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Music therapy in the treatment of children with cancer

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We declare to have written this thesis on our own and that we have stated every source of literature we used. We also declare, that neither of the authors has any conflict of interest.

Zuzana Agathangelou wrote the first chapter of the theoretical part, read through texts written in English, created the attachments and executed the additional analysis. She also translated the entire thesis from Slovak and Czech to English. Linda Horváthová wrote the second and third chapter of the theoretical part, the introduction of the practical part and described the entire research construction process. Every step of the research process was carried out and discussed by both authors, with the help of the third researcher (JK) when needed, in order to reach consensus and to fulfill the high standards of quality required to conduct the analyses. PhDr. Zuzana Svobodová helped with the search for the studies later used in the practical part. Consultations on the topic of research methodology were provided by PhDr. Miloslav Klugar, Ph.D. For the entire duration of the process of conducting research and writing, the availability of thesis supervisor Mgr. Jiří Kantor, Ph.D. for consultation and discussion was of immense help.

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I would like to thank all the children, “almost adults” and parents of these oncology patients for their trust, which gives me a chance to learn about their lives, to accompany them on their journey and to experience their own world of music.

Linda

We also feel grateful for all the health care workers in clinics around the globe, who are welcoming towards the innovative practices of music therapists.

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Linda and Zuzka

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INTRODUCTION

Each year around 150 out of every 1 000 000 children, adolescents and young adults fall ill with an oncology disease before reaching their 20th birthday. For this age group oncology diseases are the third leading cause of death. Currently, thanks to multi-modal treatment – consisting of surgical procedures, chemotherapy, radiotherapy and immunotherapy – it is possible to cure more than 75% pediatric patients (Kolenová, 2014). However, this treatment is not easy to get through. Its demanding nature and lengthy duration cause physical collateral damage as well as bruises on the soul.

Psycho-social-spiritual care is therefore an essential part of treatment in pediatric oncology. In the course of treatment, patients are often hospitalized for long periods of time and socially isolated. Music therapy in the oncology department uses music in prophylactic, curative as well as in palliative care and holds potential to help a broad spectrum of patients who suffer from treatment side-effects, writes Stanczyk (2011) and continues: "*Although music therapy does not affect the disorder directly, it has a big impact on patient's mood and sometimes improvements can be observed in the ways they cope with feelings concerning their illness."* Bringing joyful experiences and a "different culture" into the hospital environment can therefore benefit the patients in improving their adaptation to hospitalization, strengthening their coping strategies, which in turn promotes better cooperation with the medical personnel.

In this thesis we therefore focus on mapping the effectiveness of musical interventions on the physiological and psychological aspects during the treatment of pediatric and adolescent patients with oncology diseases.

The theoretical part consists of an introduction to pediatric oncology, as well as its relation to developmental psychology. Further on we discuss the family as a vital component of whole course of treatment. The last chapter in this section considers defining music therapy and its incorporation into the hospital environment.

The goal of the practical section was to describe the process of conducting our research. We chose to construct an umbrella review – in other terms a systematic review of systematic reviews – which can be useful when multiple systematic reviews of varying quality have been constructed on the same topic. An umbrella review, among other things, critically appraises existing systematic reviews and informs the practice of "the real effectiveness" (Klugar, 2015).

We would like this thesis to present an overview on the importance of adding music based interventions into common medical practice.

PART I. - THEORY

1 THE SPECIFICS OF PEDIATRIC ONCOLOGY

According to the website of the J. E. Purkyně Czech Medical Association: *"Pediatric oncology is a medical field dedicated to the diagnostics and treatment of solid tumors and hematological malignancies in children from 0 to 15 years of age and adolescents from 15 to 19 years of age. The foundation of the pediatric oncology field was shaped by the recognition of fundamental differences between tumors of the adulthood and childhood ... not only in their incidence but also in etiology, biology, clinical behavior, treatment and outcomes thereof."* (Starý, 2017).

The first difference in the care for pediatric as opposed to adult oncology patients stems from the nature of physiological processes, which changes during the process of maturation. Children do not just grow in size. Their organs and functionality thereof still continue to develop. This fact has a bright side as well as a darker one. According to Starý (2017), wound healing is a much faster process for children than it is for adults, comorbidities with other ailments are rare and their organs tend to be healthier than adults. However, he adds that for those reasons, the intensity of treatment, which could lead to unfavorable outcomes later on and influence overall development, has to be considered carefully.

The etiology of oncology diseases is driven by a series of cumulative genetic and epigenetic alterations (Takeshima and Ushijima, 2019). These tend to accumulate in time and that is why they can be found in adults with a much higher frequency. From the total number of diagnosed malignancies, pediatric cancers make up for 1-1.5% of all cases. Their incidence is however on a constant, slight rise (Starý, 2017). As opposed to tumorous growths in adulthood, the etiology of most pediatric cases remains unknown. It cannot be explained by the cumulative negative environmental effects and in about 90% genetic factors are not the cause either (Zhang, 2015).

1.1 ONCOLOGY DISEASES IN CHILDHOOD

A hypothetical graph of prevalence of oncology disorders in childhood and adolescence would have two peaks. The highest percentage of cases occur within the first three years of life, after which incidence steadily declines until 9 years of age. After this period another increase in cases can be observed which peaks during late adolescence (Davidoff, 2010). These two distinct age groups of pediatric oncology patients present different types of diagnoses. Since various types of cancer exist, each type has a distinctive age representation. Overall it can be said that children 0-5 years old most often present with leukemia; lymphomas; tumors stemming from undifferentiated tissue – embryonal tumors such as neuroblastoma and sarkoma; tumors of the connective tissue (Bajčiová, 2014). Among pubescent and adolescent patients Hodgkin lymphoma and germinal cell tumors (testicular cancer) are some of the most common diagnoses. It is in the latter patient cohort where the yearly incidence of oncology disorders is steadily on the rise for non-Hodgkin lymphoma; osteosarcoma; Ewing sarcoma; cancer of the thyroid; melanoma and soft tissue rhabadomyosarcoma (Davidoff, 2010).

Tumor growth in childhood is much more aggressive than in adulthood and metastases form faster as well. An early diagnosis and treatment are therefore of utmost importance. The Czech Oncology Association of the J. E. Purkyně Czech Medical Association states, that childhood oncology disorders should be viewed as acute rather than chronic illnesses (Bajčiová, 2014). Treatment is however much more effective in children than adults. This gives oncology patients and their parents hope, which can guide them throughout the lengthy and demanding treatment process.

1.1.1 Leukemia

Leukemia is a malignancy of the blood. In their article on hematopoiesis, Jagannathan-Bogdan and Zon (2013) describe the process of the origins of blood and its components. All human blood cells are produced in bone marrow. Red blood cells transfer oxygen and other substances through the blood stream into every tissue of the body. Platelets play a vital part in blood clotting processes and white blood cells are an integral part of our immune system. (The authors are aware of the major simplification of this description, however for the purpose of this thesis they have decided not to

elaborate further.) Each type of blood-cell originates from stem-cells – undifferentiated blood-cells in the earliest stage of their development. Stem-cells differentiate as they reproduce into multiple kinds of blood cells, such as lymphocytes or neutrophils. According to Chappelear (2017) in the case of leukemia, white blood cells lose the ability to mature and further differentiate. This leads to an overproduction of one cell type, which then replaces healthy blood cells and can lead to bone marrow failure. Abnormal white blood-cells flood the circulatory system, lymphatic pathways and organs of the body, meaning that the body loses its ability to fight infections and blood-clotting as well as nutrient transport are disrupted.

Leukemia can be an acute as well as a slowly progressing disease. Starý (2017) states, that the most common form in children is acute lymphoblastic leukemia (ALL); which is responsible for 80% of all leukemia diagnoses and 25% of pediatric malignancies. Other types of leukemia, which occur in childhood are acute myeloid leukemia (AML) – about 15% leukemia diagnoses; myelodysplastic syndrome (MDS) – about 5% leukemia diagnoses; and chronic myeloid leukemia (CML) – about 2-3% leukemia diagnoses.

As mentioned above, acute lymphoblastic leukemia is by far the most common oncology disease of childhood. According to (Chappelear, 2017) it affects 6 out of every 100 000 children and usually between the 3rd and 7th year of age. This type of leukemia used to be classified in 3 further sub-types, depending on which how the impaired blood-cells looked under a microscope. However, in 2016 the World Health Organization updated this system according to new cytogenetic and cytometric tests, which can provide a more accurate diagnosis and treatment planning. The three main categories of this new system are: B-Cell ALL; T-Cell ALL; Mixed Lineage ALL (American Cancer Society, 2018).

ALL is the outcome of an excessive multiplication of immature lymphoblasts, which push out healthy blood-cells. Silverman (2009) lists its symptoms. An afflicted child is more prone to infections and excessive bleeding, because cancerous cells get transferred from bone marrow into the circulatory system; lymphatic tissue; the spleen and other vital organs. Chappelear (2017) adds, that on the outside, the child can seem fatigued; lethargic and have difficulties breathing due to an insufficient amount of red blood-cells to transport oxygen. They can bruise more easily; suffer from a higher propensity to infections; pains in their joints and limbs; swollen gums; frequent nose-bleeds; small red dots on their skin; fever; weight loss and palpitations.

ALL is usually treated with chemotherapy – oral, intramuscular or intravenous administration of anticancer drugs. According to Kolenová (2014) treatment is introduced in three phases. The first stage of remission induction lasts approximately 4 weeks and in the majority of cases the child needs to be hospitalized throughout. A bone-marrow test is conducted towards the end of this period, in order to find out, whether the disease is in remission. This stage is followed by consolidation/intensification and can begin once the illness starts to remiss. Silverman (2009) describes consolidation therapy as a treatment which follows initial therapy after cancer has disappeared, in order to kill any remaining cancer cells in the body. It may include radiation therapy or a stem cell transplant. The same goal is stated by the aforementioned resource in the third stage of treatment – the maintenance phase. Chappelear (2017) writes, that lower doses of cancer medications are given at this point and the child does not need to be hospitalized and can partake in every day activities. Maintenance treatment can span up to 2.5 years after the initial diagnosis.

According to Chappelear (2017), radiation therapy may be used in cases where the cancer has or may spread into the central nervous system or the testicles. He continues to say, that if a bone marrow transplant is needed, radiation therapy may be administered in preparation. In cases of relapse a stem cell transplant can be necessary. It is described by Marcus and Haas-Kogan (2009) as a form of therapy for patients with cancers or other diseases, which involves taking cells from bone marrow (stem cells), filtering those cells, and administering them to the patient in need, after their own unhealthy bone marrow has been treated to kill the abnormal cells.

1.1.2 Lymphomas

Malignant lymphomas stem from transformed lymphatic cells. Since they usually affect the whole organism, they belong to the group of systemic diseases (Reiter and Ferrando, 2009). Since lymphomas can affect bone marrow as well, a differential diagnosis of from leukemia can be difficult (Kolenová, 2014). Lymphomas are the third most common malignancy in childhood and account for approximately 10% of all malignancies, which arise before the age of 18. Around 60% of those cases are classified as non-Hodgkin lymphoma, 40% as Hodgkin lymphoma (Reiter and Ferrando, 2009). Authors also explain, that both kinds of lymphomas develop from white blood cells (lymphocytes) and can arise in any organ comprised of lymphatic tissue. Without medical treatment, both types are usually lethal.

According to Yiallouros (2009), for treated Hodgkin lymphoma the long-term survival rates of children and teenagers are over 90%. The incidence of Hodgkin lymphoma peaks at 15 years of age. The gender ratio differs in sources. Kolenová (2014) states a ratio of 4:1 with the incidence for boys being much higher than for girls. Yiallouros (2009) gives a much more equalized ratio of 1,2:1.

Reiter and Ferrando (2009) write, that non-Hodgkin lymphomas tend to spread from their primary affected organ to many other sites, including the central nervous system or bone marrow, and can behave very similarly to acute lymphoblastic leukaemia. There are various kinds of Non-Hodgkin Lymphomas and in childhood almost all of them spread very fast and are therefore highly malignant. The highest incidence can be observed at 15 years of age as well with boys being about twice more likely to be affected than girls (Yiallouros, 2009).

1.1.3 Solid Tumors

As the name suggests, solid tumors create solid masses of cells in individual organs of the body as opposed to whole systems as was the case with leukemias and lymphomas. They can spread to other organs either through direct growth in the surrounding tissue or by forming metastases (Yallouros, 2009). Depending on a multitude of factors they can be both benign or malignant. Treatment depends on the type and stage of tumorous growth and is usually a combination of surgical procedures, chemotherapy and radiation therapy. According to Kuzma (2006), the most common types of solid tumors found in children are found in the autonomous nervous system (neuroblastoma); kidneys (nephroblastoma); bones (osteosarcoma) and the retina (retinoblastoma). Kline and Sevier (2003) add rhabadomyosarcoma to the list.

Neuroblastomas are malignant solid tumors. They arise from degenerate immature cells of the sympathetic nervous system, which is part of the autonomous nervous system. In about 50% of cases the tumor develops in the medulla of the adrenal gland. The sympathetic trunc at any spinal level can be affected as well – about 75% are found in the abdomen (Shusterman and George, 2009). Kolenová (2014) states that 90% of neuroblastoma occurs in children younger than 5 years of age. According to Yiallouros (2009), there is a slightly higher incidence in boys. They further state that along with tumors of the central nervous system it is the most frequent solid tumor type for children and adolescents. This type of tumor is problematic due to its unpredictable behavior. It can regress spontaneously in very small children or be resistant to intensive

chemotherapy in older children (Shusterman and George, 2009). Some neuroblastomas do not grow further than their original site, others can spread into lymph nodes. Kline & Sevier (2003) write, that the children with localized tumors and those, who fully recover after the initial treatment have a much higher likelihood of long-term survival and a life without the disease. However, about half of the patients show metastases at initial diagnosis (Yiallouros, 2009). For these reasons, the 3 year survival rate is less than 30% (Kolenová, 2014).

Accounting for up to 85% of cases, Wilms tumor (nephroblastoma) is the most common type of kidney tumors in childhood (Yiallouros, 2010) and the second most common solid tumor of children under 15 years of age after neuroblastoma (Kolenová, 2014) with the highest incidence (50% cases) within the first 3 years of life (Kuzma, 2006). The prognosis of Wilms tumor is quite good with 80-90% patients getting cured (Kolenová, 2014).

Osteosarcoma is the sixth most common tumorous growth in children and the third most common in adolescents and young adults. Their peak incidence in adolescence is theorized to be caused by fast bone growth in this age group (Kline and Sevier, 2003). Epidemiological data shows, that patients with osteosarcoma are generally taller and the growth occurs in places with the greatest bone elongation. Boys are more affected than girls (Yiallouros, 2009). Girls are affected in earlier years of life, which correlates with their earlier growth spurt (Kolenová, 2014). In more than 50% cases the growth occurs around the knee and in about 70% cases they metastasize in the lungs (Yiallouros, 2009). Janeway, Gorlick and Bernstein (2009) write, that in the past, amputations of the shoulder or lower limb were inevitable. These interventions can be avoided today in most cases and in favorable conditions it is possible to remove part of the affected bone and replace it with endoprosthetics. Most osteosarcomas grow and spread very quickly. Without an appropriate treatment, the disease is fatal (Kuzma, 2006).

Retinoblastoma is a rare neuroektodermal malignant eye tumor arising from the embryonal neural retina (Kolenová, 2014). Therefore it almost exclusively occurs during childhood, about 80% of patients are diagnosed before reaching 4 years of age (Yiallouros, 2016). It can develop in one (70-75% cases) or both eyes (25-30% cases) (Kuzma, 2006). All bilateral and 20% unilateral tumors are hereditary. In families where the hereditary form occurs, it is essential to screen for this disease regularly from neonatal age (Kolenová, 2014). Mukai et al. (2009) add, that people with the hereditary form are also prone to other types of cancer, such as pineoblastoma or osteosarcoma.

The growth stays within the area of the eye at first but may grow very fast and spread along the optic nerve into the central nervous systems. Later it may spread via blood or the lymphatic system into other parts of the body. If untreated, it is fatal for 98-98% of patients (Yiallouros, 2016). If treated it is possible to preserve eye-sight by radiation therapy. If diagnosed in time, about 80% of children can be cured (Kuzma, 2006).

