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The Effect of Music on Pain in Adult Patients with Cancer: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

PURPOSE: The purpose of this review is to synthesize the current literature on music's effect on pain in adult patients with cancer. From the information compiled in this review, potential clinical implications and future avenues for research can be made clear.

METHODS: A review of literature published after 2000 was conducted using two databases: PubMed and CINAHL. The following terms were used: (cancer OR oncology) AND (music) AND (pain OR cancer pain). Across both databases and searches, 193 articles were identified. After removing any articles that were not randomized controlled trials, screening titles and abstracts, and screening full text articles, 10 articles met criteria for inclusion in the review.

RESULTS: The articles identified provided data to be reviewed. Various music interventions have the potential to reduce pain in adult patients with cancer. There were three main types of music interventions investigated: active music, passive music, and music therapy. Both the music therapy interventions (3 studies) and active music interventions (5 studies) found mixed results, while passive music interventions (2 studies) provided significant pain reduction in adult patients with cancer. Five studies investigated short term effects of music on pain and all five found a statistically significant reduction in pain, while the five studies that investigated long term effects included three that provided significant pain reduction, and two that provided no significant reduction in pain.

DISCUSSION: There is preliminary evidence that music has the potential to be an effective adjunctive pain reduction tool in adult patients with cancer. More research needs to be conducted on which music interventions, given over what duration and consistency, can provide the most effective pain relief in this population.

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Chapter 1

Problem

Within the last thirty years, global cancer prevalence has increased from 8.1 million new cancer cases in 1990, to 19.3 million new cancer cases in 2020 (Parkin et al., 1999; Sung et al., 2021). This number is only projected to continue increasing, with an estimated 28.4 million new cases in 2040 based on the rate of increase over the past quarter century (Sung et al., 2021). Furthermore, in 2023, the American Cancer Society projected there would be just under two million new cancer diagnoses in the United States alone (Siegel et al., 2023). With a cancer diagnosis comes many different forms of medical treatments, including but not limited to biopsies, insertion of multiple intravenous lines, invasive procedures, and treatments such as chemotherapy, radiation, and surgery. Due to these treatments, as well as the cancer disease process itself, pain is one of the most reported symptoms associated with cancer, with 20-50% of adult patients with cancer reporting pain (2025). Furthermore, 44.5% of patients report moderate to severe pain that can last up to three months after their last treatment (Snijders et al., 2023). This highly prevalent, long-lasting pain can have a detrimental effect on these patients' quality of life (2025). Even with this high reported prevalence, it is important to note that patients with cancer oftentimes downplay their pain and are reluctant to report information about their pain to their providers (Cluxton, 2019). Given this data, the prevalence, frequency, and severity of pain experienced by patients with cancer warrants further attention.

A common way to manage and treat this pain is pharmacological treatment, typically opioids such as morphine (Makhlouf et al., 2020). While this achieves pain reduction in many patients, there is a lot of resistance and poor compliance with patients to this modality due to fear of drug addiction, poor medication tolerance, and the oftentimes harsh side effects of commonly

used opioids; and providers can have resistance due to fear of over-prescribing strong medications (Makhlouf et al., 2020). Additionally, pharmacological pain management does not always result in full pain reduction, with over 50% of patients with cancer worldwide reporting inadequate pain relief (Thota et al., 2011). With poor compliance for pharmacological pain treatment and inadequate pain management, it is pertinent to look into other pain management therapies and techniques that may benefit patients in addition to pharmacological therapies. In doing so, it may be possible to achieve the best method of pain reduction, whether through strictly pharmacological, or a combination of nonpharmacological with pharmacological to improve outcomes.

Nonpharmacological pain reduction strategies are necessary to treat cancer pain, and acupuncture, yoga, massage therapy, aromatherapy, and guided imagery are all successful strategies for helping achieve pain reduction (Singh & Chaturvedi, 2015). Music, on the other hand, is typically used as a psychological relief tool to help with symptoms such as anxiety and depression (J.-M. Zhang et al., 2012). While studies have focused on the relationship between music and mental health, this systematic review aims to synthesize research evidence on the effect of music as a nonpharmacological treatment option for pain, specifically in adult patients with cancer. Though research is progressing, it is unclear whether music can reduce the pain related to a cancer diagnosis and treatment, therefore improving quality of life for patients with cancer.

Significance

As briefly mentioned above, pain is a very common symptom associated with cancer. Almost two million people were diagnosed with cancer just last year in the United States, and almost 50% of these patients experience moderate to severe pain related to the disease process and treatment (Siegel et al., 2023; Snijders et al., 2023). With the high prevalence of cancer

diagnoses, and the frequent reporting of pain, it is important to understand the significance of this pain and its impact on patients.

