptom clusters: headache, fatigue, loss of appetite, and nausea	Subjective analysis through the oncologists' observations	No adverse effects were attributed to H15* in 19 patients. Children who reported an improvement in their general health state amounted to 5/19; 3/17 patients presented a mainly transient improvement of neurological symptoms, such as hemiparesis and ataxia.
Thrane <i>et al.</i> 2017 <sup>(43)</sup> USA	To examine the viability and acceptability of Reiki in children undergoing palliative treatment and the effect of Reiki therapy on pain and anxiety	16 patients (8 verbal and 8 non-verbal) (11 girls and 5 boys) Age: 7 to 16 years old (mean age: 12.6 years old)	Use of Reiki / The intervention consisted of two 24-minute Reiki sessions at the child's home, with a minimum of 1 and a maximum of 3 days between sessions. Each Reiki session used a protocol of 12 hand positions performed for 2 minutes each. The child was comfortably dressed and the parents were invited to watch the sessions. The interventionist was a pediatric nurse with 12 years of experience, who wrote down in a registry the number of minutes for the session, including any deviations from protocol or uncommon occurrences	- Clinical outcomes: heart and respiratory rate - Symptom clusters: pain and anxiety	- VAS† - Wong-Baker FACES® Pain Scale - The Children's Fear Scale - Children's Anxiety and Pain Scale	All mean scores of the outcome variables (pain, anxiety, heart, and respiratory rate) decreased after treatment with the two Reiki sessions. Significant reductions in pain during treatment 1 in non-verbal children (p = .063) and for respiratory rate of treatment 2 in verbal children (p = .009). The size of Cohen's effects was medium and high for most outcome measurements.
Weekly <i>et al.</i> 2019 <sup>(44)</sup> USA	To explore the impact of therapeutic massage on symptom overload and use of medication in pediatric patients undergoing palliative care, describe the impact of therapeutic massage on the suffering of the family caregiver and report the perception of the nursing team of the impact of therapeutic massage for the children and their families	53 patients (17 girls and 36 boys) Age: 6 months to 8 years (mean age: 3.8 years old)	Use of therapeutic massage / The massage intervention occurred during a scheduled period of 30 minutes in the participant's hospital room. The massage was performed by a certified pediatric massage therapist, with a focus on hands, feet, arms, scalp, head, and shoulders of the participants. Relaxing music was used during the intervention to minimize the noise from the hospital ward. The family caregivers were encouraged to watch the intervention. The mean duration of a massage was 10.5 minutes, with a minimum duration of 3 minutes and maximum duration of 22 minutes.	- Clinical outcomes: use of pain medication "if necessary" - Symptom clusters: pain, anxiety, dyspnea, and nausea	- NCCNS Distress Thermometer Scale - FACES Pictorial Scale - BARF   Pictorial Scale - Dalhousie Dyspnea Scale - McMurtry Anxiety Scale - FLACC¶ Scale	The difference in the scale face, legs, activity, cry, and child consolation (FLACC¶) was significant (p < 0.0001) with a median (interquartile interval - IQI) before the FLACC¶ score being 2 (1-3) and after the FLACC¶ score 0 (0-1). The difference in use of medication for pain "if necessary" in the 24 hours before and after the massage was statistically significant (p = .0477). The mean difference for the level of suffering of the family caregiver with massage was 3.0 (IQI = 2.0, p < 0.0001). All nurses reported that massage is a significant way of providing care to patients and families.