1.1.4 Tumors of the Central Nervous System

Tumors of the central nervous system are a heterogeneous group both from the biological and histological standpoint, ranging from localized growths with low malignancy up to highly malignant growths which may spread to other parts of the body (Kolenová, 2014). They originate in the brain or the spinal cord and are the second most common group of malignancies in childhood (about 24%). The most common symptoms according to Sharma and Sharma (2020) are caused by increased intracranial pressure and therefore present as headaches, vomiting, drowsiness, confusion, nausea, sixth nerve palsy, papilledema, generalized seizures and cognitive impairment. In an overview, Kieran et al., (2009) list gliomas, medulloblastomas, rhabdoid CNS tumors, pineoblastomas, ependymomas, and choroid plexus tumors among to most common types. This is a very simplified distinction. Sharma and Sharma (2020) give a much more precise list, however the description of each type according to them would be too extensive for the purpose of this thesis.

Kieran et al., (2009) describe gliomas as tumors which originate from glial cells in the central nervous system. As there are more kinds of glial cells, there are more kinds of gliomas, such as astrocytomas, oligodendrogliomas, mixed oligo-astrocytic, and mixed glioneuronal tumors. The World Health Organization (WHO) categorizes gliomas from grade 1 (lowest grade) through grade 4 (highest grade), based on various characteristics – low grade gliomas (grade 1 and 2) showing lesser malignancy than high grade gliomas (grade 3 and 4) (Forst et al., 2014). For simplification purposes, only the latter distinction is further explained.

Low-grade gliomas are a diverse group of brain tumors with a better prognosis than high-grade gliomas due to their generally indolent course (Forst et al., 2014). Most low-grade gliomas can be found in the cerebellum and central regions of the cerebrum, such as the optic pathway and the hypothalamic-pituitary axis. They are the most common CNS tumors in children and adolescents, accounting for about 50% of all CNS tumors in this age group (Yiallouros, 2007). The unpredictability of growth of low-

grade gliomas can cause complications. Most of the time these tumors are localised and their growth is slow. In some patients they can halt completely for a while. They may also grow very fast and aggressively, however, and therefore they can become life-threatening in the course of the disease (Kieran et al., 2009). Most low-grade tumors have a good prognosis and can be cured by surgical procedures, however the potential benefits of treatment must balance out the potential risks specific for this age group (Forst et al., 2014).

High-grade gliomas show highly malignant behavior. They usually grow fast and frequently destroy healthy brain tissue. For this reason, they can lead to death within months without proper treatment, which can be difficult due to their rapid and permeating growth (Kieran et al., 2009). 15 to 20 % of CNS tumors in children and adolescents are high-grade gliomas with boys and girls equally affected. Incidence is similar throughout age groups, with the exception of children below 3 years of age where this condition is rarely found (Yiallouros, 2007).

Medulloblastoma and other neuroektodermal tumors are the most malignant tumors in children and adolescence (Kolenová, 2014). They account for approximately 3% of paediatric malignancies and about 12% of all CNS tumours in this age group. Patients most often diagnosed are between 4 and 7 years of age (Sharma and Sharma, 2020). They originate from undifferentiated ‚embryonal' cells of the central nervous system, which proliferate at a high rate. This is the cause of their very fast growth (Yiallouros, 2021). Their primary center is in the cerebellum but with growth they can spread into the brain stem or the ventricles. Because the cancerous cells spread via cerebrospinal fluid, they can metastasize for example in the spinal canal. Approximately 30% of patients present with metastases at initial diagnosis (Sharma and Sharma, 2020). is a highly malignant, solid tumor that develops due to a malignant transformation of cells of the cerebellum, a part of the brain (Yiallouros, 2021).

1.2 THE ONCOLOGY TREATMENT OF CHILDREN

The diagnostics and treatment of oncology diseases in childhood is complex. It involves treatment of the tumor (somatic treatment), as well as care for the psychological, social and spiritual aspects of personality. An oncology diagnosis, along with its somatic treatment severely impact the social and psychological attributes and vice versa – the psyche and adequate social support influence how well the patient can

cope with the somatic treatment. Besides that, encountering a life-threatening disease, questions concerning spirituality naturally arise. Therefore a holistic treatment should dedicate time to these topics as well.

1.2.1 Somatic Treatment

Depending on various circumstances, the somatic treatment can involve a combination of surgical interventions, radiotherapy, chemotherapy, immunotherapy, hormonal therapy and supportive treatment. Its focus lies in treating the tumorous growth itself or its potential metastases. It can be sub-divided into local treatment (operations; radiotherapy) and systemic treatment (chemotherapy; immunotherapy; hormonal therapy; supportive treatment). Individual methods can be used separately or in various combinations and their succession varies depending on the diagnosis; treatment protocol or clinical studies (Koutecký and Cháňová, 2003). Authors further elaborate on specific types of somatic treatment:

Surgical treatment – viable only in the treatment of solid tumors. In some cases, however, even delimited tumors are not indicated of this kind of treatment. This can occur in cases, where the tumors have grown into vital organs; spread into surrounding tissue and organs; if surgery would create a severe functional impairment; or if the operation would be technically impossible for other reasons (Koutecký and Cháňová, 2003). Kuzma (2006) adds, that when an operation is not possible due to the tumor's size, other methods such as cytostatics or radiation therapy can be used to reduce its size, after which the operation might be feasible.

Radiotherapy takes advantage of the destructive effects of radiation on live cells. It can be used as a curative, as well as a palliative form of treatment. The full radiation dose is prescribed by a radiologist, depending on the type of tumor; its size; location; sensitivity to radiation and the child's age and the overall state of their health. The dose is divided in a process called fractionation into daily doses, called fractions (Koutecký and Cháňová, 2003). Kuzma (2006) lists possible adverse reactions to radiation: skin irritation; hair loss; loss of appetite; head aches; diarrhea; and irritation of the oral mucosa.

Chemotherapy uses chemical substances – cytostatics – which have the capability to destroy cancer cells. Their administration can be intravenous; intramuscular; intratectal or oral. The treatment consists of several consecutive days of therapy, followed by a break, after which the cycle repeats. One of the difficulties of

chemotherapy is the limited spectrum of effectiveness of each cytostatic agent. They are therefore administered in various combinations, based on clinical trials. In this way, the tumor's sensitivity to the cytostatics (chemosensitivity) and chemoresistence is determined (Koutecký and Cháňová, 2003). According to Kuzma (2006), a child undergoing chemotherapy has an increased risk of infections, light anemia and bleeding, because the treatment decreases the number of leukocytes, erytrocytes, as well as thrombocytes.

Immunotherapy utilizes the natural antitumor immunity response of the body by increasing its capability to attack and destroy the malignant growth. According to Butterfield, Kaufman and Marincola (2021) this treatment can be administered orally, topically, intravenously or intravesically. There are two main approaches of immuno-oncology: passive immuno-therapy (eases and strengthens the existing immune reaction through checkpoint inhibitors) and active immuno-therapy (directs the body's own immune cells to recognize, attack and destroy cancer cells via antitumor vaccines). As of today, passive immunotherapy shows better results. ESMO (2017) explains immunity checkpoints as the body's natural defense against autoimmunity. They are meant to switch off the immune response in order to prevent collateral damage of healthy cells by "deactivating" (or in some cases destroying) an activated lymphocyte – such as a T-cell – immediately after recognizing and destroying a cancer cell. Koutecký and Cháňová (2003) continue, that as opposed to chemotherapy, which attacks cancer cells directly, immunotherapy with checkpoint inhibitors acts "indirectly" by taking advantage of the patients own immune system. Due to its ability to block the body's natural protective mechanisms, which prevents the immune system from over-activation, immunotherapy can influence healthy tissue as well and cause undesirable side-effects. As immunotherapy is quite novel, the entire extent of their side-effects along with their long-term duration is still unknown.

1.2.2 Psycho-social-spiritual Care

Care for the child oncology patient's psychology, social well-being and spirituality is an integral part of their treatment. Being diagnosed with an oncology disorder along with its treatment brings about changes on all of these levels. That is why the help of a team of experts such as special and treatment pedagogues; educators; psychologists; play therapists; social workers; volunteers; various support groups; associations and organizations etc. – is crucial.

Kearney and Salley (2015) define the standards in psycho-social care for the parents of children with oncology diseases as the necessity of an initial and ongoing evaluation of their needs for a healthy psychological growth. According to them, access to appropriate interventions can help parents, children and the entire family system to cope with the situation in a better way. Standards of psycho-social care for children with oncology diseases according to Kupst (2015) affirm the necessity of systematic evaluations of their psychological and social needs and add: monitoring of neuro-psychological deficits during and after treatment of children with brain tumors; an annual screening of educational, social and psychological problems and risky behavior in children post-treatment; financial advice; psycho-education or a support system for siblings. "*In some cases, the aide of a psychiatrist or a psychotherapist, interpreter (in case of a language barrier) or spiritual guides, who can help families to cope with the demanding life situation, is needed.*" states the handbook of SIOPE (2009, pg. 18,19) which also lists the factors, helpful to promote the best quality of life possible for the patient and their family:

- Planned social, psychological and educational pedagogy care.
- Access to extensive information on the disease, its treatment and the effects on the family.
- Offering information to children, suitable for their age and level of understanding.
- Upholding the child's activity level and preservation of the most normal way of life possible, which the treatment process can allow.
- Ensuring the child's re-introduction into the school collective and society as a whole.

  Within the framework of psycho-social care, it is essential for an expert team to offer help for patients and their families during the treatment process, as well as subsequently if necessary, or in the course of palliative care. This can help to cope with stress, to foresee a possible crisis and to strive for a higher quality of life overall.

1.2.3 Pain Management

According to Koutecký and Cháňová (2003, pg. 87): *„Oncology diseases pose many difficulties for those affected, which have a major impact on their physical and mental condition"* Fear is the first in line of this vast array of issues and appears without exception. *"The second condition is pain, which can be just as frightening, as the anguish about whether the disease will be fatal."* The causes of pain can vary. It is influenced by the tumor itself, medical examinations, and other treatment methods. *"Inevitable pain is always easier to bear, when not accompanied by fear of the unknown."*

The International Association for the Study of Pain (IASP, 1994) defines pain as an uncomfortable sensory and emotional experience, which is associated with an existing or potential tissue damage, or marked by the duration of such impairment. The level of pain in children is influenced by emotional and situational factors, and therefore it is not possible to expect the same level of pain even in children with identical diseases or medical procedures. The manifestation of behavior caused by pain change throughout development as well (Vágnerová, 2012).

Pain can be procedural, acute and chronic (Bužgová, 2019). Procedural pain occurs during medical procedures. Sharp and sudden pain, which did not originate from tissue damage caused by medical interventions is classified as acute pain and tends to be connected to injury or an illness and can subside in a matter of days. Chronic (persistent) pain lasts longer (continuous or intermittent) and can arise without an apparent cause as well. The American Pain Society (2000) classifies pain linked to oncology diseases as chronic pain, further sub-classified.

Pain plays a critical role in the efforts to achieve health and well-being. Lee (2016) says, that if left untreated, it can among other things lead to a decline in mobility; strength and functioning of the immune system and to various issues in the social and psychological spheres. Considering its negative impact on everyday life, it has a strong influence on the overall quality of life.

WHO (1996) codified the basic principles of pain management. „*The analgesic ladder presents schematic instructions when choosing a suitable analgesic according to the pain intensity. For a long time, there has been a tendency to increase the stress on the aspect of pain intensity whilst choosing analgesics, as opposed to its etiology, or the ailing child's prognosis."* Bužgová states (2019, pg. 44).

The occurrence of pain in oncology patients varies from person to person. Koutecký and Cháňová (2003) explain, that it is influenced by the tumor's growth rate; damage to the nerves, bones and other organs; the pain threshold; tolerance for pain and the overall psychological state. Pain is perceived through nerve endings in the affected organ, as well as the brain. This explains why some unfavorable circumstances, such as fear; anxiety; depression; fatigue or insomnia, can increase pain perception and why anxiolytics; antidepressants; hypnotics and corticosteroids (medicaments, which limit inflamation and swelling) are an integral part of treatment.

Regarding pain accentuated by psychological states, there is an ongoing debate concerning non-pharmacological means of its reduction. More on this topic can be found in chapter 3.1.3 (Music and Pain).

1.3 TREATMENT COMPLICATIONS OF ONCOLOGY DISEASES

Among the oncology treatment components is the competence to foresee complications and apply the appropriate treatment in the right time, in order to diminish adversities. *"Even a seemingly mild symptom can be a signal of a potentially serious complication."* (NFDO Krtek, 2008, pg. 64). Children with oncology diseases can go through difficult, many times life-threatening complications of treatment, which can vary with each case. Once a child is cured, difficulties can still arise in the form of late onset side-effects of treatment and treatment complications. In case the treatment is unsuccessful, treatment moves into the area of palliative care. For this reason, a chapter about this type of care has been included our thesis.

1.3.1 Acute Complications of Treatment

Each type of somatic treatment brings about specific side-effects. These come in a vast array, and therefore only basic acute complications which can accompany treatment are listed below (NFDO Krtek, 2008; Koutecký and Cháňová, 2003):

- damaged hematopoiesis due to cytostatics (depending on the type of hematopoietic cells this can exhibit as leukopenia or neutropenia, which greatly lowers resistance to infections; thrombocytopenia, which causes bleeding,

excessive bruising or petechiae; anemia, which causes fatigue, palpitations, a propensity to fainting),

- bacterial infections (inducing fever; cough; swelling; abdominal pain; shingles) or viral infections (sheeppox pose fatal danger for oncology patients),
- nausea, vomiting (which lead to a decline in the state of nourishment),
- diarrhea (as a result of damage to the colon mucosa or an infection),
- constipation,
- damaged mucosa of the oral cavity and throat – mucositis,
- temporary hair loss (alopecia),
- dry skin, eczema,
- neurological and psychological complications (neuropathy; hearing impairment; ileus – a temporary lack of normal muscle contractions in the intestines; urinary retention; brain tissue damage – encefalopathy; apathy; night blindness – nyctalaopia),
- damage to the heart (cardiotoxicity, cardiomyopathy, hypertension), lungs (pneumotoxicity), kidneys and the urinary tract (nephrotoxicity, urotoxicity),
- adverse effects on the genitals and fertility,
- adverse effects of corticosteroids (disorders of water and salt retention; increased appetite; irritation of stomach lining; muscle weakness; increased blood sugar; skin strength disruption; higher blood pressure; loss of potassium; irritability; insomnia; changes in the psychological state – increased sensitivity; mood swings; aggression; sadness).

1.3.2 Late Onset Adverse Reactions to Treatment

Thanks to prognoses getting better for an increasing number of patients and therefore a higher number of people finishing oncology treatments, the topic of late onset adverse effects became one of the more serious problems of these patients. *"Most authors distinguish between long-term and late onset adverse effects of oncology treatment. Whereas long-term side-effects persist during as well as after treatment, late onset side-effects are such, which are not present during treatment, but arise with a la-*

tency of some years after the treatment has finished." (Mladosievičová and Rečková, 2015, pg. 2).

According to them, among the most often affected are patients treated who had received high doses of chemotherapy and a subsequent stem cell transplant, anthracycline and radiotherapy (specifically after 35 or more Gy). It is important to take into account the inter-individual variability in treatment responses as well (genetic determinants of toxicity and other risk factors, which add to the treatment's toxicity).

Kolenová (2014) lists the most common symptoms that occur in former child oncology patients as growth and developmental disorders; neurocognitive damage (a cognitive dysfunction called "the chemobrain" with impairments of memory; attention; concentration; expression; planning and other abilities); pain; sleep disturbances; reproductive and sexual disorders; muscle-skeletal problems; endocrinological disorders; impairments of the immune system; dental and facial problems; impairments of the skin and other organs and tissues; fatigue; anxiety; depression; fear and other psycho-social disruptions.

Some of the most common life threatening complications and consequences of anti-tumor treatment in childhood are secondary malignancies; cardio-toxicity and pneumo-toxicity, writes Mladosievičová (2009, pg. 3) and adds: "*Among the most serious inadequacies in monitoring late onset adverse reactions in our country, as well as the rest of the world, are not only the insufficient awareness of cured patients and their families, but of their primary doctors as well and the lack of medical workers in care centers, who would be dedicated to dealing with this issue."*

Hand in hand with the development of research in the area of late onset adverse effects, psycho-oncology research on the topic of adaptation to those effects is developing too. Most adults, who survived an oncology disease in childhood, become well adapted. These is, however, a great number of survivors with psychological difficulties. In this area, coping strategies to help manage those issues are the main topic of research. Wenninger et al. (2012) summarize research findings on this topic, which show that avoidant behavior; negative emotional representations of the disease; and a heightened awareness of adverse reactions correlate with higher levels of distress. Searching for information; personal engagement; and a sense of coherence correlated with lower levels of distress. The ability to face painful memories and emotions supports acceptance of the past, which can be an important prerequisite to start focusing into the future and the development of hope.