Living in constant pain often negatively impacts mental health, leading to anxiety or depression (Ozkan, 2010). Pain can also be isolating, causing a person to be stressed or angry. Cancer related pain is typically related to higher levels of psychological distress, and patients experiencing this pain are more prone to emotionality (Ozkan, 2010; Stiefel, 1993). A study conducted by Glover and colleagues compared mood states of patients with cancer that were experiencing pain and patients with cancer that were not experiencing pain (1995). Patients experiencing cancer related pain reported significantly higher levels of anxiety, depression, and anger (Glover et al., 1995). Similarly, a study conducted by Ahles and colleagues found significantly more depressive symptoms in patients with cancer related pain (Ahles et al., 1983). Living with heightened depression, anxiety, and anger places more strain on patients with cancer bodies and minds, leading to a further diminished quality of life.

Pain has detrimental effects on physical health as well. Cancer related pain is often chronic and can last for three months or longer. This pain interferes significantly with daily activities, and reduces how active patients with cancer can be (Dorrepaal et al., 1989). This type of pain is also associated with poor cardiovascular function leading to hypertension, reduced sleep quality, and impaired sexual function (Fine, 2011). All these comorbidities place stress on patients' long term health outcomes and quality of life (Fine, 2011). Patients also miss out on social relationships and interactions due to consequences of poor physical health, lack of sleep, or mental health (Calati et al., 2015). When a person misses out on social opportunities because of physical pain, this can cause them to feel resentment towards their own bodies, leading to further negative mental health conditions (Calati et al., 2015).

This impact extends to the families and friends of the patients experiencing cancer related pain. As care shifts from the hospital to the home, these people become informal caregivers for the patients, taking on sudden and oftentimes complex caregiving responsibilities (Yuen & Wilson, 2021). This need for care can disrupt family balance and cause role changes that come with unpredictable consequences (Karimi Moghaddam et al., 2023). Though a caregiving relationship can be positive, providing care for a patient with cancer is also burdensome both mentally, physically, and financially (Yuen & Wilson, 2021). Informal caregivers are at risk for a decreased quality of life due to the stress and demands adding up over time (Mishra et al., 2021). Anxiety, depression, and stress are all common in this population, as it can be difficult to take care of themselves and manage their own mental health while caregiving for a patient with cancer. Worrying about the patient, spending time running errands for medications and hospitalizations, and balancing work and social life outside of caregiving places disrupts daily routines and leads to negative mental and physical health (Karimi Moghaddam et al., 2023).

With this big issue of mistreated pain and its effects on the patient and their family members or caregivers, it is pertinent to examine how it is currently managed. Pain management for cancer is most commonly opioids. Opioids are a mix of synthetic and natural drugs that are used both legally, through prescriptions for pain, and illegally, such as street drugs like heroin (2024b). Due to the misuse of prescribed opioids, and the rampant illegal use of opioids, America has been facing an opioid crisis since 2013, and since 2017 it has been declared as a national public emergency (Salmond & Allread, 2019). The drugs abused are most commonly oxycodone, hydrocodone, and morphine (Stoicea et al., 2019). Opioids are very addictive due to their no ceiling effect, and patients with cancer that are prescribed opioids for pain are at a higher risk for nonmedical opioid use (NMOU) due to getting addicted while using the drugs for pain

management (Dalal & Bruera, 2019). In addition, this population is also more at risk for developing opioid use disorder (OUD) during or after their cancer treatment (Ganguly et al., 2022). A study by Liu and colleagues showed that in a large study with over 3.39 million adult patients diagnosed with cancer, nearly 25% showed evidence of recreational misuse of their prescription (2013). Recreational misuse of these opioid prescriptions is an indication of drug tolerance and addiction, and puts this population more at risk for opioid associated hospitalizations, and deaths (Liu et al., 2013). It creates a surplus of patients in hospitals that are not equipped financially or with the right resources to treat them. High costs for opioid pain management and high influxes of opioid associated hospitalizations lead to depletion of resources and strain on hospitals. Mitigating the opioid crisis may help the number of opioid related hospital visits and help reduce overdoses (Ganguly et al., 2022). This is where nonpharmacological strategies, like music, can come into play. With there being over 50% of patients with cancer worldwide reporting inadequate pain relief, patients may turn to abusing the opioid prescription in a desperate attempt to soothe their pain (Thota et al., 2011).