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Reference/ Country	Objective	Sample	Complementary therapy / Intervention protocol	Clinical outcomes/ Symptom clusters	Instruments	Main results
Ofir et al., 2019 <sup>(45)</sup>  Israel	To analyze the short-term efficacy and safety of <i>Cannabis sativa</i> (marijuana) (M)†† in pediatric oncology patients undergoing palliative care	50 patients (19 girls and 31 boys) Age: 7 months to 19 years (mean age: 13 years old)	Use of marijuana / The first dose of marijuana for all patients was 20 grams per month (cannabis through dry inflorescence) used for inhalation / smoking or a basis for oil production. Marijuana (M)†† was offered to 30 patients through oil drops (60%) and to 11 through smoking (22%), followed by vaporization, capsules, or combination of various routes	- Clinical outcomes: quality of life - Symptom clusters nausea and vomit, loss of appetite, mood, sleep disorders, and pain	- VAS† - NRS** - FLACC¶	Positive effects were reported by children and parents in 80% of the cases related to the symptoms nausea and vomit, sleep disorders, pain, appetite, and mood. Five (10%) patients who smoked reported burning throat and anxiety attacks; 4% reported stomach pain, but it was not clear whether these complaints were caused by marijuana (M)†† or by the children's medical conditions.
Genik et al. 2020 <sup>(46)</sup>  Canada	To perform an intervention of therapeutic massage to determine the acceptability of the intervention and its initial effects on pain classification, reduction of worry, and quality of life	8 patients (3 girls and 5 boys) Age: 10 to 17 years (mean age= 14.5 years)	Use of therapeutic massage / The MT†† intervention consisted of four weekly massages performed by a massage therapist with experience in palliative care services. The massages were performed in the hospital or at home, abiding by the contract between the massage therapist and the hospital's palliative care service. Each massage had approximately 60 minutes in duration. A balance between intervention and individualization was attempted. For example, special considerations or alterations were applied to the MT†† session when these were related to physical care and the child's well-being, such as cancer type, site of metastases, adverse reactions to treatments, skin fragility, edema, and pressure or inflammation lesions.	- Clinical outcomes: quality of life - Symptom clusters pain and worry	-PedsQL§§- Cancer Module -PainSquad app - FPS-R    - CFS¶¶	The participants reported significant pain reductions after two MT†† sessions (p = 0.03) and in worry after one session (p = 0.03). No statistically significant differences were found for symptoms pain and quality of life between baseline and follow-up (p>0.05)

Acronyms: \*H15- Special extract of *Boswellia Serrata*; †VAS – Visual Analogue Scale; §NCCN - The National Comprehensive Cancer Network; ||BARF - Baxter Animated Retching Faces; ¶ FLACC - Face, Legs, Activity, Cry, Consolability; \*\* NRS- Numerical Rating Scale; ††M- Marijuana; ††MT- Massage Therapy; §§PedsQL- Pediatric Quality of Life Inventory; |||FPS-R - The Faces Pain Scale; ¶¶CFS- The Clinical Frailty Scale.

## CANCER SYMPTOM CLUSTERS EVALUATED IN THE STUDIES

The total of research participants in the studies<sup>(42-46)</sup> included in this systematic review was 146 patients, and samples varied from 6 months to 19 years of age (mean age of 10 years and a half). With regards to the use of complementary therapies in the included studies, two were verified to use therapeutic massage<sup>(44,46)</sup>, one used reiki<sup>(43)</sup>; one study used boswellic acid<sup>(42)</sup> and another one<sup>(45)</sup> evaluated the use of *Cannabis sativa* (marijuana) for the management of symptom clusters in children and adolescents with cancer undergoing palliative care.

Regarding the symptom clusters evaluated in the five included studies, the oncological pain was verified to be the most evaluated symptom by four studies<sup>(43-46)</sup>, followed by the symptom nausea, evaluated by three studies<sup>(42,44-45)</sup>. The symptoms loss of appetite<sup>(42,45)</sup> and anxiety<sup>(43-44)</sup> were also evaluated by two studies, respectively. Cancer-related fatigue was evaluated by a single study<sup>(42)</sup>, as was the symptom sleep disorder<sup>(45)</sup>. The most often evaluated clinical outcome

was quality of life, analyzed in two studies<sup>(45-46)</sup>. Regarding the time of follow-up, all studies presented a short period, with intervention protocols varying among the studies<sup>(42-46)</sup>. None of the five included studies presented a control group or randomization of research participants. The instruments used to evaluate the symptom clusters in children and adolescents with cancer undergoing palliative care, only one study was verified not to use validated instruments to measure such symptom groups, using subjective analysis through the oncologists' observation<sup>(42)</sup>. The most often reported instruments were VAS<sup>(43,45)</sup>, FACES<sup>(43-44)</sup>, and FLACC<sup>(44-45)</sup>.