1.3.3 Palliative Care

How to keep hope on the other end of the treatment outcome spectrum – in a situation, where the child cannot be cured – is a big question mark in the field of palliative care. Mojžíšová and Benešová (2019) present its definition according to the World Health Organisation, which understands this way of treatment as an attempt to improve quality of life in patients, who are facing problems linked to a life-threatening disease. By an early recognition, qualified appraisal and the treatment of pain, it aims to prevent and ease the suffering of those in need and their families as well. *"A life-threatening or limiting disease changes the child's needs or ways to satisfy those needs."* Sikorová, Lokaj and Husovská (2019, pg. 36) write. Setting the goals of palliative care of a specific child is best realized along with the entire close family – including their siblings – and a multidisciplinary team of experts. However, the key point of holistic care is to minimize symptoms (Sikorová, Lokaj and Husovská, 2019).

"Psycho-social support of a child, along with communication about the topic of dying, depends on the way they perceive their illness." (Bužgová and Staňková, 2019, pg. 112). With some children, communication is not possible due to the factors of mental development and cognitive impairment. In those cases, dialogue is lead mostly with their parents. They continue to explain, that *"The goal of communication with these children tends to be general reassurance, providing emotional support and to satisfy the needs of safety and positive assurance."*.

McSherry et al. (2007) state, that emotional problems, which develop in children and adolescents with a life-threatening disease mainly stem from changes and losses, which the ailment brings about, and presents three topics of childhood loss, which pose the biggest stress: loss of control of one's own body; loss of personal identity; and the loss of interpersonal relationships. Bužgová and Staňková (2019) continue, that of all ages with varying degrees of cognitive abilities are capable of perceiving stress, coming from their parents; siblings; medical personnel; and other people they come in contact with. It is therefore important to give them truthful information, let them further their own needs and wishes and mediate contact with their peers. No matter how ill, children still need to play, imagine, have privacy, keep their secrets and continue in their daily activities.

2 THE CHILD AND THEIR FAMILY DURING CANCER TREATMENT

It is evident, that pediatric cancer pervades the life of the entire family. The ways in which their members adapt to the new life situation depends on many factors. Some factors, which play a role in how the illness is perceived and in the adaptation to it are relatively stable though – especially the stage of development which the affected child is at and their level of cognitive development.

2.1 THE IMPACT OF CANCER ON CHILDREN THROUGHOUT STAGES OF DEVELOPMENT

The understanding of a chronic disease in patients of any age is linked to less fear and chaos; greater contentment with medical care; better adherence to treatment and a better emotional state, all of which are key factors of a better quality of life and promote health, states Matley (1997) and goes on to say, that the lack of information can lead to chaos; increased anxiety and feelings of loss of control.

The emotional reactions of children to a disease and subsequent hospitalization depend on the type and amount of stress which they experience. They are influenced by a countless number of variables: age; inner balance and level of development; adaptability; coping strategies; fears; worries and fantasies, brought on by the ailment; type of hospitalization; necessary medical procedures; the stance and reactions of their parents; attitudes of the medical personnel; conditions of their home environment, etc. (Nagera, 1978). All of these factors can make the situation easier or more difficult for the child.

Age is the most commonly cited variable used to explain changes in the child's understanding of the illness. Piaget's cognitive development theory provides some clarity in understanding these changes. According to this theory, a child's thought processes show qualitative changes when passing from one stage of thinking to the next. In the course of development, the understanding of a disease becomes less concrete, less egocentric and less easily influenced by external stimuli or reactions (Crisp, 1996). The second variable the author puts forth is their experience with being sick. The level of understanding an illness can differ in two individual children on this basis, even when they belong to the same age group. The experience with chronic illness can make the

understanding of its causes easier, even though it is not clear, which specific aspects of this experience have an impact.

Depending on the child's developmental level, consequences of hospitalization and treatment can vary on the psycho-social-spiritual level as well. This chapter further elaborates on how a malignancies affect children of various ages.

2.1.1 Infancy

The attachment bond between parents and a child is determined in infancy. At 3-6 months of age, a child can form attachments to various people – attachment figures. As Cassidy (1999) explains, it is important for those figures to be able to understand the child's signals, to react to them accordingly and offer the infant feelings of safety and trust. The mother and father are very important for small children in this context, however other people can fill this role as well, such as nurses.

Every painful intervention, causing anxiety in this early age, has to be viewed as a potentially harmful or stressful experience. The stress which parents experience can influence the attachment bond itself (Cassidy, 1999). Parents can be worried about the health and life of their child. Therefore the medical personnel should help minimize painful experiences and the baby's separation from from its parents. According to Vágnerová (2012) presents the signs of stress in this age group, which often show as troubles eating and unthriving. Sleep disturbances and irritability can occur as well. Hägglof (1999) adds, that strong stress and neglect can lead to depression, reactivity and disruptions in interpersonal contact. Among other typical signs are constant crying, fearful behavior, screaming outbursts, acute panic and somatic signs of anxiety, such as frequent urination, diarrhea or vomiting.

2.1.2 Toddler Age

Vágnerová (2012) writes, that this life stage is distinctive by the prodigious development of motor skills, communication capabilities and the ego. The child takes control over its bodily functions as well, such as urination and defecation. Thinking is egocentric and often unstable. Empathy begins to develop as well, the child starts to understand other perspectives and a higher form of emotional reactions starts to emerge. It is still difficult to inform children of their treatment at this age.

Among the stressful situations, which can occur in the hospital environment for toddlers are painful procedures, immobilization and separation from parents, writes Hägglof (1999) and continues to explain, that the ability of the parents to cope with the situations can influence the ways in which they set limits for their children. Development can be delayed in multiple areas, and psychosomatic symptoms can occur in the form of difficulties with feeding; stomach pain; sleep disturbances; hyperactivity or irritable mood.

2.1.3 Preschool Age

According to Cassidy (1999), children in this age group are more easily separated from parents, in comparison with toddlers. Empathy increases and play within a group of peers develops. This period is important for the development of sexual identity. Magical thinking is common, which can mean, that fantasy can be worse (scarier) than reality.

Reactions to the placement in a hospital environment are similar to those in toddler age. As Hägglof (1999) writes, painful procedures, separation from the family and immobilization are fear inducing. Stressful experiences can affect sexual development. A common reaction to stress is stomach pain. Hyperactivity can also arise due to stress, especially in boys (Maté, 1999). Girls tend to be more introverted and exhibit anxious behavior. Secondary encopresis, enuresis or daytime incontinence can occur as well.

2.1.4 School Age

The child's thinking in this developmental stage slowly leads up to being more based in reality and magical thinking subsides. Cassidy (1999) writes about the attachment bonds in this age, that children can understand non-verbal communication and therefore any provided information should be fair and truthful. Children should of course not stay without hope. She continues, about the importance for social development in this age, where they come into contact with a network of people outside the family. Children start comparing themselves to others and begin to understand their social standing within peer groups. Those who are different from others (for medical reasons for example) can feel lonely (Vágnerová, 2012). They start to think about existen-

tial questions (death, disease, war,…), but the ability to cope with such topics is not well developed yet. Worries about their illness are important for them.

Hägglof (1999) adds, that for this age group, a stay in the hospital environment means separation from friends, school and everyday activities as well, which are of utmost importance for the child. Stressful situations evoke symptoms linked to stress, such as anxiety; depression; stomach pain; headaches; hyperactivity; attention deficits; secondary enuresis; incontinence or encopresis.

A common tendency is to interpret their disease as punishment for their bad behavior. This kind of thinking can persist until their eighth to tenth year of age. These fantasies can sometimes stay, even though they can understand their situation in a more realistic way, says Nagera (1978).

2.1.5 Adolescence

Teenagers tend to think about themselves and reflect on their thinking as well. Forming an identity is one of the basic tasks of this age. People other than their parents move into the center of their focus (friends, teachers, famous personalities,…). They cast doubt on the values and opinions of their parents (Graber and Brooks, 1996). A malignancy can pose a threat in the development of their identity. Teenagers want to be active and included in the discussion about their disease. Within the family, parents tend to protect them.

Coping with the disease in this age can cause a vast array of symptoms linked to stress. Emotional and behavioral symptoms can arise in addition to psychosomatic difficulties. Girls show more emotional symptoms, whereas boys have a tendency to react more often in terms of behavioral symptomatology (Hägglof, 1999).

2.2 THE FAMILIES OF CHILDREN WITH CANCER

As was mentioned previously, an oncology diagnosis of a child has a major impact on the life of their entire family. It introduces parents to heavy existential immediately. They can become overwhelmed by fear of the life-threatening disease, the stress of treatment itself along with it's consequences, as well as a change in socioeconomic status, loss of contacts, and limitations of daily activities, which gave their life meaning. Long term treatment limits leisure activities (which often times

function as coping mechanisms for handling commonplace difficulties) and employment – many times leading to a complete loss of employment and professional roles. The disease has an enormous impact on siblings, friends and distant family members as well. A high quality standard of help for families who end up in such situations requires a good understanding for these circumstances, along with ways of managing them, when they arise.

2.2.1 Coping Strategies

The reactions of parents to the loss of certainty have been well documented as of today. The first influential figure, who analyzed and ordered the states of experiences people go through when death is nearing (which can be applied to life-threatening diseases as well) into specific phases, was Kübler-Ross (2015).

She described the first phase as denial. It is characterized by shock, confused thinking and exaggerated emotional reactions. *"It is the first psychological defense attempt, the goal of which is to stabilize and find firm ground again. An impending loss of the most valuable possession we have – our own life – leads to the denial of reality."* writes Tschuschke (2007, pg. 207).

In the second stage Kübler-Ross describes the lament over one's fate and negotiation. Apart from repetitive denial, the dying person attempts to renegotiate the prolonging of their life with a higher power.

Anger and wrath dominate the third stage of this model. These feelings are a symptom of the fundamental fight for life. Patients are often very exhausted and come face to face with their physical limits. Feelings of anger can be the outcome of great fear.

The fourth stage then follows and presents as depression, sadness. Apathy, distance and loss of physical energy are typical for this phase. "*One of the doctors' tasks is to determine, whether depression in individual cases is part of the natural process of giving farewell to the world, or whether it has become pathological,"* writes Tschuschke (2007, pg. 210).

The last stage is acceptance. It is characterized by finding balance, accepting responsibility, constructive solutions and participating in treatment. A new life order arises in terms of adapting to a life with the disease, searching for new outcomes and solutions in the future of the family and the child. Each step towards the internal and external

management with one's own feelings is a step on the road to departure (Tschuschke, 2007). However, today we know, that these stages do not always follow this hierarchy, but can appear in a different succession and many times repeatedly.

The strain of caring for a person with a physical handicap is described in professional literature by the term "care-load" (Khanna et al., 2012). It is linked to long term emotional load and can have many negative consequences on the afflicted person's care-givers. In the field of care for pediatric oncology patients, these are specifically:

- Learning and multiple roles – for patients undergoing a curative or palliative treatment parents often take on the roles of care-givers as well as teachers, especially if the care takes place in the child's home environment,
- A bad economic situation – at least one parent has to stop carrying out their occupation and becomes reliant on social benefits,
- Relationships and divorce rate – treatment of these patients is characterized by long term isolation outside, as well as inside the family,
- Losses and restrictions – these arise for the family in multiple areas: personal; interpersonal; activities and future perspectives…,
- Normality and societal discrimination – it can happen, that the family starts to identify with the role of a "sick family" as a result of their losses and restrictions.

Severe stress and frustration can stimulate defense mechanisms, which were first described by Anna Freud. *"The defense model stems from psychoanalysis. The goal of the defense is to push threatening fantasies and feelings into the unconscious mind. The defense is unconscious, meaning that the ones affected do not utilize this mechanism purposefully or consciously. The defense tends to dissolve on its own once the threat, or the situation which is perceived as threatening, is resolved."* writes Tschuschke (2007, pg. 94).

These subconscious or unconscious strategies are usually ruled out of the sphere of conscious management, the inner workings of which are described by the term coping. *"The coping model originated from the research of stress. The theory of coping derives from the notion, that crisis management is associated with the process of adaptation to a new reality. Contrary to defense mechanisms, it is carried out consciously and is linked to specific behavior. We can deduce the patient's coping strategies from their*

behavior. However, in order to activate them, the patient needs appropriate defenses as well," writes Tschuschke (2007, pg. 99).

The term coping relates to adaptive (constructive) coping strategies, meaning strategies which lower stress. When a strategy adds stress instead, it becomes maladaptive and can be termed as mismanagement. The term coping further denotes reactive coping – a reaction to coping, which follows a stressor. This is distinct from proactive coping, the goal of which is to neutralize future stress factors. However, many authors present varying definitions.

Lazarus and Folkman (1988) state, that coping strategies and defense mechanisms overlap. They have divided coping strategies into four groups as follows: problem-focused coping; emotion-focused coping; appraisal-focused coping (searching for support) and occupation-focused coping (searching for meaning). Billings and Moos (1981) add the avoidance of coping as a type of emotion-focused coping.

Vágnerová (2004) on the other hand defines coping merely as active and passive. An active style can be searching for help; an active attitude towards solving the situation at hand; searching for resources. A passive style is a form of escape from the situation – trivialization of symptoms or denial of the disease; substitution.

Atkinson (1990) speaks about denial as a refusal to acknowledge a serious and uncomfortable reality. She understands repression in terms of expelling an uncomfortable reality from memory. If this happens involuntarily, we speak about repression. When this process is voluntary, it is called suppression (Balcar, 1991).

Rationalization can be understood as an effort to find rational reasons for absurd thoughts or situations; or in other terms, excusing one's own behavior, which their social environment would see in a negative way (Atkinson, 1990).

Transfering the reason's of one's failures on another person or target is called projection (Drhlíková, 1992).

Intellectualization is the striving to gain emotional distance from a stressful situation by coming to terms with it through intellectual means (Atkinson, 1990).

Langton (2000) stresses the importance of the mutual appreciation of marital roles, which strengthens the family and promotes its resilience. The family gives security to a sick child. It helps them to adapt to the oncology disease, to manage its treatment and the adverse effects thereof. In order to achieve a positive treatment outcome, a good handling of the situation by the family is crucial.

Apart from all the negative changes, dealing with the disease can bring about positive changes as well, in the form of transformation and growth. The term of post-traumatic growth can be found in literature on this topic, which describes the positive outcomes of overcoming a traumatic event. It can result in emotional and cognitive growth, better functioning and a deeper understanding of life, which can manifest internally, as well as externally by changed behavior, different interpersonal relationships or by embarking on a new life path. It is a positive positive identity transformation (Marešová and Mareš, 2008). Often times, development can arise in the area of spirituality and the competence of all family members, changes can be seen in their life philosophy, understanding of essential values, mutual understanding and therefore the relationships within the family can improve (Evans, Darrah and Galambos, 2010; Green, 2007). Parents of children with cancer sometimes feel proud to have survived such a heavy life challenge (Gibbins et al., 2012). A common topic of studies focusing on the families of children with cancer is the strive to maintain hope, courage and a positive attitude (Mu et al., 2015; Gibbins et al., 2012).

2.2.2 The Siblings of Children with Malignancies

All family members can undergo positive, as well as negative changes. Parents can get excessively attached to the sick child during treatment and forget the healthy ones. However, those have their own needs too, of course. It is important for siblings to know about the disease and that their parents provide necessary information, not strangers. It is possible for the siblings of the sick child to change during treatment (Šrámková, 2016). Children's reactions depend on a multitude of factors. Among those are their age, level of cognitive development and their relationship.

Excessive demands have a negative influence on the psycho-social development of a child. They can lead to developmental disorders, disobedience or even aggression (Kovalčíková, 2002). The absence of the parents can cause changes in their emotional life. Children can experience feelings of jealousy, injustice, anger, sadness, guilt for being healthy, etc. They can become concerned about their body, which can border on panic even when common illnesses occur. According to Eiser (2004), their school performance can be impaired, as well as their functioning within their social collective. Their interests can change too. On the other hand, they can become more mature and determined, based on their experience of taking care of their ill sibling.

However, with good parental support, children can adapt to the traumatizing circumstances. An open dialog helps to vent all negative feelings. Contentment can be brought about by stability in other areas of daily life: upholding the domestic regime; common rules in everyday activities; making the least possible amount of changes.