Opioids can also be very stressful and physically harmful to patients with cancer when used as pain management. Side effects such as constipation, nausea, vomiting, dizziness, and respiratory depression have made it difficult to justify long term use of opioids to manage cancer related pain (Benyamin et al., 2008). Due to the already harmful side effects patients face from cancer treatment, side effects of opioids are not typically tolerated well in this population.

Cancer related pain is also financially draining for patients (Malhotra et al., 2020). Some pain-related costs for patients with cancer include expenditures that are incurred from the direct treatment of pain, analgesic medications, medical procedures and technology, hospitalizations related to pain, use of emergency department services and ambulances, and physician office

visits for pain (Fortner et al., 2003). Patients with advanced cancer pain are likely to have prescribed opioids to help manage the pain and a lot of insurances do not cover them due to the opioid crisis mentioned above (Langa et al., 2004). In 2003, common costs of opioids were reported as follows: fentanyl was $204 per month, intravenous morphine cost $381 per month, and hydromorphone was $726 per month (Fortner et al., 2003). Overall, this study reported that patients with cancer reported an average spending of $10,000 per year for total pain-related costs (Fortner et al., 2003).

Cancer related pain additionally makes it difficult for patients to work due to their physical pain and oftentimes poor mental health (Halpern et al., 2022). Patients with cancer experiencing moderate to severe pain often move to working part time hours, do not pursue promotions, retire earlier than planned, or stay at a nonpreferred job in fear of losing health insurance (Halpern et al., 2022). In the study conducted by Halpern and colleagues, it was reported that the odds of adverse employment outcomes were much greater among patients with cancer experiencing severe pain (2022). The additional costs that cancer related pain inflicts upon patients with cancer and their families, coupled with the difficulty of adverse employment outcomes, the financial burden of cancer related pain proves to be an issue requiring attention.

This financial stress extends to healthcare systems as well (Chandler & Payne, 1998). A study conducted by Chandler and Payne found that hospitals spend an average of five million dollars annually for pain management in patients with cancer due to long hospital stays and frequent hospitalizations (Chandler & Payne, 1998). This financial burden is shared by a big portion of society through taxes, however patients with cancer and their families take on a portion of this cost through insurance plans, deductibles, co-payments, and other services not covered by third parties (Fortner et al., 2003).

Given the substantial impact of cancer-related pain on patients, families, and caregivers, including physical and mental health, social connection, and financial burden, research on cancer pain management must be understood better. The current pharmacological treatment does not achieve adequate pain reduction and therefore the issue of cancer related pain continues to burden this population of adult patients and the healthcare system. If complementary or alternative pain management can be coupled with pharmacological pain management, there is a possibility for greater pain reduction and an increase in quality of life in this population.

While some nonpharmacological therapies have already been added to pain management care plans such as aromatherapy, massage, and acupuncture; there is still further need for greater pain reduction in this population of adult patients with cancer. Music has the potential to be used as an adjunctive therapy to pharmacological pain management, similarly to other nonpharmacological methods. This review will aim to gather the existing research and reach a conclusion on its effectiveness.

Study Purpose

The purpose of this systematic review is to synthesize the existing randomized controlled trials on the effect of music on cancer related pain in adult patients with cancer. Randomized controlled trials were exclusively included in this review because the process of this research is rigorous in its efforts to minimize bias, examine cause and effect relationships, and are considered the gold standard for effective research. By compiling the existing research, the aim is to provide directions for possible clinical implications and to recommend future research directions. In reviewing the evidence, it may be possible to advocate for the addition of a more holistic approach to pain management with a combination of nonpharmacological and pharmacological strategies to achieve greater pain reduction in adult cancer patients, thereby reducing the side effects and compliance issue of pharmacological pain management, achieving

greater pain reduction in this population, and promoting quality of life for adults as they live through a cancer diagnosis and treatment.

Chapter 2: Literature Review

This chapter discusses the existing research evidence on cancer, cancer treatments, cancer-related pain, and the consequences of cancer-related pain on patients, families, caregivers, and the healthcare system. This information will provide insights into the need for pain management within this population. This chapter also explores the current pain management techniques used for various cancers and determines barriers to these implementations and treatment success. In conclusion, the importance of understanding and furthering pain management in the field of oncology will be addressed and summarized.

Cancer

In 2020, there were roughly 19.3 million new cancer cases globally, with approximately 10 million cancer deaths (Sung et al., 2021). The ten most prevalent cancers are female breast cancer, lung cancer, prostate cancer, nonmelanoma skin cancer, colon cancer, stomach cancer, liver cancer, rectum cancer, cervix cancer, and esophagus cancer (Sung et al., 2021). Currently for men, lung cancer is the leading cause of cancer death, followed by liver and colorectal; while for women, breast cancer is the leading cause of cancer death, followed by lung, colorectal, and cervical cancers (American Cancer Society, 2024).