## CHARACTERISTICS OF STUDY INTERVENTIONS

Therapeutic massage was evaluated in two promising studies<sup>(44,46)</sup>. In one study, there was an acceptability and pre-/post-test efficacy associated to the impact of therapeutic massage on pain, worry, and the overall quality of life of patients<sup>(46)</sup>. The participants reported significant short-term reductions in pain (p = 0.03) (after two sessions of therapeutic massage) and

worry ( $p = 0.03$ ) (after one session), when compared to baseline measurements<sup>(46)</sup>. The other study on therapeutic massage<sup>(44)</sup> had as a main characteristic the verbalization of children on the intervention, such as “I want to feel better” or “I want to relax” before the first session of therapeutic massage. Family caregivers were encouraged to watch the patients’ massage to obtain instructions on massage techniques which could be used by the family. Patients undergoing pediatric palliative care who received a massage completed the National Comprehensive Cancer Network Distress Thermometer Scale 5 minutes before and after the intervention. The participants received a validated visual scale spreadsheet for each symptom, suiting their age. The spreadsheet was provided to the child with numerical classifications in each of the following figures: FACES pictorial scale, Baxter Animated Retching Faces (BARF), Dalhousie Dyspnea Scale, McMurtry Faces Anxiety Scale, and Face, Legs, Activity, Cry, Consolability Scale (FLACC) for non-verbal children or those with cognitive problems pre- and post-massage<sup>(44)</sup>. In this study, there was a statistically significant difference in the use of medication for pain “if necessary” in the 24 hours before and after the massage ( $p = .0477$ )<sup>(44)</sup>.

The application of the Reiki intervention required informed consent from parents and the children’s consent, and the Reiki therapy sessions were carried out as desired by the family. Pain, anxiety, heart, and respiratory rate were registered immediately before and after each Reiki therapy session<sup>(43)</sup>. This study’s findings point that all the mean scores of the outcome variables (pain, anxiety, heart, and respiratory rate) reduced after the two Reiki sessions. Also, pain reduced significantly among non-verbal children ( $p = .063$ )<sup>(43)</sup>.

The use of boswellic acid as a palliative effect was evaluated for clinical and radiological responses. The subjective relief of symptoms such as headache, fatigue, loss of appetite, and nausea was monitored. Objective criteria such as vomit, body weight, and evolution of neurological deficits such as paresis, ataxia, impaired coordination, and sensory deficits were documented by repeated oncological exams<sup>(42)</sup>. In this study, no adverse effects which could be attributed to boswellic acid were observed in the 19 patients; 26% ( $n=5$ )

reported an improvement in their overall health status with the use of boswellic acid<sup>(42)</sup>.

The other intervention used *Cannabis sativa* (marijuana extract). After receiving a license in that country (Israel), parents and children were trained on how to use the medication and instructed of possible side-effects. Specifically, the parents were informed orally by the assistant physician of the possible side-effects of marijuana, such as an increase in sleepiness, slight reduction of cognitive skills and concentration, and allergic reactions, such as cutaneous eruption and wheezing, as well as dry mouth and dizziness. The marijuana was manufactured with support of the Israeli Ministry of Health. Marijuana was introduced and monitored gradually in patients to provide symptom relief while avoiding dependence<sup>(45)</sup>. This study with no control group had positive effects reported by children and parents in 80% of the cases regarding the symptoms nausea and vomit, sleep disorders, pain, appetite, and mood. However, 14% patients who smoked reported burning throat, anxiety attacks, and stomach pain<sup>(45)</sup>.

### INTERNAL VALIDITY OF THE INCLUDED STUDIES

Regarding the risk of bias of the studies selected and evaluated by the tool ROBINS-I, which evaluates the internal validity of non-randomized clinical trials of interventions, most studies ( $n= 3$ )<sup>(42,44-45)</sup> were classified as serious risk of bias, i.e., such studies presented important problems (and this occurs when the study is considered as low or moderate risk of bias for most domains, but presents serious risk of bias in at least one of the domains of ROBINS-I). The other two studies were judged as being moderate and with a higher reported methodological consistency<sup>(43,46)</sup>. No study was classified as low risk of bias, receiving a score in all domains for this category. Among the domains of ROBINS-I, those which were classified as serious were related to selection biases (participant recruitment and incomplete data/losses) and measurement biases (classification and intervention bias). In Chart 3, the methodological evaluation of each study is shown in detail in a chronological order.