3 MUSIC THERAPY AND PEDIATRIC ONCOLOGY

In the scope of psycho-social-spiritual care of oncology patients, the use of music is clearly substantiated in any treatment phase. The aim of this chapter is to discuss the ways in which music therapy is currently being used in oncology care.

3.1 MUSIC THERAPY IN HEALTH CARE

In many European or American hospitals, music therapy has become a common part of the so called supportive therapies during treatment of (not only) oncology diseases. Research has shown the inclusion of music therapy into the treatment process to be beneficial. *"In the midst of the chaotic hospital environment it can help to find a sense of normality and hope."* (O'Callaghan, 2013).

3.1.1 Music Therapy and Art Therapies in Health Care

Music therapy falls into the category of art therapies (sometimes known as creative, expressive or complementary therapies). In recent years the use of music in health care has grown in popularity. Music is being used as an intervention for various ailments, for all age groups, before procedures or operations and thereafter, and for lowering anxiety or pain. Is is often used in conjunction with other activities, educational programs or during massage for the purpose of relaxation (Evans, 2002).

The way in which music can change the perception and experiences of people in distressing or painful situations point to the phenomenon of its capability to serve as a distracting stimulus with the goal of diverting attention away from the discomfort. A basic presumption lies in the fact, that music is a form of communication and can be viewed as a kind of universal language. It can offer an escape from negative stimuli, such as pain and anxiety, by offering something pleasant and uplifting (Nilsson, 2008). Avers, Mathur and Kamat (2007, pg. 576) present the therapeutic potential of music therapy in pediatric care. *"The use of music therapy in a hospital environment can be effective for children coping with their stay in an unknown environment, which can bring about many new and scary things."* It offers them an opportunity of choice and control during the therapeutic encounter. This can be invaluable, because the choices patients can make in a hospital are limited.

Music therapy allows pediatric patients to cope with their pain, anxiety and fear, states Malchiodi (1999, pg. 13) and mentions, that art in general can *"ease the impact of trauma and strengthen physical health of pediatric patients."* Art therapies can improve the experience of hospitalized patients by diverting their focus onto something else than their disease. It can also offer hope and an opportunity to learn to withstand pain through examining their fears of medical procedures. The art-therapeutic process provides hospitalized children an opportunity to examine what is going on: it gives them a visual language, thanks to which they can communicate their experiencing with others. Artistic creation can give children a space where they can prepare for medical procedures (through the means of visual depiction, musical composition etc.), which can ease their anxiety.

Councill (2012, pg. 225) notes that many hospitalized children do not suffer from psychological disorders, and therefore the goal of art therapy in the hospital environment lies in its general ability *"to reveal the qualities of their strength, coping mechanisms and resilience".* Malchiodi (1999) states, that children have to cope with many factors during their hospital stay, such as the loss of independence; pain caused by their treatment; changes in body image; the fight to come to terms with the trauma stemming from the situation and to comprehend, why they fell ill. The process of art therapy can make it easier for them to examine all of these questions and help them feel stronger in a situation, which generally evokes feelings of helplessness.

For the purpose of artistic creation, which is at the core of complementary therapies, medical equipment or sounds of the environment can be utilized in the hospital environment. By their incorporation into the creative process they can transform into a new work of art. An artifact, which can provide the patients with feelings of control over their surroundings.

The experience of a disease is described as a traumatic experience in literature on the topic. Councill (2012, pg. 232) notes, that many children and their families experience symptoms of trauma and *"can feel frightened, helpless and vulnerable" a*s soon as they receive the diagnosis or in the course of treatment. The disease tends to appear unexpected, which adds to the traumatic experience of the situation. Art can be especially beneficial in the treatment of trauma, as it brings patients into the present moment by pointing their focus on the sensory qualities of various artistic modalities. Hospitalized children, which show signs of trauma can therefore arrive into the "here and now". The shared process of creation helps the therapist to build a relationship to the patient as well, by forming a safe environment where the child can feel comfortable and where

they can share their feelings. Art can help patients integrate their experiences in a non-verbal manner.

3.1.2 Music Therapy and Music Medicine

In professional literature, which describes the effectiveness and use of music and its elements within the framework of health care we can often encounter the term music medicine. It is important to differentiate between this intervention method (and its practical use) from the interventions of music therapy. To practice music therapy it is required to complete a long-term systematic education course. This is not a requirement for the practice of music medicine.

Dileo (2013) says that music medicine involves the use of music by medical personnel in order to ease anxiety, pain, autonomic system reactivity and to improve the mental state and relaxation in patients. Prerecorded music is most commonly used and is chosen by the doctor or patient from what is available and according to the patient's preference. Even though a relationship between these two persons is possible, this relationship does not evolve through the musical experience. It is based on the provided medical care. This offers a definition of music medicine as passive listening to recorded music provided by medical personnel in order to achieve non-musical goals. Music is usually played in headphones and the patients can but do not have to be involved in the choice of music (Dileo and Bradt, 2005).

In contrast to this, Dileo (2013) defines music therapy as an intervention, which can be used in a broad spectrum of medical specialties, as well as in various fields outside of medicine. The goals of music therapy can be of a physical; psychological; spiritual; cognitive; developmental or social character. Music therapy differs from other practices involving music by: utilizing the therapeutic process (initial assessment, the therapeutic process itself, final assessment); the extent of musical experiences offered to the patient; and the therapeutic relationship, which is developed by musical means. The interventions of music therapy, provided by trained experts, are significantly more effective than the interventions of music medicine (Dileo, 2005). This distinction can be attributed to the fact, that music therapists personalize their interventions in order to fulfill the specific needs of each patient, let the patients to actively participate in the creation of music and guide the systematic process.

Around 20% of music therapists work within the context of health care. Among the common objectives of working in health care are: socialization; communica-

tion; self-respect; managing adversities and coping with stress (or stress reduction). Frequently used music-based interventions include musical relaxation; improvisation; songwriting; lyric analysis; and movement to music. These musical interventions are often used alongside common psychotherapeutic practices (Silverman, 2007). Music therapists are often asked to partake in situations, where psychopharmacological treatment shows limited results. It is also recommended for patients with low levels of motivation. It has also been proven successful with patients, who do are not responsive to verbal (group) therapy. Music therapy can mitigate the management of symptoms and enable the individual to release suppressed feelings linked to their experience. Research shows, that this is a result of the affective, motivational nature of music on mediating the therapeutic and behavioral change (de l´Etoile, 2002).

One of the components in the health care context is working with pain. The next chapter is a continuation of the information on pain in oncology diseases provided in chapter 1.2.3 (Pain management). The following segment focuses on the subject matter of pain from the stand point of music therapy.

3.1.3 Music and Pain

Pain is an important alarm signal, which should however not sound for too long and cannot exceed a tolerable threshold. If left untreated, the pain and suffering of a child with a life-threatening disease has a major impact on the quality of life of the child, along with their entire family, Bužgová (2019) states.

The Center for Disease Control and Prevention nevertheless argues, that pain management is currently focusing on decreasing the use of opioids and other medicaments, in a pursuit to identify and increase the use of nonpharmacological strategies (CDC, 2018). A multitude of such strategies exists in the form of relaxation; deep breathing techniques; massage; accupuncture; or the use of art, to name a few, which can be potentially beneficial in cases where pharmacological treatment has been ineffective or contraindicated (U.S. Department of Health and Human Services, 2019). *"Such approaches reduce the perception of pain along with the need of pharmacotherapy."* (Bužgová, 2019, pg. 47)

The use of music is one of these non-pharmacological strategies with a swiftly developing support. LiKamWa (2020) writes, that a myriad of research has already established the positive effect of music in managing pain, albeit the mechanisms of its action are yet unknown. Key theories have been put forth though, which help to clarify

these mechanisms. They talk about the activation, modulation and modification of painful stimuli. Knox presents two main hypothetical explanations, which support the use of music in managing pain: *"The capacity to use music freely any time and at any stage of pain – which induces feelings of control, and the capacity to do something in order to detach from a negative experience. The second explanation is aimed at the disconnection of focus from pain, where the external stimuli leave no space for pain perception."* (Knox, 2011)

Lee (2016) adds, that multiple studies base their research in the gate control theory of pain, as proposed by Ronald Melzack and Patrick Wall. In this theory they discuss the flow of nerve fibers into the central nervous system. Pain perception is controlled by a gateway system in the spinal chord, which can be open or closed, and therefore controls the transition of information about pain into the brain. People's reactions to equally painful stimuli can vary. The theory postulates, that this level of pain is determined by the amount of painful stimuli, which enter the brain through the "gate of painful input in the spinal chord". One of the key points of this theory is, that sensory, cognitive and affective processes are able to initiate descending nerve signals, which "close the gate". In this way, non-painful stimuli (such as music for instance) can close the gate, thereby lowering the activity of pain-transfering cells, which can in turn lead to reduced pain perception. Even though the gate control theory of pain has remained the most influential and most important theory for our understanding of pain to this day (Mendell, 2014), it does not take into account the complex interactions of the psychological and social aspects of pain.

The bio-psycho-social model of pain therefore seeks to bridge this gap in explaining the function of pain transfer, modulation and perception. Attention and emotion are two key elements, forming the basis of the analgesic effect which occurs while listening to music (Lunde et al., 2019). The theory of selective attention claims that when a person is focusing on one subject while ignoring others, the sensory input from the ignored stimuli dissipates (Isbell et al., 2017). Distraction can also be intensified through the stimulation of affective brain regions and by invoking positive emotions (Koelsch, 2014). The limbic system – responsible for emotional processing – is thus important for the therapeutic use of music, especially the amygdala, which consolidates memories linked to feelings (Gerlichová, 2021).

3.2 THE SPECIFICS OF MUSIC THERAPY WITH PEDIATRIC ONCOLOGY PATIENTS

Music therapy in oncology utilizes music in the preventive, curative and palliative forms of treatment and can be very helpful for a broad spectrum of patients with various types of cancer. Although music therapy does not influence the disease directly, it has a big impact on the patients' mood and may help them to cope with and accept their illness too. Within the context of oncology, the aim of music therapy is on the physical as well as psychological needs relating to the illnes, along with the adverse effects of cancer treatment (Stanczyk, 2011). According to Huang (2010), music therapy has shown to be effective in promoting a positive self-image and supporting healthy relationships, as well as in lowering the need of analgesics. On the following pages we take a closer look at the use of music therapy in various situations, which may arise throughout the treatment of oncology diseases.

3.2.1 Music Therapy in the Course of Treatment

Many of the disease symptoms and the side effects of oncology treatment impact the life quality of the patients along with their whole families. Those include food intake disorders; difficulties swallowing; nausea; vomiting; itching; constipation; diarrhea; dyspnoea – troubles breathing; fatigue; insomnia; muscle weakness; and loss of sensitivity. Research results clearly imply that people with oncology diseases experience significantly higher levels of psychological distress and depression in reaction to their diagnosis and treatment (Dileo and Bradt, 2005).

Individual experiences with adverse effects of chemotherapy, along with their influence on well-being differ nonetheless from patient to patient, even when administered the exact same treatment. This leads to the conclusion, that non-pharmacological factors may play an important role in the way patients perceive or interpret physical symptoms in the duration of treatment, Dileo and Bradt (2005) continue and further add: *"The interventions of music therapy and music medicine are put to use in order to reduce the symptoms and adverse effects of treatment, as well as to meet the psycho-social needs in people with cancer. In music medicine interventions, the patient regularly listens to pre-recorded music, offered to them by a medical professional. Music therapy on the other hand requires the involvment of a trained*

music therapist, who implements musical interventions, sets goals and creates a tailored therapeutic process."

Research dedicated to the effects of music and music therapy in patients have grown in number immensely and their results are being applied in various fields of expertise (Dileo, 2006). In patients suffering from cancer, music is being used to lower anxiety before or during surgical procedures; to decrease stress during chemotherapy or radiotherapy; reduce their side effects; enhance mood; as well as to ease pain management; improve the immune system functioning; and thus to promote their quality of life in general, lists Dileo (2006) and on another page, he writes: *"It is common knowledge, that musical elements, such as rhythm and tempo, pitch, timbre, melody and harmony influence people's physiological and psychological – emotional reactions."*

While working with oncology patients, music therapists assess the process in its duration and apply personalized interventions to patients and their families. In the context of the therapeutic relationship, bio-psycho-social issues and needs can be addressed through the means of music therapy (Magill, 2009; McClean, 2012).

O'Callaghan et al. (2012) address the importance of a dialogue concerning the musical history of a patient before they had received their diagnosis; their musical preferences; how they listen to music and what they usually do while listening; the felt effects of music; changes in their musical behavior (the physical, emotional, financial and environmental influence of the oncology disease along with its treatment on their musical history; the alterations in their musical preferences and their behavior while listening to music); resilience and adaptability (the beneficial affects of music after being diagnosed and while receiving treatment); and wisdom (through shared experiences: sound and music based support strategies suggested by adolescents may be provided to help further patients). Based on the patient's preference and their assessment during treatment, music therapists accustom and adjust their interventions, aiming at finding solutions for their symptoms and areas of discomfort. They use music alongside verbal interventions to create the opportunities for self-expression and communication; reminiscence; to process thoughts and emotions; and to support symptom management (Magill, 2011). The music therapeutic environment oftentimes provides the space and time, in which patients along with their families can experience social connection, enhance their self-realization and amass effective coping strategies.

Reid (2018) presents the main focal points, which often emerge for children and adolescents with oncology diseases. He divides them into three categories: goals relating to treatment and hospitalization (preventing distress; stress and anxiety reduction;

developing coping strategies; providing comfort; motivation to physical activity and rehabilitation; relaxation; diverting attention; aid during procedures,…); social and emotional goals (engagement in positive musical experiences in connection with others; supporting the healthy aspects of the child; improving mood; promoting social interactions; reducing loneliness; eliciting entertainment and the feeling of normalcy) and musical goals (supporting natural musical development; enhancing creativity; bringing joy; improving musical dexterity).

He further lists five basic methods used in practice, which aim to achieve these goals: songwriting; active music therapy; receptive music therapy; improvisation and the use of technique. O'Callaghan (2015) uses other criteria in listing the musical methods and techniques:

- listening to live, improvised or pre-recorded music
- performing music on a musical instrument
- spontaneous musical improvisation with the use of voice or an instrument
- musical composition
- using songs (singing, songwriting and lyric analysis)
- imagination and relaxation accompanied by music

Studies describe the utility of music therapy in the field of pediatric oncology. In order to support its usage, constant research is however still needed in this specific context. Close cooperation with medical and nursing personnel can help raise the significance and integration of music based strategies into practice within hospitals (Hilliard, 2006).

3.2.2 Music Therapy in Palliative Care

One of the elements in the reality of patients, families or experts dealing with cancer is the possibility of an untimely death. Although death is a natural outcome of life, it is being viewed as taboo in the culture of our society Non-pharmacological care of a dying patient and their family (as well as of other patients, their families and specialists, when talking about palliative care in general hospitals) is called palliative accompaniment. At its core lies active listening and closeness (Holosová, 2021). Listening to children can be understood on multiple levels, states Amery (2017):

- Listening to words, which suddenly gain much deeper meaning for the child. We need to find out, what exactly they mean for them.
- Listening to dreams. Stories and fears from real life, which the child does not dare to discuss directly get reflected in their dreams, which the child can explain easier than their experiencing, because metaphorical verbalizations are less delicate and painful.
- Listening to "inquisitive sentences". It can help us to unveil the child's pursuit of meaning in what is happening, and by following up on them we can reach their deeper substance.
- Listening to their thoughts about the path they are approaching. The child will often use metaphorical references to death, which is expressed by words like journey, departure. These discussions are very heavy, albeit immensely significant for the child, as they need to confirm their supposition, that they are dying.

One of the interventions, which are well suited for accompanying the dying, is the use of music. *"It is essential to accommodate the faith of the dying person and their family, because many times they wish to sing spiritual songs, which stem from their convictions and opinions concerning life and death, or possibly the life after death. Families and relatives often do not want to or cannot manage to sing, so this becomes the main calling of the music therapist in such situations, in order to assume their feelings onto themselves and to sing or play instead of them, while the ones close to the dying hold their hand or can join in to sing as well. In these moments, it is essential to approach all that are present with a great dose of respect, kindness and love."* (Holosová, 2021, pg. 36).