The term “cancer” refers to the disease resulting from the abnormal and rapid division of cells that spreads to and invades other local tissues (World Health Organization, 2018). Oncology is the branch of medicine focusing on the diagnosis and treatment of cancer (National Cancer Institute, 2011). Cancer cells can spread to other parts of the body through either blood or lymph, resulting in damage to important body systems and causing a variety of symptoms such as

unexplained fluctuations in weight, weakness, malaise (general weakness), fatigue, and pain in affected body parts. Over 100 different types of cancer have been diagnosed, and cancer types are specified and named based on what part of the body the cells originate in (World Health Organization, 2018).

The abnormal growth of cells that occurs results in tumors, or clusters of cancerous cells in the body (World Health Organization, 2018). These tumors can either be metastatic or nonmetastatic, meaning they can rapidly grow and spread throughout the body, or they just stay in one place (Ganesh & Massagué, 2021). Metastatic cancer has a much higher mortality rate and can be much more difficult to treat, oftentimes requiring more intensive and invasive treatments (Ganesh & Massagué, 2021).

Common Cancer Treatments

The most common cancer treatments include surgery, radiation therapy, and chemotherapy (American Cancer Society, n.d.). Surgery is often used for the nonmetastatic cancer discussed above. If the tumor is localized to one part of the body, surgery will be used to cut out the cancerous tumor, ideally removing all the cancer completely. However, commonly surgery is unable to remove every cancerous cell, and a patient is likely to receive radiation therapy or chemotherapy before or after surgery to shrink the tumor prior to surgery, or to remove any remaining cancerous growth in the body after surgery (American Cancer Society, n.d.)

Radiation therapy is another local cancer treatment, as it targets a specific site to destroy cancerous cells. This therapy uses high energy particles to make small breaks in the DNA of cancer cells, destroying them and causing them to divide much slower (American Cancer Society, n.d.).

Chemotherapy is a systemic cancer treatment, meaning it travels all throughout the body to work. These drugs are most often given by mouth or through an intravenous line. Chemotherapy work by targeting different parts of the cell cycle to stop growth and maturation of cells or destroy them all together (American Cancer Society, 2024). The rapid growth of cancer cells give chemotherapy more time to target and attack them since there are more frequent cell cycles to detect and identify (American Cancer Society, n.d.).

While these treatments have success in managing and treating cancer, there are often very dangerous side effects associated with each. Some of the most common side effects of surgery are bleeding, blood clots, damage to nearby tissues, pain, and infections (American Cancer Society, n.d.). All these side effects can cause very serious and potentially life-threatening complications for a post-operative patient. Radiation therapy has harmful side effects as well. This therapy can affect nearby healthy cells when targeting the growth of cancer cells. A very common side effect is also fatigue and local skin reactions such as redness, itchiness, or swelling (National Cancer Institute, 2022). Chemotherapy is also notable for its side effects. Since it works systemically, it has a wide range of side effects in the body. Nausea and vomiting are among the most frequently reported symptoms, along with fatigue, decreased appetite, hair loss, dry mouth, and constipation (Altun & Sonkaya, 2018). All together these side effects and complications put patients' bodies under a lot of stress and pain, often leading to a diminished quality of life while receiving this life saving treatment.

Cancer Related Pain

Pain is one of the most commonly reported symptoms among patients diagnosed with cancer, with 44.5% of patients reporting pain during the disease process and treatment (Snijders et al., 2023). Cancer pain is related both to the disease process and treatment (Russo & Sundaramurthi, 2019). In terms of disease process, the most painful cancers are bone, pancreas,

head, and neck (Seladi-Schulman, 2021). It can be classified as nociceptive or neuropathic pain (Caraceni & Shkodra, 2019). Nociceptive pain arises from damage to tissues, while neuropathic pain arises from damage to sensory nerves (Armstrong & Herr, 2025).

Nociceptive pain is further broken down into somatic versus visceral pain. Somatic cancer pain results from the spread of malignant, or cancerous, cells into tissue, skin, and bones, while visceral pain results from organ damage such as distention or inflammation (Russo & Sundaramurthi, 2019). In cancer diagnoses, somatic pain can be caused by superficial injury related to cancer treatment such as incisional pain or deep pain such as bone marrow infiltration by cancer cells (Caraceni & Shkodra, 2019). Visceral pain in cancer diagnoses include pleuritic chest pain, which is chest pain caused by pleural effusion, or excess fluid in the lungs, secondary to cancer cell infiltration in the lungs (Russo & Sundaramurthi, 2019).