**Chart 3** – Evaluation by consensus of ROBINS-I between two reviewers per bias domain.

Study	*Domains ROBINS-I							Overall judgment ROBINS-I
	Confounding bias	Participant selection bias	Classification of intervention bias	Bias due to intervention deviations	Incomplete data bias	Outcome measurement bias	Selective outcome reporting bias	
Janben <i>et al.</i> <sup>(42)</sup>	Moderate	Serious	Serious	Moderate	Serious	Serious	Moderate	Serious
Thrane <i>et al.</i> <sup>(43)</sup>	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
Weekly <i>et al.</i> <sup>(44)</sup>	Moderate	Serious	Moderate	Moderate	Serious	Moderate	Moderate	Serious
Ofir <i>et al.</i> <sup>(45)</sup>	Moderate	Moderate	Serious	Serious	Moderate	Moderate	Moderate	Serious
Genik <i>et al.</i> <sup>(46)</sup>	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate

Acronyms: \*ROBINS-I, Risk of Bias In Non-randomized Studies.<sup>(41)</sup> \*\* The global judgement of ROBINS-I is systematized and attributed as follows: a) Low risk of bias, in which the study is comparable to a well-designed randomized trial (the study is considered as low risk of bias for all domains); b) Moderate risk of bias – the study is consistent with a non-randomized study design, but cannot be considered comparable to a well-designed randomized study (in this case, the study is considered as low or moderate risk of bias for all domains); c) Serious risk of bias – the study has some important problems (the study is considered as low or moderate risk of bias for most domains, but presents serious risk of bias in at least one of the domains); d) Critical risk of bias – the study is too problematic to provide any evidence (the study is considered as critical risk of bias in at least one domain); e) No information – when no information is available to provide grounds to any judgment of risk of bias (missing information on one or more domains)<sup>(41)</sup>.



## DISCUSSION

This systematic review aimed at synthesizing and critically evaluating the evidence on complementary therapies effectiveness in symptom cluster management of children and adolescents with cancer undergoing palliative care. Overall, out of five quasi-experimental studies which met the inclusion criteria, two used therapeutic massage<sup>(44,46)</sup>, one used reiki<sup>(43)</sup>, one evaluated the effect of boswellic acid<sup>(42)</sup>, and another one evaluated the effects of *Cannabis sativa* (marijuana)<sup>(45)</sup>. Three studies (using therapeutic massage and Reiki) presented statistically significant results for managing the cluster pain-anxiety-worry-dyspnea.

### THERAPEUTIC MASSAGE

Care directed at children and adolescents concentrated on optimization of quality of life and reduction of suffering for those with severe diseases, including cancer<sup>(44,47)</sup>. Unfortunately, management of diverse cancer symptom clusters experienced by this population in palliative care are frequently mismanaged, focusing mainly on pharmacological intervention, which results in increased suffering and a reduced quality of life<sup>(48-49)</sup>. To meet the psychosocial well-being and manage the overload of cancer symptom clusters which are concomitantly faced by these patients, complementary therapies must be incorporated, e.g., therapeutic massage<sup>(44,48)</sup>.

Therapeutic massage is a low-risk manipulative physical intervention included among complementary health approaches<sup>(49)</sup>. This is also a low-cost intervention and is currently being used in pediatric oncology services, showing positive effects in adults and children with chronic diseases, including cancer<sup>(23,50-51)</sup>. Its administration is accessible and easily performed, providing the benefits of muscle relaxation and, consequently, tension reduction. Therapeutic massage had positive effects on diverse health conditions, such as in the integumentary, musculoskeletal, nervous, circulatory, lymphatic, respiratory, and endocrine systems<sup>(49)</sup>. Symptoms such as pain, worry, and fear are common in children with cancer under palliative treatment and the most appropriate management of these symptoms is particularly hard<sup>(47,52)</sup>. One possibility is the use of therapeutic massage<sup>(50-51)</sup>.

In this review, two studies evaluating the use of therapeutic massage presented positive and effective results<sup>(44,46)</sup>. The difference between the scores in the FLACC scale was significant ( $p < 0.0001$ ) comparing the moments before and after the intervention, showing an improvement in the overall comfort of the child after receiving therapeutic massage. The difference in the use of medication for pain "if necessary" in the 24 hours before and after the massage was statistically significant ( $p = .0477$ ), and such need was reduced after the intervention<sup>(44)</sup>. In the other study about therapeutic massage, the participants reported significant reductions in pain after two sessions of therapeutic massage ( $p = 0.03$ ) and in the worry after one session ( $p = 0.03$ )<sup>(46)</sup>.