When using interventions of music therapy, the main goal stems primarily from the goals of palliative care (the improvement or sustenance of the quality of life on the highest level possible, up until the moment of death). *"Partial goals, which are derived from the main goal are first and foremost the satisfaction of the client's specific needs, the emphasis on human dignity in any state of the client, the reduction of pain and the mental, as well as psychological suffering of the client and their loved ones,"* writes Holosová (2021). Amtmannová (2007) lists three levels of goals in music therapy: the first one is the effort to sustain the patient's state; the second one attempts to modify it;

and the third one aims for improvement. In palliative care, the first level of goals can be viewed from the biological perspective, as in this area the only target is to sustain the same state of the client because it cannot be improved, changed or cured. From the psychological, emotional and social standpoints it is possible to talk about further music therapeutic levels of goals, as seen from this perspective, change or an improvement of the patient's state may ensue (Holosová, 2021).

Gerlichová (2014) defines the needs of the client, long with their loved ones and family, and suggests ways to satisfy the individual needs with the help of music therapeutic techniques. Among these individual needs of clients in the terminal state of illness are:

- Lowering pain – music therapy is not able to put an end to pain or its causes. What it can achieve though, through various techniques, is to change the perception and reactions to pain from the client's perspective. It can ease pain with the help of music therapeutic relaxation methods, as singing or good music offer a distraction from pain and suffering (Boyle et al., 2012). People in this stage of illness tend to prefer a slower tempo and calm rhythm.
- Improving the quality of breathing and decreasing shortness of breath – people who spend almost all day in bed often encounter breathing difficulties, so it is advisable to strengthen the lungs merely by singing, which contributes to more intense breathing and promotes the intake of higher oxygen levels.
- Processing emotional experiences in a safe environment – for the expression of one's accumulated emotions, simply singing, improvisation on a musical instrument or listening to music of the client's choosing can be helpful. Through song lyrics, clients can express themselves easier than with their own words. Especially when the client feels the need to talk about difficult and serious topics, with the aid of music or songs this becomes much easier for them (Peters, 2000). Jacob (2008) also writes, that melodies alone or song lyrics are oftentimes connected with the client's past and remind them of certain people, places or moments in life. The client does not always be the one who sings. Singing can be offered by the therapist, where the client chooses the song on their own and thereafter, if the client is ready for it, a discussion about the emotions evoked by the song or melody may follow.
- Managing stress and anxiety through musical stimuli – it is important to connect to the positive experiences from the past, to songs, which the client knows or knew how to sing, to the melodies which they enjoyed. Words are

not always necessary, sometimes it is enough to play nice music for the client or to play a musical instrument and connect this to breathing or massage exercises.

- Strengthening the client's self-confidence, self-respect, offering space for self-expression – a suitable technique here is playing a musical instrument, which the client can play or learning to play an instrument, if they do not know how to play and it has been a dream of theirs to learn it. Boyde et al. (2012) state, that some people feel good, when they can teach a new song to someone, in which they can pass something on, be it in general or to a specific person.
- Providing support (personal, psychological, spiritual,…) - it is always necessary to recognize the client's present state and to build on its basis. Some like to talk, whereas others prefer nonverbal means.
- Aiding relaxation and rest – music works well for relaxation, therefore it is good to use music alongside relaxation exercises. For this purpose it is vital to choose melodies in slower tempo and calm rhythm.

Not only does palliative care tend to the dying, but also to their family and loved ones, who are in need of support and an opportunity to express their feelings during this time as well. Music therapy may provide an amicable medium, which can take care of those needs of the grieving and has the ability to help them in their search for a path to move on.

PART II. - RESEARCH

4 RESEARCH THEORY

Recently there has been a surge of new research taking place in the field of medicine. Thousands of new studies are getting published each year and their quality and results can vary greatly. This is why systematic reviews have gained in importance and at this time multiple systematic reviews can be found, researching the same topic, the quality of which can also vary.

The main goal of creating an umbrella review is to critically appraise existing systematic reviews and inform practitioners about the real effects of the medical interventions in question (Klugar, 2015). At the same time umbrella reviews seek to gather available knowledge, find and describe what is yet unknown and propose recommendations for practitioners and further research. This type of summarizing systematic review can be found under different names in literature: umbrella systematic review; review of reviews or a meta-review.

4.1 DEVELOPING AN UMBRELLA REVIEW

In the area of research, Cochrane Collaboration and JBI have historically focused on reviews which find information about effectiveness of interventions or therapies. There are many reasons for creating an umbrella review. The main reason is to summarize findings from multiple systematic reviews to further understanding of a topic at hand. Findings can entail an analysis of the effectiveness of various interventions for a given population or studies which research one intervention but give varying results. The main focus of an umbrella review should be to summarize existing research syntheses on the topic of interest or research question, not to re-synthesize the results of existing reviews or syntheses or syntheses with meta-analyses (meta-syntheses), as the Methodology for JBI Umbrella Reviews (2014) states. Aromataris and

Munn (2020) write *„The wide picture obtainable from the conduct of an umbrella review is also ideal in highlighting if the evidence base around a topic or question is consistent or if contradictory or discrepant findings exist, and in exploring and detailing the reasons why. Investigation of the evidence with an umbrella review allows assessment and consideration of whether reviewers addressing similar review questions independently observe similar results and arrive at generally similar conclusions,“.*

One part of constructing an umbrella review is the protocol, which needs to be registered officially and should contain basic information on how the study will be constructed. The protocol for our study can be found in the first attachment.

4.1.1 The Methodology of an Umbrella Review

When writing this type of research it is necessary to start by creating a protocol to be registered. The topic is chosen according to the professional interests of the researchers as well as what is needed to be found in the field. It is essential to form a good research question. *„Although the umbrella review may aim to examine existing research syntheses for different types of interventions or phenomena of interest with the same condition, or different outcomes for the same intervention or phenomena of interest, the PICO and PICo mnemonic should be used to generate a clear and meaningful title and question. Ideally, the title for a quantitative umbrella review may incorporate some of the PICO elements, including the Population, the Intervention, the Comparison and Outcome, and the PICo elements if considering a question or topic that lends itself to qualitative data, including the Population, the Phenomena of Interest and Context,“* Aromataris and Munn (2020) write and elaborate further, that if an umbrella review intends to review both quantitative and qualitative systematic reviews, both the intervention and phenomena of interest need to be clearly specified in the protocol.

The next section of the protocol is the introduction. This segment should most importantly contain information about the researched topic, as well as outline clear borders of the inclusion criteria, which will provide the basis for the inclusion and exclusion of studies for the umbrella review and should be therefore clearly defined. *„These criteria provide a guide for the reader to clearly understand what is proposed by the reviewers and, more importantly a guide for the reviewers themselves to base decisions about the studies to be included in the umbrella review,*“ (Aromataris and Munn, 2020).

The search strategy of an umbrella review should aim to identify all research syntheses relevant to the review question. The extent of the keywords used should be broad enough to capture all relevant research. According to Aromataris and Munn (2020) a three-phase search process is commonly used: *„First, initial keywords are identified followed by analysis of the text words contained in the title and abstract, and of the index terms to describe relevant reviews. The additional terms as meta-analysis or systematic review need to be included in the key terms for searching. Second, database-specific search filters for each bibliographic citation database stipulated in the protocol are constructed, and finally the reference list of all included reviews should also be searched. A comprehensive search for a JBI umbrella review should also encompass a search for grey literature or reports that are not commercially published.“*

The umbrella review protocol should also describe the process of study selection. This process has multiple stages and procedures for solving disagreements between reviewers.

Research syntheses that are eligible for inclusion in a JBI umbrella review must be assessed for methodological quality. *„Ideally, only high quality systematic reviews should be included in an umbrella review. There are a variety of checklists and tools available to assess research syntheses and systematic reviews. It is the JBI policy that all systematic reviews need to be critically appraised using the standard JBI critical appraisal instrument for Systematic reviews and Research Syntheses,“* (Aromataris and Munn, 2020). In case consensus cannot be reached by the two researchers, a third reviewer should be consulted.

The next step in developing an umbrella review is data extraction. What is meant by this is the procedure for extracting relevant details from the systematic reviews and meta-analyses included in the umbrella review. The standardized JBI data extraction tool should be used to extract data from the reviews in question and to avoid risk of bias, state Aromataris and Munn (2020) and they continue: *„Extraction and presentation of data for a JBI umbrella review should be limited to the results and findings presented by the included research syntheses; in this regard it is not recommended that the researchers conducting the umbrella review retrieve primary studies (original research) in an included systematic review, for example, to access extra data.“*

Heterogeneity of primary studies within the reviews should be recorded and evaluated. In the presence of large between-study heterogeneity, results of the meta-analyses may

not be representative of true effects and cannot produce reliable recommendations for future research (Papatheodorou, 2019).

As mentioned above, the aim of an umbrella review is to present a summary of existing research syntheses relevant to a particular topic or question. There is no further synthesis or meta-analysis. „*To this end, the results of all included studies should be presented to the reader to allow for a ready and easily interpretable overview of the findings. Tabular presentation of findings is recommended when overall effect estimates extracted from systematic reviews or other similar numerical data are presented. Where quantitative data is being presented, the number of studies that inform the outcome, the number of participants and the heterogeneity of the results of included reviews should also be reported,"* (Smith et al., 2011). When qualitative systematic reviews are included in an umbrella review, the results and findings should be presented in tabular form with sufficient information regarding their context. A summary of findings should be included as well, so that it can be clearly visible that all findings were interpreted (Aromataris and Munn, 2020).

When searching through the databases we noticed, that many systematic reviews have been written, which focus on the use of music-based interventions in patients with oncology diseases. At the same time it also became clear, that some of these systematic reviews are of questionable methodological quality. Out of the large number of reviews, the focus of which was unclear, we started to suspect research waste, and therefore we decided to utilize the methodology of an umbrella review. In addition to that, we have written this review to summarize the results of available systematic reviews in higher complexity. The entire process of its creation is described in the following text.

5 THE EFFECTIVENESS OF MUSIC-BASED INTERVENTIONS IN CHILDREN AND YOUTH WITH CANCER: AN UMBRELLA REVIEW

In this chapter, the results of our research are presented, the protocol of which (Attachment 1) is registered in PROSPERO (reg. number: CRD42021259529). The following division into sub-chapters fulfills the methodological criteria for JBI umbrella reviews.

5.1 The Review Question

We sought to answer the following question: „What is the effectiveness of music-based interventions for children and youths with cancer on physiological and psychological outcomes?“

5.2 Inclusion Criteria

The chosen inclusion criteria were quite strict. This has proven to be very limiting in the process of study selection, which found very few results. The criteria went as follows:

Types of participants

Only those studies were included, which synthesized research on children and adolescents with oncology diseases in any stage of treatment. All studies, which researched the adult population only, or together with children, were excluded.

Interventions/phenomena of interest

We only considered studies which contained music interventions or any use of music in our chosen context. Among those were the interventions of music medicine, such as listening to recorded music administered by medical personnel before or during medical procedures; relaxation with music etc. as well as music therapy interventions,

such as songwriting, lyric analysis, improvisation etc. Studies, which did not include any music based interventions were excluded.

Comparators

Any comparator was found appropriate for our review. Those could be for example standard treatment, psychotherapy, other expressive therapies and others.

Types of studies

Only quantitative systematic reviews of effectiveness were included. Other types of reviews (with mixed methods or qualitative methodology for example) were excluded. Reviews without meta-analyses were excluded, unless they stated a specific reason for not conducting the meta-analyses.

Types of outcomes

Studies researching any physiological (heart rate, oxygen levels, etc.) or psychological outcomes (sleep quality, anxiety, quality of life, pain perception, etc.) in the context of treatment (before, during or after procedures in any stage of treatment, etc.) were included in the analysis.

5.3 Search Strategy

A systematic literature search was conducted using Epistemonikos, Scopus, WoS, ProQuest and gray literature. Finally, the reference lists for systematic review articles identified in the original search were examined to find relevant articles. There was no limitation in language or publication period. The following keywords were used: children, youth, cancer, oncolog*, music. The search strategy for all databases in its entirety can be found in attachment 2.

5.4 Study Selection

Texts had been screened by two reviewers independently, first at abstract and later at full-text level. Screening was conducted using the Zotero research tool. Any duplicates were excluded using an automated tool within the program. Any

disagreements had been solved by consensus or by the decision of a third reviewer. Reasons for elimination included no randomization, no control group, no meta-analysis and adult age of participants. Screening results are presented in the PRISMA flowchart from Aromataris and Munn (2020) which can be found in attachment 3.

5.5 The Review Methodology

To construct this review we have used JBI methodology. Screening, critical appraisal, data extraction and data summary have been conducted independently by two reviewers.

Assessment of methodological quality

The assessment of methodological quality was done independently by two reviewers using the JBI critical appraisal instrument for Systematic Reviews and Research Syntheses (attachment 4). As the JBI Manual for Evidence Synthesis (Aromataris, Munn, 2020) states *"Ideally, only high quality systematic reviews should be included in an umbrella review,"*. As written in the protocol, reviews were not excluded solely on the basis of low quality. The reason for this decision was based on the presumption of the occurrence of a small number of high-quality systematic reviews in this field.

Data extraction

Data had been extracted independently by two reviewers from the eligible reviews using JBI Data Extraction Form for Review for Systematic Reviews and Research Syntheses (Aromataris and Munn, 2020). The extracted data contains study details (author; objectives; participants: characteristics and number; setting; interventions), search details (number of studies included; types of studies included), appraisal (instruments used; rating) and analysis (method of analysis; outcome assessed; result and findings; significance/direction; heterogeneity; comments). *"Individual study level data should not be reported in an umbrella review, except where an outcome is only informed by one included study,*" (Aromataris and Munn, 2020). Unfortunately, we had no choice but to use this exception, as is further explained below.

Data summary

The aim of the JBI umbrella review is to present a summary of existing research syntheses relevant to a particular topic. For this reason, the results of each included review are presented in a narrative style and in a tabular form to allow for an overview of relevant data, which can be interpreted easily.

5.6 Results

Relevant studies were identified by a systematic literature search using Epistemonikos, Scopus, WoS, ProQuest, gray literature and reference lists of studies selected for full-text screening. Our search strategy identified 1242 systematic reviews. After removing duplicates, reviews which did not meet inclusion criteria and reviews not possible to retrieve, 27 systematic reviews remained for full text review. Each article was carefully reviewed against the inclusion criteria and 24 more studies were eliminated. Reasons for exclusion were identified as: lacking meta-analysis or a reason why it was missing; wrong type of systematic review; not a systematic review; wrong patient population; wrong kind of intervention. After completing this process only 3 systematic reviews remained.

Description of the studies

Only one of the three studies eligible for analysis was examining music interventions exclusively (Nunes da Silva Santa et al., 2021). The focus of the two remaining reviews (Jong et al, 2019; Thrane, 2013) was much broader, grouping various interventions from the field of complementary and alternative medicine (such as hypnosis; massage; art therapy etc.), one of which is music.

Articles included had a total of 429 individuals (one study (Nguyen 2010) was included in all of the analyzed reviews – duplicate participants were not included in the final number). Ages ranged from 0 to 18 years old of any gender or ethnicity, with any type of cancer (acute and/or chronic oncology diseases) and at any point in the cancer trajectory from being newly diagnosed, in ongoing treatment, long-term survivors, or nearing the end of life.

Interventions were provided in clinical settings for children undergoing cancer treatment in nursing departments; intensive care units and/or outpatient clinics; day-care; nursing and/or ICU treatment and during painful procedures (such as lumbar puncture).

Of the two studies which focused on CAM (complementary and alternative medicine) in general, both used the same primary study to examine the effectiveness of music as an intervention (Nguyen, 2010) – a randomized control trial which used listening to music as an intervention before a painful procedure and was conducted on 40 pediatric patients with leukemia. Other interventions in these studies were based on different modalities (hypnosis; mind-body techniques; virtual reality; creative arts therapy; massage etc.). This primary study was included in Nunes da Silva Santa et al., (2021) as well.

In other primary studies, active music interventions offered by trained music therapists had been used, as well as passive music interventions such as listening to pre-recorded music, which were offered by medical staff. Types of music used for the interventions varied and included lullabies, relaxing music and classical music. Outcome measures of primary studies were summarized into three categories of pain reduction, anxiety and quality of life.

Methodological quality

Eligible reviews were assessed by two independent reviewers (ZA and LH) for methodological validity prior to inclusion into the review using standardized JBI Critical Appraisal Checklist of Systematic Reviews and Research Syntheses (Aromataris and Munn, 2020), which consists of 11 questions designed to evaluate the quality of execution of the review question; inclusion criteria and strategy; appraisal of methodological quality and elimination bias. This assessment revealed that studies were of moderate to high quality with scores ranging from 8 to 10. Any disagreements between the reviewers had been resolved through mutual discussion, or by consulting the third reviewer (JK).

Table 1. Assessments of the methodological quality of studies included in the analysis

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Thrane, 2013	Y	Y	Y	Y	N	N	N	U	Y	Y	Y
Nunes da Silva Santa et al., 2021	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Jong et al., 2019	Y	Y	Y	Y	N	N	Y	Y	Y	U	U

Y=yes, N=no, U=unclear

Questions of JBI Critical Appraisal Checklist of Systematic Reviews and Research Syntheses (Aromataris and Munn, 2020): 1. Is the review question clearly and explicitly stated? 2. Were the inclusion criteria appropriate for the review question? 3. Was the search strategy appropriate? 4. Were the sources and resources used to search for studies adequate? 5. Were the criteria for appraising studies appropriate? 6. Was critical appraisal conducted by two or more reviewers independently? 7. Were there methods to minimize errors in data extraction? 8. Were the methods used to combine studies appropriate? 9. Was the likelihood of publication bias assessed? 10. Were recommendations for policy and/or practice supported by the reported data? 11. Were the specific directives for new research appropriate?

The review findings

Results shown in this chapter focus on answering our research question: „What is the effectiveness of music-based interventions for children and youths with cancer on physiological and psychological outcomes?“

For the analysis we used the data extraction method according to JBI methology, as seen in Attachment 4.

First we define the outcomes which were found in the primary studies of our chosen systematic reviews. We found physiological outcomes, such as heart rate, blood pressure, respiratory rate and oxygen saturation. As psychological outcomes we found pain perception, fatigue, sleep quality, anxiety, distress, emotional regulation, active participation, vitality and overall quality of life.

In the analysis of the results of our chosen reviews we saw three main areas of outcomes: anxiety, pain and quality of life. They form the basis on which we formulate the effectiveness of musical interventions. These outcomes have been found in the three systematic reviews chosen for primary analysis. Two of these (Jong, 2019; Thrane, 2010) show a very high heterogeneity of interventions which included other modalities

of complementary alternative medical practices, such as massage, hypnosis etc. In this umbrella review only musical interventions were taken into consideration. The two above mentioned systematic reviews have only contained one primary study which was included in both of them (Nguyen, 2010).

The music interventions have divided the use of music into receptive and active. Passive interventions included listening to music with headphones or a speaker in a quiet room and were used before or during medical procedures, as well as before sleep with the goal of supporting better sleep hygiene. The selection of music varied from classical, relaxational, instrumental only to children's songs according to the patient's wishes. Time duration of musical interventions ranged from 10 to 30 minutes.

Among the active musical interventions we found were singing, playing different instruments and music listening together with the therapist. This came as a surprise to us, because the last mentioned intervention is classified among receptive interventions in music therapeutic literature. Parents could be present, if the child had wished for it. Active music interventions were conducted before or during medical procedures as well. Both forms – passive and active – were synthesized in the systematic reviews only as 'music interventions'. Therefore we use this umbrella term in our review as well, instead of dividing interventions into more detailed categories.

In the analyzed reviews we found that music is effective for reducing pain (SMD − 1.51; CI 95 % − 2.76− 0.26 N = 160= I 2 = 90 %) and anxiety (SMD − 1.12; CI 95 % − 1.78− 0.46 N = 199 = I 2 = 77 %) during clinical procedures performed on children and adolescents undergoing cancer treatment. A lesser but still significant effect can be observed in the quality of life outcome as well (SMD -0.96; CI 95 % − 1.17, − 0.74 N = 402= I 2 = 3 %).

These results are supported by results of all analyzed reviews. Five primary studies from the three systematic reviews included in our analysis researched pain reduction. For the anxiety outcome 5 studies were found in two of our chosen reviews and for quality of life we found 5 studies within one systematic review.

An analysis of the effects of music on heart rate in children undergoing cancer treatment brought forth three studies. In one study no difference was observed when compared to the control group. However, two studies registered a reduction in heart rate after the musical intervention. These inconclusive results can be attributed to the small number of studies focusing on heart rate in this population. In our analysis we view this result as a very small effect (SMD − 0.23; CI 95 % − 0.72− 0.27 N = 158= I 2 = 49 %).

Heterogeneity of the primary studies was moderate to high. This poses a limit to the generalizability of results and the creation of practical recommendations. Additional studies on this population with comparable techniques which can be reliably repeated are needed for a more accurate evaluation of the effectiveness of music interventions in pediatric oncology.

Table 2. Tabular presentation of quantitative findings for pain reduction

Interventions	Author/year	Number of studies/participants	Results/findings	Heterogeneity
Music interventions	Nunes da Silva Santa, 2021	3/115	-1.51[-2.76,-0.26]	A
	Thrane, 2010	1/40 (Nguyen, 2010)	Not calculated	N
	Jong, 2019	1/40 (Nguyen, 2010)	Not calculated	N

Table 3. Tabular presentation of quantitative findings for lowering anxiety

Interventions	Author/year	Number of studies/participants	Results/findings	Heterogeneity
Music interventions	Nunes da Silva Santa, 2021	4/154	-1.12[-1.78, -0.46]	A
	Thrane, 2010	1/40 (Nguyen, 2010)	Not calculated	N

Table 4. Tabular presentation of quantitative findings for quality of life

Musical interventions	Author/year	Number of studies/participants	Results/findings	Heterogeneity
Music Interventions	Nunes da Silva Santa, 2021	5/245	-0,96[-1,17,-0,74]	A

Table 5. Tabular presentation of quantitative findings for lowering heart rate

Musical interventions	Author/year	Number of studies/participants	Results/findings	Heterogeneity
Music Interventions	Nunes da Silva Santa, 2021	3/97	-0,23[-0,72,-0,27]	A

Summary of evidence

The following segment presents a table in which a significant effect of musical interventions on pain reduction, anxiety and higher quality of life (evaluation based on improved sleep quality, higher initiative and active participation and lower anxiety levels) can be observed. Lowering of heart-rate due to musical interventions had very little to no effect.

Table 6. Summary of Evidence from quantitative research synthesis

Phenomenon of interest	Author/ Year	Pain	Anxiety	Quality of Life	Lower heart rate
Music Interventions	Thrane, 2013 Jong et al., 2020 da Silva Santa et al., 2021				

"stop-light" indicator: green = effective intervention, amber = no difference in the investigated comparison

While constructing this umbrella review it quickly became evident that it would be very difficult to fulfill our primary goal – to analyze systematic reviews of effectiveness with meta-analyses focusing on the use of musical interventions on the population of pediatric oncology patients – according to the strict criteria set in the protocol. Since we were following the JBI methodological guidelines, we were strict in appraising the reviews. A large portion of systematic reviews found for full-text screening had to be excluded because they did not fit the inclusion criteria. In our final study selection, which only contained 3 systematic reviews we encountered another issue. All of them contained the same primary study (Nguyen, 2010) and two of them contained no other primary studies which researched music interventions. This skewed our findings drastically. For these reasons we decided to conduct an additional analysis of previously excluded systematic reviews from those chosen for full-text screening.

The goal of this analysis was to determine the reasons for the low number of studies, which fulfilled our criteria. While conducting the primary analysis it came to our attention, that one study (Nguyen, 2010) was repeatedly used in all of the analyzed reviews. For this reason we wanted to examine our hypothesis about the existence of a small number of primary studies dedicated to this field and age group. Therefore we identified the primary studies used in other systematic reviews of lower quality, which could not be used in the primary analysis. We determined their total number and the

number of repetitions across the reviews we chose for full-text screening. We also examined the sources they searched in and languages used for their search, in order to determine the scope and extent of their search strategies. To determine the methodological quality of these reviews we focused of whether or not the research question was clearly stated according to the PICO guidelines and what the type of the reviews was (mixed-methods review, review of literature etc.).

Studies chosen for additional analysis were any reviews, which researched effectiveness of music interventions on the population of pediatric oncology patients and the outcomes of which were any physiological and psychological effects. Among those were quantitative systematic reviews of effectiveness without meta-analysis or a given reason for its absence; scoping reviews; narrative reviews and mixed methods systematic reviews. One study (Bradt and Dileo, 2016) was included even though it did not discriminate between adults and children as its objective. Because of its primary focus on musical interventions and a vast array of primary studies focusing on music, it contained 5 studies targeting the pediatric population and gave specific recommendations for further research for this population.

12 studies were included in the additional analysis, which found 32 primary studies combined (attachment 4). Of those primary studies 20 were randomized controlled trials and 12 were non-randomized. As one can anticipate based on the high number of systematic reviews relative to the number of primary studies, some (13) primary studies have been analyzed by more than one systematic review: Kemper 2008 3x; Nguyen 2010 5x (in studies included for additional analysis and 3x in studies included for primary analysis); Sepulveda, 2014 2x; Robb, 2003 2x; Robb, 2008 3x; Robb, 2014 4x; Barry, 2010 4x; O'Calagan, 2011 2x; Uggla, 2016 2x; Uggla, 2018 3x; Barrera, 2002 3x; Burns, 2009 3x.

We therefore drew our attention to the analysis of search strategies (attachment 6) used in these reviews next. We wanted to understand whether the low number of primary studies found was due to inadequate or inappropriate search strategies or a deficit of studies of this problematic. Upon completion of this step we found that 10 reviews used PubMed and the 2 which did not (Landier and Tse, 2010; Bradt et al., 2016) used MedLine, both of which search the same database. Only 2 reviews (O'Connor and Halkett, 2018; Bradt et al., 2016) searched referenced literature. Those 2 reviews had the highest number of researched databases (13 and 10) and also included manual search in following journals and websites: Australian Journal of Music Therapy, Australian Music Therapy Association Bulletin, Canadian Journal of Music Therapy,

The International Journal of the Arts in Medicine, Journal of Music Therapy, Musik-,Tanz-, und Kunsttherapie (Journal for Art Therapies in Education, Welfare and Health Care), Musiktherapeutische Umschau, Music Therapy, Music Therapy Perspectives, Nordic Journal of Music Therapy, Music Therapy Today (online journal of music therapy), Voices (online international journal of music therapy), New Zealand Journal of Music Therapy, The Arts in Psychotherapy, British Journal of Music Therapy, Music and Medicine, Approaches, Journal of Medical Radiation Sciences, The Radiographer, Journal of Medical Imaging and Radiation Sciences, Journal of Radiotherapy in Practice, Radiography (2010-2015), Radiation Therapist, National Institute of Excellence in Health and Social Services (website), the NIHR Health Technology Assessment Programme (website), the CMA Infobase and the Directory of Good Practice Recommendations (website) and French-speaking consensus conferences.

Only one study was found to have searched in gray resources as well. (Bradt et al., 2016). Four reviews searched 2-4 databases; six reviews searched 6-9 databases.

When examining the languages used for search we found that articles were searched in languages of European origin only (mainly English, French, Spanish, Portuguese). This means that most studies conducted in Asian or African countries would not have been found.

Other aspects we evaluated were whether or not the reviews followed the PICO guidelines when forming their research question as we can see (3Y, 9N) – in attachment 7; if there was any kind of appraisal of quality or bias (6Y, 6N) – in attachment 8; if the review had a published protocol (3Y, 9N) – in attachment 9. These findings point to the conclusion that the quality of the analyzed reviews was quite low.

Furthermore, merely 4 of those (González-Martín-Moreno, 2021; Knott, 2016; Facchini, 2020; Bradt, 2016) were researching music interventions only. Other studies included other interventions from the field of complementary alternative medicine. Those four reviews found 28 of the 32 primary studies found in all 12 reviews we analyzed:

- The review by González-Martín-Moreno et al. (2021), Music Based Interventions in Paediatric and Adolescent Oncology Patients: A Systematic Review found 10 primary studies.
- The review by Knott et al. (2016), Music in the Care of Children and Adolescents with Cancer: Integrative Review found 7 studies.

- The review by Facchini et al. (2020), The Role of Music Therapy in the Treatment of Children with Cancer: A Systematic Review of Literature found 17 studies.
- The review by Bradt et al. (2016), Music Interventions for Improving Psychological and Physical Outcomes in Cancer Patients found 5 studies.

Based on the results of these four studies, music-based interventions improve anxiety, fatigue or pain in pediatric and adolescent oncology patients during diagnostic procedures and during hospitalization. Studies induct that music-based interventions improve also state of mind, self-esteem, decrease depressive symptoms, stimulate adaptive coping strategies by decreasing social isolation during radiotherapy and hospitalization, allow to cope better with the hospital environment and the therapy to which they are subjected to and improve quality of life. Access to our favorite music activates creativity, fun and laughter, whose value is incalculable, when cancer becomes a limiting life factor. Despite these positive findings, one review (Facchini, 2020) suggests that the benefits of MT in terms of relaxation and pain perception during the medical procedures are still discordant.

Music-based interventions have beneficial effects on vital signs, decreasing heart rate, respiratory rate and blood pressure before and after lumbar puncture. However, this reduction is rather small and therefore may not be clinically significant. No evidence of effect was found also for distress, mood, physical functioning, spiritual well-being or oxygen saturation (Bradt, 2016). However, only a small number of trials investigated the effects of music on these outcomes. Results from single trials suggest that music listening in cancer patients undergoing surgery may reduce anesthetic and analgesic consumption and reduce the length of hospital stay, but more research is needed before drawing solid conclusions. Results from a single study furthermore suggest that post-surgery recovery time may be shortened when a music therapist offers live, individualized music before and during surgery.

Listening to music was the most frequently used intervention in the studies. However, when a qualified music therapist was involved in the intervention, more complex techniques such as active music engagement were used. Music therapy in the context of pediatric oncology can be easily implemented and readily accepted by children, parents and medical staff.

5.7 Discussion

The findings of the primary analysis (Nunes da Silva Santa et al., 2021; Jong et al., 2019; Thrane, 2013) confirm the high effectiveness of musical interventions on psychological (pain, anxiety, quality of life, etc.) and physiological (heart rate, etc.) outcomes when working with children and adolescents undergoing oncology treatments.

These results are supported by the findings of numerous primary studies, as well as systematic reviews, which focus on the adult population. In their randomized control trial, Cassileth, Vickers and Magill (2003) found, that music therapy can improve anxiety, depression and mood disturbances in patients undergoing autologous stem cell transplantation. Hilligard (2003) found significant improvements of the quality of life in palliative care patients who received music therapy, compared to the control group. Moreover, the quality of life of the experimental group increased over time, whereas the quality of life in the control group decreased. Capeda, Carr, Lau and Alvarez (2006) have synthesized the findings of multiple primary studies focusing the effects of music on pain perception. Their systematic review concludes, that music can reduce perceived pain and lower the intake of opioids, however the magnitude of these benefits remains unclear due to the high heterogeneity of included studies. In another systematic review, Bradt, Dileo and Shim (2013) have found, that listening to music can reduce anxiety before operations. This can be explained by its impact on the autonomic nervous system and the endocrine and psychological stress response (Thoma et al., 2013). Even though these findings are congruent with those of studies focusing on children, we should not make the mistake of deducing, that children react in the same way. More primary research on this population is needed.

The results of the additional analysis (O'Connor and Halkett, 2018; Myers et al., 2005; Poder and Lemieux, 2013; Velez-Florez et al., 2018; González-Martín-Moreno et al., 2021; Knott et al., 2016; Xavie et al., 2019; Lopes-Júnior et al., 2015; Coughtrey et. al., 2017; Facchini and Ruini, 2020; Landier and Tse, 2010; Bradt et al., 2016) confirm our hypothesis of research waste in the field of music therapy in pediatric oncology. Reviews are being published, which do not fulfill the criteria of quality research (the absence of published research protocols, the PICO question, critical appraisal) and which analyze identical primary studies.

Implications for practice

The results of analyzed research confirm, that the use of music interventions has a positive impact on a number of outcomes in the target population. They also point out the need for a greater implementation of findings into practice. Standards of psycho-social care for patients are well established in psycho-oncology. Creating guidelines for music therapy practice in this target group would be helpful for providing interventions which could be easier to replicate and to conduct research on. Without further research, stating further clinical recommendations would be unfounded.

Implications for research

As previously stated, further research into musical interventions on psychological and physiological effects on children and adolescents is needed. A larger number of studies have been published on the effects of music in the adult population of oncology patients. However, there is still a great need for more research targeting children and adolescents.