These findings are in line with two recent systematic reviews<sup>(53-54)</sup>. The first review which aimed at understanding the effects of therapeutic massage on children with cancer

has shown that the authors of the evaluated primary studies used different massage techniques (Swedish massage, effleurage, petrissage, frictions, pressure), obtaining benefits in symptoms (pain, nausea, stress, and anxiety reduction) and increase in leukocytes and neutrophils<sup>(53)</sup>. The second systematic review of clinical trials in the pediatric oncology population identified nine studies investigating the efficacy of therapeutic massage and found encouraging and beneficial evidence for various symptoms, especially for oncologic pain and anxiety<sup>(54)</sup>.

Regarding the symptom pain, authors<sup>(55)</sup> show that pain perception by patients undergoing palliative care is reduced and lasts for 18 hours after the application of therapeutic massage, whereas other researchers<sup>(56)</sup> indicate that the intervention, conducted by a nurse with expertise in therapeutic massage for 45 minutes in children with osseous metastases reduces anxiety and pain and its effects are long-lasting. Based on previous studies with both adult and pediatric populations with chronic diseases, including cancer, therapeutic massage may help reducing unpleasant symptoms, such as pain, fear, anxiety, and fatigue, as well as improving the individual's functional capacity<sup>(23,50,51,54,57)</sup>.

### REIKI THERAPY

Concerning the use of Reiki as a complementary therapy for the management of symptom clusters in children and adolescents with cancer undergoing palliative care, the findings of the study evaluating Reiki therapy in this population shows that all mean scores for the outcome variables (pain, anxiety, heart and respiratory rate) reduced after two Reiki sessions ( $p = .063$ )<sup>(43)</sup>.

The findings in this review corroborate a recently published pilot study, conducted to test the viability and efficacy of Reiki to provide pain relief among pediatric patients submitted to hematopoietic stem-cell transplants. In this study, the effect of 88 sessions of Reiki therapy in nine patients was analyzed through a short, medium, and long-term perspective. Variance analysis of repeated measures has revealed a significant difference between the three periods ( $F = 17.17$ ,  $p < 0.0001$ ); pain reduction was achieved during the experimental period in short and medium term, whereas in the follow-up period the level of pain was stable<sup>(58)</sup>. The authors of the pilot study have concluded that nurses trained in pediatric and adolescent oncology may insert Reiki into their clinical practice as a valid instrument to reduce suffering caused by cancer in children and adolescents. Still, studies on Reiki are emphasized to be scarce so far, especially for the pediatric and adolescent oncology population undergoing palliative care<sup>(43)</sup>.

Among various complementary therapies, those related to energy are particularly promising<sup>(58-59)</sup>. Reiki has no religious doctrine and does not depend on any innate personal capacity for cure; it is taught by Reiki masters and practiced by those who have learned Reiki hand positions and who were attuned to open their body's energy channels<sup>(60)</sup>. Reiki is a relaxing form of cure therapy which is applied through a gentle, non-invasive, non-manipulative touch<sup>(61)</sup>. It is defined by the National Center for Complementary and Integrative

Health (NCCIH) as “a complementary health approach in which practitioners place their hands lightly on or just above a person, with the goal of helping to facilitate the person’s own healing response”<sup>(61)</sup>.

Non-invasive care that the Reiki therapy approach evokes is appropriate even for very fragile patients<sup>(59)</sup>, such as pediatric patients undergoing palliative care. Among adult patients, Reiki therapy emphasized relevant and positive clinical properties<sup>(62)</sup>, but, among children, studies are still too scarce to draw precise conclusions<sup>(58)</sup>. The few available pediatric studies discuss Reiki treatment for hospitalized children caregivers, especially those submitted to surgery<sup>(63-65)</sup>. Reiki as a complementary therapy in pediatric oncology has been growing worldwide, but still requires more robust evidence to be better accepted by the scientific community<sup>(58)</sup>.

### BOSWELLIC ACID

Boswellic acids are extracted from the resin of the *Boswellia* tree<sup>(42)</sup>. *Salai Guggal* is the Indian incense prepared with *Boswellia serrata*, which is still used in traditional popular Indian medicine (Ayurveda) in treating inflammatory and rheumatic diseases. In biochemical analysis, this Indian incense represented a standardized mixture of various boswellic acids and a minor component of dienes and terpenes<sup>(66)</sup>. *In vitro*, acetyl-11-keto-boswellic acid was shown to be the most efficient component of all boswellic acids<sup>(67)</sup>.