If further systematic reviews are to be carried out, we recommend searching for primary studies in languages other than European and call for a higher methodological quality thereof. Under these conditions, further reviews may be relevant. If these findings were to confirm the low number of suitable primary studies, we would recommend conducting more primary research. Studies should primarily focus on the pediatric population, as it has its own characteristics in treatment and symptom management. Furthermore, we recommend focusing on various music therapy forms (examining active and receptive music therapy individually) and methods (interpretation, improvisation, composition, listening to music) in regards to the age of the children and adolescents, as well as on the specific stages and types of treatment. Research could also focus more specifically on the type of cancer (such as neurological music therapy in children with cancer of the central nervous system, etc.). We recommend monitoring more specific social outcomes, or the inclusion of music therapy in medical rehabilitation (in cooperation with physiotherapists). In terms of social outcomes, we see the importance of focusing research on relationships and their transformation during long-term hospitalization and isolation, and the role of music therapy in supporting the maintenance of the quality of existing, as well as new interpersonal relationships.

To fully use the potential of musical interventions specialized academic and clinical training is required, as well as careful selection of intervention techniques to meet the client's needs. In the studies we analyzed music interventions were performed by music therapists, as well as health professionals not certified in music therapy, such as doctors, nurses or physical therapists.

Music therapy practitioners use predominantly musical techniques based on scientific evidence to meet specific needs of their patients, be they physical; psychological or social in nature, and to enhance life skills such as forming relationships; increasing motivation; attention; relaxation; self-expression; organization and learning to increase the quality of life. On this we base our next recommendation for further research: to conduct studies using interventions administered by music therapists and to separate them from those using interventions administered by health care professionals. When evaluating music therapy, specific guidelines for music-based interventions should be established. In order to establish music therapy as an evidence-based intervention, more research of superior quality is needed. When a firm basis of primary research has been built, guidelines can be constructed for safe and consistent methods to be used in clinical practice.

Study limitations

The strong suit of our research is, that we were following the guidelines of the standardized JBI methodology, including publishing a research protocol. We worked together with supervisors and a multidisciplinary team, including an information specialist, who conducted the database search.

Already while choosing studies eligible for this review it became clear that our results will be limited by the low number of systematic reviews which would fulfill our search criteria, and the extremely low number of high quality reviews. Another aspect limiting a robust synthesis was the high heterogeneity of musical interventions and their use. However, those findings lead us to reach one of the important conclusions for further research. More primary studies are needed for a better understanding of the effectiveness of specific music interventions for children undergoing cancer treatment.

Another limitation of our research lies in the fact, that we did not search in the literature written in non-European languages and we did not contact authors for missing information (14 full-texts not retrieved). The results of this study are influenced by the

small number of quality systematic reviews in the given research field, but therefore our study is enriched with an additional analysis, which is usually not conducted.

CONCLUSION

This thesis discusses the possibilities of using music interventions, primarily music therapy, in pediatric and adolescent cancer patients. It presents a general theoretical basis of the field of pediatric oncology, providing an insight into the specifics of children's and adolescents' responses to the disease with respect to this age group. It focuses at the use of music-based interventions in health care – examining the relationship between music and pain and the difference between music medicine and music therapy. Finally, it provides a theoretical view of the application of music therapy in this target group.

We attempted to document the effectiveness of these interventions in the second part of the work. In the practical part, we analyzed the available systematic reviews, examined their quality and evaluated the effects of musical interventions in children and adolescents with cancer based on their results. It appears that in this area, there is a lack of quality systematic reviews and a small number of primary studies worldwide. The recommendations based on our research therefore clearly support further conduct of primary research, carried out on the basis of direct work with clients. The information available so far thus shows that music-based interventions in pediatric oncology are of significance for a wide range of therapeutic goals and provide the means necessary for their fulfillment.

The effectiveness of musical interventions on reducing pain and anxiety and improving quality of life in children undergoing cancer treatment is backed by evidence. Yet the area of interpersonal relationships and interventions implemented directly by the music therapist has been documented to a far lesser extent. We also feel there is a need to support research aimed directly at the pediatric and adolescent population. It is possible that such studies have been published in non-European languages, which neither we nor the studies we have analyzed have searched through. Therefore, we find it important to in these languages as well.

Based on these findings, musical interventions can be recommended as non-pharmacological therapy within the complex care for pediatric oncology patients. It would make us happy to see our work contributing to the publication of research, which could further examine their effectiveness, and thus in time to contribute to the

standardization of care or the development and implementation of guidelines, essential for the consolidation of their practice.

ANNOTATION

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Music Therapy in the Treatment of Children with Cancer

Doc. Mgr. Jiří Kantor, PhD.

Number of characters: 132 112

Number of attachments: 9

Number of used sources of literature: 119

Key words: music therapy, music, oncology, cancer, children, adolescents.

This thesis discusses individual treatment aspects of oncology diseases in childhood and adolescence. Its primarily focus is on non-pharmacological procedures while accompanying patients and their families during treatment and in terms of palliative care, specifically the use of music, music medicine and music therapy in the process of accompaniment. The practical part is comprised of an umbrella review, which maps the currently available systematic reviews in this area and evaluates thus acquired data in order to answer the question: What is the effectiveness of using musical interventions in children and adolescents with oncology diseases on their physiological and psychological reactions, which occur in the course of treatment.

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LIST OF ATTACHMENTS

Attachment 1 – Study protocol registered in PROSPERO with the registration number CRD42021259529

Effectiveness of Music-based interventions in children and youths with cancer: umbrella review protocol

Introduction:

Cancer is a large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably, go beyond their usual boundaries to invade adjoining parts of the body and/or spread to other organs. The latter process is called metastasizing and is a major cause of death from cancer, writes WHO (2021). The International Agency for Research on Cancer estimates that globally, 1 in 5 people develop cancer during their lifetime (GLOBOCAN, 2020). Cancer is the second leading cause of death, particularly in developing countries (WHO, 2021). In 2020, 279 419 children and youth (from 0 to 19) were diagnosed by cancer worldwide (GLOBOCAN, 2020).

Cancer often results in extensive emotional, physical and social suffering. Goal of cancer treatment is not only cure or prolong life, but also quality of life. Current cancer care increasingly incorporates various psychosocial interventions to improve quality of life. This can be achieved by supportive or palliative care and psychosocial support, is written in Cancer Key Facts published by WHO (2018).

APA Dictionary of Psychology defines psychooncology as *„the study of psychological, behavioral, and psychosocial factors involved in the risk, detection, course, treatment, and outcome (in terms of survival) of cancer. The field examines responses to cancer on the part of patients, families, and caregivers at all stages of the disease.“* (APA, 2020) Evidence-based research on psycho-oncology in last three decades lays emphasis upon the critical role of psychological services for better illness adjustment, improved quality of life, reduced distress and cognitive problems among the rapidly increasing pediatric cancer population (Huang et al., 2010). Music therapy as non-invasive method is often used as complementary intervention to standard cancer treatment.

„Music therapy in oncology uses music in preventive, curative and palliative cancer care and is very helpful to a wide variety of patients who suffer from a large range of neoplasms. While music therapy does not actually affect the disease itself, it has a great impact on the their mood, and sometimes can make a difference in the way the patient copes with and feels about their disease. The effectiveness of music therapy for oncology patients has been documented in numerous descriptive and experimental studies. A number of publications have described the specific benefits of music therapy interventions. Music therapy in cancer care focuses on both physiological and psychological needs arising from the disease as well as from side-effects of cancer treatment", sais Stanczyk (2011). Music therapy interventions have been used to alleviate symptoms and treatment side effects and address psychosocial needs in people with cancer. Music therapy requires the implementation of a music intervention by a trained music therapist, the presence of a therapeutic process and the use of personally tailored music experiences (Bradt, 2016). Interactive music therapy was found to promote a positive self-image and healthy relationships and decrease the intake of analgetics (Huang, 2010). In the chaotic hospital environment it may help institute a sense of normalcy and hope (O'Calaghan, 2013).

Increased interest in providing systematic reviews of this topic is visible in last years. There are many reviews (Osterman, 2012; Archer, 2015; Nightingale, 2015; etc.) but their focus is still too general. There is no change in understanding more the context of different population or cancer characteristics. However, many studies has confirmed healing effect of music-based interventions in this setting. Because of it, we want to make analysis of effectiveness of music and music therapeutic interventions to understand them more.

Conduct of an umbrella review offers the possibility of addressing a broad scope of issues related to a topic of interest. The wide picture obtainable from the conduct of an umbrella review is also ideal in highlighting if the evidence base around a topic or question is consistent or if contradictory or discrepant findings exist, and in exploring and detailing the reasons why. Investigation of the evidence with an umbrella review allows assessment and consideration of whether reviewers addressing similar review questions independently observe similar results and arrive at generally similar conclusions.

PROSPERO, OSF and Epistemonikos were searched for systematic reviews and umbrella reviews. No ongoing or finished umbrella review was found, however there is a considerable amount of systematic reviews focused on cancer and music-based

interventions. Our aim is to explore the effectiveness of music-based interventions for children and youths with cancer on physiological and psychosocial outcomes.

Methods

Review question: „What is the effectiveness of music-based interventions for children and youths with cancer on physiological and psychological outcomes?“

We have found out that there is no umbrella review on this topic done. However we found a large number of systematic reviews that lead us to consider of possible presence of research waste or other research gap. Our aim is to explore the effectiveness of music-based interventions for children and youths with cancer.

Inclusion criteria:

Population: children and youth with cancer, without limitation by the type of cancer

Intervention: all music-based interventions, e.g. interactive music therapy, music imaginary, song writing, listening to music, music medicine...

Outcomes: any physiological and psychosocial outcome, e.g. depression, anxiety, pain, fatigue, quality of life...

Comparators: any type of comparator, e.g. control groups using standard treatment, psychotherapy, other art therapies, relaxation...

Setting: type of setting without limitation, e.g. children hospital, day care centre, care provided at home...

Type of systematic review: only systematic review of effectivness (with meta-anaylsis from studies with any quantitative design).

The JBI methodology for umbrella reviews will be used (Aromataris and Munn, 2020).

Search strategy: The database Epistemonikos, Scopus, Wos and grey literature is included to search strategy. Initial keywords to be used will be: children OR youth AND cancer OR oncolog* AND music. There will be no limitation in language or publication period. We will screen also the reference lists of all relevant studies.

Study selection: Texts will be screened by two reviewers independently, first at abstract and then at fulltext. Any disagreements will be solved by consensus or by the decision of a third reviewer. Reference lists of eligible texts will be searched for relevant systematic reviews. Screening results will be presented in a PRISMA flowchart (Aromataris and Munn, 2020).

Assessment of methodological quality: Selected eligible reviews will be assessed by two independent reviewers (JK and LH) for methodological validity prior to inclusion

in the review using standardized JBI Critical Appraisal Checklist of Systematic Reviews and Research Syntheses (Aromataris and Munn, 2020). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer. Reviews will not be excluded solely on the basis of low quality.

Data extraction: Data will be extracted from the eligible reviews using JBI Data Extraction Form for Review for Systematic Reviews and Research Syntheses (Aromataris and Munn, 2020). The data extracted will include study details (author, objectives, participants: characteristics and number, setting, interventions), search details (number of studies included, types of studies included) and appraisal (outcome assessed, result and findings). If there are data missing or incomplete, the authors of reviews will be contacted. Two reviewers will extract data independently.

Data Summary: The aim of the JBI umbrella review is to present a summary of existing research syntheses relevant to a particular topic. To this end, the results of all included reviews will be presented narratively and in a tabular form to allow for a ready and easily interpretable overview of the findings.

Literature:

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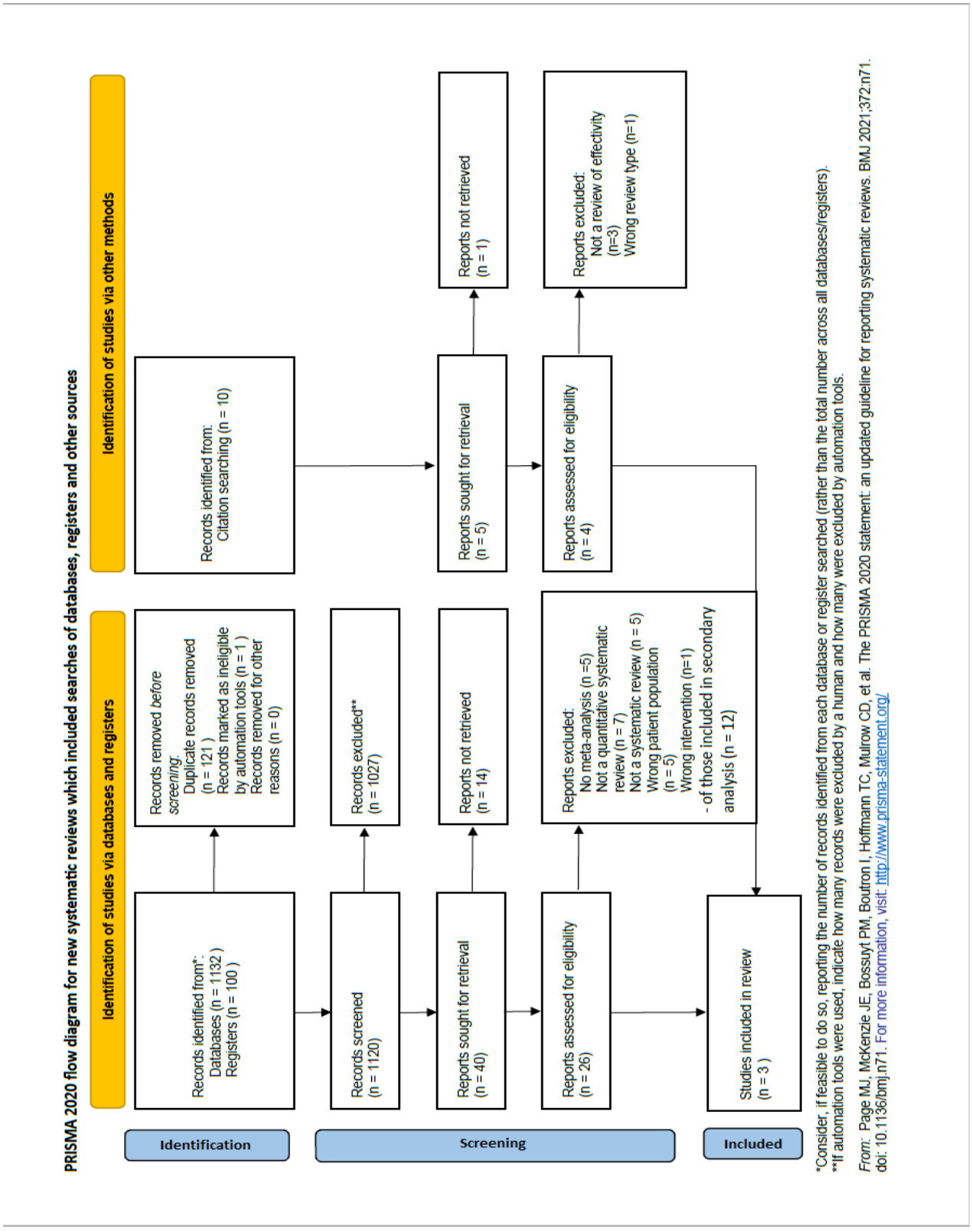
Attachment 2 – Search strategy

(advanced_title_en:(child* OR adolescent* OR youth OR young* OR teen* OR pediatr* OR infant*) AND (cancer OR neoplasm* OR tumor* OR tumour* OR carcinoma* OR leukemia OR leukaemia OR malignan* OR oncolog*) AND (music* OR music intervention* OR music therap* OR music imaginar* music engagement* OR song writing OR listen* to music OR music medicine*) OR advanced_abstract_en: (child* OR adolescent* OR youth OR young* OR teen* OR pediatr* OR infant*) AND (cancer OR neoplasm* OR tumor* OR tumour* OR carcinoma* OR leukemia OR leukaemia OR malignan* OR oncolog*) AND (music* OR music intervention* OR music therap* OR music imaginar* OR song writing OR listen* to music OR music medicine*)) [Filters: protocol=no, classification=systematic-review]

Attachment 3 – Picture 1. PRISMA Flow diagram for Study selection for umbrella review



Attachment 4 – Data Extraction

MUSIC INTERVENTIONS IN PEDIATRIC ONCOLOGY: Systematic review and meta-analysis

Study details	
Author/Year	Ivone Nunes da Silva Santa, Mariana Cabral Schveitzer, Maria Lucia Barbosa Maia dos Santos; Ricardo Ghelman and Vicente Odone Filho 2021
Objectives	Identify the therapeutic effects of music interventions in psychological and physiological terms and on the quality of life of children undergoing cancer treatment.
Participants (characteristics/total number)	429 children, whose ages ranged from 1 month to 18 years of either gender and any race, with acute and/or chronic oncology diseases, undergoing outpatient, day-care, nursing and/or ICU treatment.
Setting/context	clinical settings for children undergoing cancer treatment in nursing departments, intensive care units and/or outpatient clinics
Description of Interventions/phenomena of interest	studies that examined music interventions and measured pain, anxiety and quality of life
Search details	
Number of databases/sources searched	6 databases: Excerpta Medica dataBASE **(**EMBASE); Literature of the Latin American and Caribbean Health Sciences (LILACS); National Library of Medicine National Institutes of Health (PubMed); Scientific Electronic Library Online (SciELO); and Web of Science. Search for unpublished studies: ClinicalTrials.gov.
Range (years) of incl studies	2008-2020
Number of studies included /	11
Types of studies included	Randomized Controlled Trials and Quasi-Experimental Studies
Country of origin of incl. studies	Brazil, Sweden, Vietnam, China, Italy, Canada, Indonesia, Mexico, 2x USA, Australia

Appraisal	
Appraisal instruments used	JBI Clinical Appraisal Checklist for Randomized Controlled Trials. JBI Critical Appraisal Checklist for Quasi-Experimental Studies
Appraisal rating	RCT: Moderate to high quality - scores ranged from 7 to 13 on a 13 point scale. Non-RCT: Moderate to high quality - scores ranged from 6 to 8 on a 9 point scale.
Analysis	
Method of analysis	Meta-analysis (standardized mean differences calculated in JBI SUMARI) + narrative synthesis
Outcome assessed	Anxiety, pain and quality of life
Results/Findings	Combined estimate of pain and anxiety (five studies): the use of music interventions proved beneficial, despite high heterogeneity: SMD -1.05; CI 95 % -1.70 – 0.40 N = 453 I2 = 90 %. Pain reduction: SMD □ 1.51; CI 95 % □ 2.76□ 0.26 N = 160= I2 = 90 % Anxiety: music interventions favored reduced anxiety: SMD □ 1.12; CI 95 % □ 1.78□ 0.46 N = 199 = I2 = 77 % The quality of life: benefits for music interventions: SMD -0.96; CI 95 % □ 1.17, 0.74 N = 402= I2 = 3 % (the effects observed the most were improved sleep quality, more initiative and engagement, and less anxiety). Heart rate and blood pressure: no difference comparing CG: SMD 0.23; CI 95 % 0.72 0.27 N = 158= I2 = 49 %. A reduction in heart rate after the music interventions session was only noted in two isolated studies.
Significance/direction	Music was found to be effective in pain and anxiety reduction and improving quality of life for the following procedures: chemotherapy, stem cell transplantation (CTCTH), lumbar puncture and radiation therapy.
Heterogeneity	Combined analysis of the effect of music interventions on pain and anxiety: $I^2 = 90$ Music interventions vs. standard treatment on reducing pain: $I^2 = 90$ Music interventions vs. standard treatment on reducing anxiety: $I^2 = 77$ Music interventions vs. standard treatment on improving quality of life: $I^2 = 3$ Music interventions vs. standard treatment on lowering heart rate: $I^2 = 49$
Comments	This was the only review which fully fit our inclusion criteria, and the sole focus of which were musical interventions. It is due to the small number of primary studies with robust design. Additional studies with this population and similar and reproducible standardized procedures are needed to allow more accurate evaluation of the effectiveness of music therapy on paediatric oncology population.

Development of an evidence-based decision aid on complementary and alternative medicine (CAM) and pain for parents of children with cancer

Study details	
Author/Year	Miek C. Jong, Inge Boers, Herman van Wietmarschen, Martine Busch, Marianne C. Naafs Gertjan J. L. Kaspers and Wim J. E. Tissing 2019
Objectives	To develop an evidence-based decision aid for parents of children with cancer and to help guide them in the use of complementary and alternative medicine (CAM) for cancer care.
Participants (characteristics/total number)	480 Children (0–18 years) with any type of cancer undergoing a CAM intervention. There was only 1 RCT with music as an intervention with 40 participants with leukemia.
Setting/context	Clinical settings for children undergoing cancer treatment.
Description of Interventions/phenomena of interest	- 1 study in review by Nguyen (2010): RCT evaluating music vs control group for pain and distress associated with lumbar punctures. - Pain reduction, adverse reactions to CAM.
Search details	
Number of databases/sources searched	4 databases: Pubmed, Embase, Cochrane. CINAHL
Range (years) of incl studies	1987-2015
Number of studies included /	11
Types of studies included	Randomized Controlled Trials
Country of origin of incl. studies	N/A
Appraisal	
Appraisal instruments used	N/A
Appraisal rating	N/A
Analysis	

Method of analysis	GRADE analysis (did not include music therapy)
Outcome assessed	The primary outcome was pain (any pain-related outcome), and the secondary outcome was reported CAM-related adverse events.
Results/Findings	- As compared with the control group, children in the music group had significant reduction in self-reported pain and anxiety. Significant reductions in heart rate and respiratory (during and after procedure) in music group. The exact effect size values are not stated in this review but are identical to those found in the Effectiveness of Integrative Modalities for Pain and Anxiety in Children and Adolescents With Cancer: A Systematic Review. - No evidence was found that music therapy was unsafe to treat pain in children with cancer.
Significance/direction	Authors have found only 1 RCT of music interventions, which they could include in their study. The RCT is of a high quality with a large effect for pain reduction and very large effect for anxiety. However, for a lack of other RCTs in this field, the study gives a ‚low quality effect' score to music interventions, as well as all other modalities except for hypnotherapy, for which more high quality studies have been produced in this context.
Heterogeneity	GRADE Analysis did not include the study with music therapy.
Comments	

Effectiveness of Integrative Modalities for Pain and Anxiety in Children and Adolescents With Cancer: A Systematic Review

Study details	
Author/Year	Susan Thrane 2013
Objectives	To establish which integrative modalities are most effective for reducing pain and anxiety in children and adolescents with cancer.
Participants (characteristics/total number)	- 358 children with various types of cancer, 1-18 years old at any point in the cancer trajectory from new diagnosis, to ongoing treatment, to long-term survivorship, or end of life. - There was only 1 RCT with music as an intervention with 40 participants with leukemia.
Setting/context	Clinical setting, during painful procedures common throughout cancer treatment.
Description of Interventions/phenomena of interest	- Pain reduction after undergoing treatment with various CAM. Integrative modalities included in the review are: hypnosis, mind-body techniques, virtual reality, creative arts therapy, massage, music. - 1 study in Review by Nguyen 2010: RCT evaluating music vs control group for pain and distress associated with lumbar punctures.
Search details	
Number of databases/sources searched	4 Databases: PubMed; PsychInfo; CINAHL; Web of Science; MedLine 3 Journals: Integrative Cancer Therapies; Journal of Evidence-Based Complementary & Alternative Medicine; Supportive Care in Cancer
Range (years) of incl studies	1990-2010
Number of studies included /	12
Types of studies included	Randomized Controlled Trials
Country of origin of incl. studies	Greece, Vietnam, USA
Appraisal	
Appraisal instruments used	N/A
Appraisal rating	N/A

Analysis	
Method of analysis	Narrative synthesis
Outcome assessed	Pain and anxiety reduction as a result of CAM
Results/Findings	Significant child self-report for pain during ($P <$ .001; d= 1.49) and after (P = .003; d= 1.05) procedure. Significant child self-report for anxiety before ($P <$ .001; d= 1.41) and after ($P <$ .001; d= 1.47) procedure. Significant vital signs include heart rate (HR) during procedure (P = .012; d = 0.98) and respiratory rate (RR) during (P = .009; d = 0.91) and after (P = .003; d = 1.03)
Significance/direction	In the Nguyen et al. study (2010), music was used as a distraction during an LP. Children were able to choose the type of music they would like to listen to. The large and very large effect sizes for child selfreport of both pain and anxiety during the music intervention shows very good evidence for the effectiveness of this simple intervention. - Talking about direction would hold no meaning, since this review only included 1 study with music modality.
Heterogeneity	High.
Comments	With the exception of one virtual reality study, which had a medium effect size, the remaining modalities (hypnosis, mind-body techniques, massage, creative arts therapy) in this review achieved a large to very large effect size.

Attachment 5 – Studies included in additional analysis

Author/ Year	Kemper 2008	Nguyen 2010	Sepulveda 2014	Robb 2003	Robb 2008	Robb 2014	Robb 2016	Robb 2017	Barry 2010
O'Connor and Halkett, 2018									x
Myers et al., 2005									
Poder and Lemieux, 2013					x				
Velez-Florez et al., 2018		x	x			x	x		
González-Martín-Moreno et al., 2021		x		x	x				x
Knott et al., 2016	x	x	x						x
Xavier et al., 2019									
Lopes-Júnior et al., 2015	x								
Coughtrey et al., 2017						x			
Facchini and Ruini, 2020	x	x		x	x	x		x	x
Landier and Tse, 2010									
Bradt et al., 2016		x				x			

Author/ Year	O'Calagan 2007	O'Calagan 2011	O'Calagan 2013	Uggla 2016	Uggla 2018	Bufallini 2009	Barrera 2002	Burns 2009	Burns 2010
O'Connor and Halkett, 2018									
Myers et al., 2005							x		
Poder and Lemieux, 2013	x					x	x		
Velez-Florez et al., 2018		x				x			
González-Martín-Moreno et al., 2021				x	x				
Knott et al., 2016		x	x						
Xavier et al., 2019					x				
Lopes-Júnior et al., 2015									
Coughtrey et al., 2017								x	
Facchini and Ruini, 2020				x	x		x	x	x
Landier and Tse, 2010									
Bradt et al., 2016						x		x	

Author/ Year	Colwell 2005	Cabral-Gallo 2014	Camprubi 1999	Giordano 2020	Saghaeee-Shahriari 2019	Tucquet 2014	Pfaff 1989	Docherty 2013	Polat 2015
O'Connor and Halkett, 2018									
Myers et al., 2005									
Poder and Lemieux, 2013	x								
Velez-Florez et al., 2018									
González-Martín-Moreno et al., 2021		x	x	x	x				
Knott et al., 2016						x			
Xavier et al., 2019									
Lopes-Júnior et al., 2015									
Coughtrey et al., 2017									
Facchini and Ruini, 2020							x	x	x
Landier and Tse, 2010									
Bradt et al., 2016									

Author/ Year	Haase 2019	Saghaee 2019	Giordano 2020	Caprilli 2007	Duocastella 1999
O'Connor and Halkett, 2018					
Myers et al., 2005					
Poder and Lemieux, 2013					
Velez-Florez et al., 2018					
González-Martín-Moreno et al., 2021					
Knott et al., 2016					
Xavier et al., 2019					
Lopes-Júnior et al., 2015					
Coughtrey et al., 2017					
Facchini and Ruini, 2020	x	x	x		
Landier and Tse, 2010				x	
Bradt et al., 2016					x

Attachment 6 – Analysis of search strategies

Author/ Year	Cochrane Library	Cochrane Central	Scopus	ProQuest	PubMed	Science Direct	Ovid	OVID Healthstar	Psych Info
O'Connor and Halkett, 2018	x		x	x	x	x	x		x
Myers et al., 2005					x				
Poder and Lemieux, 2013					x	x		x	
Velez-Florez et al., 2018		x	x		x				
González-Martín-Moreno et al., 2021	x		x		x	x			
Knott et al., 2016	x				x				
Xavier et al., 2019					x				x
Lopes-Júnior et al., 2015	x		x		x				x
Coughtrey et al., 2017					x				x
Facchini and Ruini, 2020			x		x				x
Landier and Tse, 2010	x								x
Bradt et al., 2016		x		x					x

Author/ Year	Web of Science	Embase	Medline	CINAHL	AMED	Mantis	Scielo	Lilacs	Dialnet
O'Connor and Halkett, 2018	x	x	x						
Myers et al., 2005				x					
Poder and Lemieux, 2013		x	x	x	x	x			
Velez-Florez et al., 2018		x					x	x	
González-Martín-Moreno et al., 2021									x
Knott et al., 2016			x				x	x	
Xavier et al., 2019	x		x	x				x	
Lopes-Júnior et al., 2015	x	x		x				x	
Coughtrey et al., 2017				x					
Facchini and Ruini, 2020									
Landier and Tse, 2010			x	x					
Bradt et al., 2016		x	x	x				x	

Author/ Year	IDICEs CSIC	BDENF	VHL	IBECS	The Science Citation index	Cancer Lit	CAIRSS for Music	Clinical Trials.gov	RILM
O'Connor and Halkett, 2018									
Myers et al., 2005									
Poder and Lemieux, 2013									
Velez-Florez et al., 2018									
González-Martín-Moreno et al., 2021	x								
Knott et al., 2016		x							
Xavier et al., 2019		x	x	x					
Lopes-Júnior et al., 2015									
Coughtrey et al., 2017									
Facchini and Ruini, 2020									
Landier and Tse, 2010									
Bradt et al., 2016					x	x	x	x	x

Author/ Year	Clinical Trials.gov	RILM	Referenced literature	Other
O'Connor and Halkett, 2018			x	Journal of Medical Radiation Sciences, The Radiographer, Journal of Medical Imaging and Radiation Sciences, Journal of Radiotherapy in Practice, Radiography (2010-2015) and Radiation Therapist
Myers et al., 2005				
Poder and Lemieux, 2013				The websites of the National Institute of Excellence in Health and Social Services, the NIHR Health Technology Assessment Programme, the CMA Infobase and the Directory of Good Practice Recommendations and French-speaking consensus conferences
Velez-Florez et al., 2018				
González-Martín-Moreno et al., 2021				
Knott et al., 2016				
Xavier et al., 2019				
Lopes-Júnior et al., 2015				
Coughtrey et al., 2017				
Facchini and Ruini, 2020				

Landier and Tse, 2010				
Bradt et al., 2016	x	x	x	Australian Journal of Music Therapy, Australian Music Therapy Association Bulletin, Canadian Journal of Music Therapy, The International Journal of the Arts in Medicine, Journal of Music Therapy, Musik-,Tanz-, und Kunsttherapie (Journal for Art Therapies in Education, Welfare and Health Care), Musiktherapeutische Umschau, Music Therapy, Music therapy Perspectives, Nordic Journal of Music Therapy, Music Therapy Today (online journal of music therapy), Voices (online international journal of music therapy), New Zealand Journal of Music Therapy, The Arts in Psychotherapy, British Journal of Music Therapy, Music and Medicine, Approaches

Attachment 7 – Presence of the PICO question in studies used for additional analysis

Author/ Year	PICO
O'Connor and Halkett, 2018	Yes
Myers et al., 2005	No
Poder and Lemieux, 2013	Yes
Velez-Florez et al., 2018	No
González-Martín-Moreno et al., 2021	Yes
Knott et al., 2016	No
Xavier et al., 2019	Yes
Lopes-Júnior et al., 2015	Yes
Coughtrey et al., 2017	Yes
Facchini and Ruini, 2020	No
Landier and Tse, 2010	No
Bradt et al., 2016	Yes

Attachment 8 – Appraisal of quality in studies used for the additional analysis

Author/ Year	**Critical appraisal**
O'Connor and Halkett, 2018	Yes
Myers et al., 2005	No
Poder and Lemieux, 2013	No
Velez-Florez et al., 2018	No
González-Martín-Moreno et al., 2021	Yes
Knott et al., 2016	No
Xavier et al., 2019	No
Lopes-Júnior et al., 2015	Yes
Coughtrey et al., 2017	Yes
Facchini and Ruini, 2020	Yes
Landier and Tse, 2010	No
Bradt et al., 2016	Yes

Attachment 9 – The presence of a published protocol in studies used for the additional analysis

Author/ Year	**Protocol**
O'Connor and Halkett, 2018	No
Myers et al., 2005	No
Poder and Lemieux, 2013	No
Velez-Florez et al., 2018	No
González-Martín-Moreno et al., 2021	Yes
Knott et al., 2016	No
Xavier et al., 2019	No
Lopes-Júnior et al., 2015	No
Coughtrey et al., 2017	No
Facchini and Ruini, 2020	Yes
Landier and Tse, 2010	No
Bradt et al., 2016	Yes