Extracts from *Boswellia serrata* gum resin and some of their constituents affect the immune system in different manners. During cell defense, boswellic acids seem to increase lymphocyte proliferation, whereas higher concentrations are inhibitive. Also, boswellic acids increase macrophage phagocytosis. Boswellic acids affect the cell defense system by interacting with cytokines production and release, inhibiting the activation of NF kappa B. Consequently, a negative regulation of TNF- $\alpha$  and a reduction of pro-inflammatory cytokines IL-1 $\beta$ , IL-2, IL-4, IL-6 e IFN- $\gamma$ , modulated by boswellic acids, have been reported<sup>(68)</sup>.

Regarding the use of boswellic acid as a complementary therapy, the one study which met this review’s criteria evaluated the palliative effect of this acid in clinical and radiological response, showing no adverse effects which could be attributed to boswellic acid in the 19 patients; 26% (n=5) reported an improvement of their overall health conditions with the use of boswellic acid<sup>(42)</sup>. The overall relief of some symptoms attributed to boswellic acid is partially explained by the fact that this substance is composed of lipophilic molecules capable of transposing the hematoencephalic barrier which may inhibit topoisomerase I and II, resulting in antiproliferative effects which have been observed in such study among patients with brain tumors<sup>(42)</sup>.

The resin of *Boswellia* species (‘incense’, ‘olibanum’) is used as an incense in religious and cultural ceremonies since ancient times. Its medicinal properties are also broadly known in treating inflammatory diseases, including cancer. Despite its historical, religious, cultural, and medicinal importance, the effects and mechanisms modulated by *Boswellia serrata* have not yet been fully clarified and deserve thus further studies for its clinical recommendation<sup>(69)</sup>. One approach

for cultivation, conservation, and preservation of important vegetal species through plant molecular biology, techniques for cultivating vegetal tissue, extensive and intensive research on the rationality and methodology of ayurvedic practices, isolation of active constituents and their development for new therapeutics, standardization, and validation of known phytotherapeutics, and other related aspects must be continuously focused<sup>(68-70)</sup>.

### USE OF CANNABIS SATIVA

With regards to the use of *Cannabis sativa* (marijuana extract), the study included in this review has shown positive effects reported by children and parents in 80% of the cases regarding nausea and vomit, sleep disorders, pain, appetite, and mood, improving thus patient quality of life. However, 14% of patients who smoked the extract reported throat burning, anxiety attacks, and stomach pain<sup>(45)</sup>. Although marijuana has no absolute contraindications, certain concerns must be considered before it is used, such as family history and dosage, since it can cause addiction; the legal issues in each country must also be observed<sup>(45)</sup>.

Although the medicinal use of Cannabis by oncology patients is mentioned in diverse international scientific publications<sup>(71)</sup>, there are still obstacles and resistance in Brazil due to the culture itself and the law number 11.343, dated August 23, 2006<sup>(72)</sup> which criminalizes the use of *Cannabis* and other substances. Currently, patients who need cannabinoids for treatment or therapeutic well-being face state bureaucracy and the path of judicialization of health<sup>(71)</sup>. Recommendation of this therapy in Brazil is thus faced with major dilemmas.

A study conducted in Minnesota, United States of America<sup>(73)</sup>, pointed that over 90% of pediatric oncologists showed desire to help children have access to medicinal Cannabis. In this study, 83% of the interviewed health professionals supported the use of medicinal *Cannabis* in cancer patients with poorly controlled symptoms<sup>(73)</sup>.

Our systematic review has some limitations. A significant heterogeneity among the included studies was noticed, specially concerning the different CT and employed protocols, which precluded data meta-analysis, as well as a broader comparison and synthesis of the data. Another limitation is the fact that different interventions are being evaluated in different tumor types, making studies heterogeneous and precluding quantitative analysis. Also, this review does not evaluate the risk of bias among studies. The absence of a control group and the short time of follow-up may have jeopardized the measurement of some study outcomes. For such, new clinical trials are suggested to be conducted, with a longer follow-up period, to verify whether the effects of complementary therapies on the management of cancer symptom clusters in these patients hold for medium and long terms. Therefore, new investigations must be conducted, especially well-designed controlled randomized clinical trials with representative population samples and low risk of bias. The small number of studies retrieved from the databases is partially justified by the difficulties that researchers face worldwide regarding ethical issues, which involve sampling and recruitment of children and adolescent patients with

cancer undergoing palliative care, and hence, such findings must be valued. Further systematic reviews must observe the pinpointed frailties and develop a more comprehensive search strategy, enabling the retrieval of a higher number of studies. However, this review is considered to present clinical significance for the management of symptom clusters in pediatric cancer patients undergoing palliative care; its results are useful for health professionals providing care to this population.

## CONCLUSION

The synthesized and analyzed evidence point out that the use of therapeutic massage and Reiki might be effective and promising for managing cancer symptom clusters, especially for the cluster pain-anxiety-worry-dyspnea in

children and adolescents with cancer undergoing palliative care. Studies evaluating the use of boswellic acid and marijuana, although showing some positive effects, are so far insufficient to precisely demonstrate the effect of such therapies on the management of cancer symptom clusters, mainly because they have shown no statistically significant differences and led to important adverse effects. Thus, further studies are necessary to clarify these findings.

This review's results may subsidize reflections of health professionals, especially pediatric nurses and oncologists, on the use of complementary therapies in addition to conventional treatment in palliative care in pediatric and adolescent oncology, seeking to contribute to their use based on evidence and demystifying these practices while, more importantly, providing a better quality of life to such a specific population.

## RESUMO

**Objetivo:** Avaliar a efetividade de terapias complementares no manejo dos *clusters* de sintomas em crianças e adolescentes com câncer em cuidados paliativos. **Método:** Revisão sistemática guiada pelo *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*, com acesso às bases de dados MEDLINE, Web of Science, Central Cochrane e PsycINFO. A identificação, seleção, inclusão, extração e avaliação metodológica foram realizadas por dois revisores independentemente. **Resultados:** Atenderam aos critérios de elegibilidade cinco quase-experimentos. As características heterogêneas dos estudos impossibilitaram a meta-análise. Dois estudos utilizaram a massagem terapêutica; um, o Reiki; um, ácido boswélico; e um, a *Cannabis sativa*, sendo que três deles (que usaram massagem terapêutica e Reiki) apresentaram resultados estatisticamente significantes para o manejo do *cluster* dor-ansiedade-preocupação-dispneia. A maioria dos estudos apresentou risco-de-viés moderado pela ferramenta ROBINS-I. **Conclusão:** A massagem terapêutica e o Reiki podem ser terapias efetivas para o manejo de *clusters* de sintomas, especialmente o *cluster* dor-ansiedade-preocupação-dispneia em crianças e adolescentes com câncer em cuidados paliativos.

## DESCRITORES

Criança; Adolescente; Cuidados Paliativos; Terapias Complementares; Enfermagem Oncológica; Revisão.

## RESUMEN

**Objetivo:** Evaluar la efectividad de las terapias complementarias para el manejo de los grupos de síntomas en niños y adolescentes con cáncer en cuidados paliativos. **Método:** Revisión sistemática guiada por *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*, con acceso a las bases de datos MEDLINE, Web of Science, Central Cochrane y PsycINFO. La identificación, selección, inclusión, extracción y evaluación metodológica fueron realizadas por dos revisores de forma independiente. **Resultados:** Cinco cuasi-experimentos cumplían los criterios de elegibilidad. Las características heterogéneas de los estudios impidieron el metanálisis. Dos estudios utilizaron la terapia de masaje; uno, el Reiki; uno, el ácido boswélico; y uno, la *Cannabis sativa*; tres de ellos (los que utilizaron la terapia de masaje y el Reiki) mostraron resultados estadísticamente significativos para el tratamiento del grupo dolor-ansiedad-preocupación-disnea. La mayoría de los estudios mostraron un riesgo de sesgo moderado según la herramienta ROBINS-I. **Conclusión:** La terapia de masaje y el Reiki pueden ser terapias efectivas para el manejo de los grupos de síntomas, especialmente el grupo dolor-ansiedad-preocupación-disnea en niños y adolescentes con cáncer en cuidados paliativos.

## DESCRIPTORES

Niño; Adolescente; Cuidados Paliativos; Terapias Complementarias; Enfermería Oncológica; Revisión.

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