Neuropathic pain results from dysfunction of the somatosensory nervous system (Russo & Sundaramurthi, 2019). Cancer typically leads to nerve damage, which can cause patients to have either hypersensitive or hyposensitive pain symptoms (Yoon & Oh, 2018). Hypersensitive symptoms include tingling, burning, or an electrical sensation, while hyposensitive symptoms include numbness and muscle weakness. Neuropathic pain also tends to last much longer than nociceptive pain, with recovery times lasting up to years after recovery from injury (Yoon & Oh, 2018). An example of neuropathic pain in a cancer diagnosis would be a tumor pressing on a nerve, causing damage to its pathways (Caraceni & Shkodra, 2019). When a nerve is damaged as such, pain fibers become abnormally sensitive, leading to the lengthy recovery often lasting long after the injury or disease has been resolved (Yoon & Oh, 2018).

Impact of Pain

The impact of cancer related pain stretches across a broad population in various aspects. It interrupts meaningful social interactions, negatively impacts patients mental health, and

financially challenges patients, their families, and the healthcare system (Halpern et al., 2022; Ozkan, 2010; Stiefel, 1993). Chronic pain is also associated with comorbidities that impair physical function and further deteriorates independence and quality of life in this population (Fine, 2011).

Patients with cancer spend a lot of the time in the hospital, leading to social isolation and feelings of loneliness. Experiencing pain on top of this can even further disrupt social behaviors and relationships, with pain often interrupting rare social outings due to discomfort, or cutting meaningful conversations short due to a lack of focus (Stiefel, 1993). Missing out on social activities and conversations leads to further feelings of isolation and distress for these patients and can be harmful to their social development (Stiefel, 1993).

Cancer pain is also often related to increased levels of psychological distress, including higher prevalence of depression, anxiety, and fear (Ozkan, 2010). A study conducted Stiefel found that people in pain were more likely to be overly emotional, while another study conducted in 1987 found that 58% of their participants reported pain having an significant influence over emotions (Stiefel, 1993). Another study conducted in 1995 found that patients with cancer pain expressed much higher levels of worry, fear of the future, and anxiety over the pain progressing (Glover et al., 1995). Patients with cancer experience these highly emotional states that can overwhelm their bodies and lead to difficulties with poor mental health and unnecessary stress (Glover et al., 1995). Patients with cancer spend considerable time in hospital, leading to social isolation and feelings of loneliness. Missing out on social activities and conversations leads to further feelings of isolation and distress for these patients and can be harmful to their social development (Stiefel, 1993).

Patient's cancer related pain can also extend into their financial wellbeing, with some literature examining the correlation between pain and working reduced hours or being unemployed entirely (Halpern et al., 2022). Pain can discourage patients with cancer from going out and finding a job, working full time hours, and can place limits on which jobs they are able to participate in. Additionally, patients experiencing cancer pain are more likely to retire early, causing them to lose money they could have earned, as well as a loss of purpose without something to do each day (Halpern et al., 2022). Pain is also a primary reason for patients with cancer to require palliative care, with 34% of adults receiving palliative care being patients with cancer, and the cost of palliative care can be expensive (World Health Organization, 2020). In 2019 it was reported that funding for palliative care was available in 68% countries worldwide, however only 40% of these countries reported that the services that were funded reached at least half of the patients in need (World Health Organization, 2020). With the financial burden of cancer treatments and hospitalizations, palliative care is yet another expense that patients with cancer and their families must support during a stressful time of their lives. Overall, cancer related pain causes psychological distress, interrupts meaningful social interactions, and financially burdens patients and their families.

Manifestation of Pain in Patients with Cancer

There are many ways that cancer pain presents and manifests. Cancer pain is not limited to but can include postoperative pain, peripheral neuropathy, bone pain, joint pain, avascular necrosis, mucositis, and osteonecrosis (2025). Sensations of this pain can manifest as stabbing, stinging, pain spasms, itching, burning, throbbing, or a constant dull aching (2025). This pain can lead to anxiety and distress, low energy or severe fatigue, increased desire to die, and overall poorer quality of life (Syrjala et al., 2014). Cancer pain can also affect a patient's body and biology. Cancer pain is associated with elevated levels of inflammatory cytokines such as TNF

alpha and interleukin one (Dunlop & Campbell, 2000). Cytokines work in the body to produce an innate immune response, which in turn inflames the part of the body under stress to send healing cells to it. However, in cancer patients, these cytokines are dysregulated, causing inflammation throughout the body and resulting in severe pain (Ott et al., 2007). It is important to also recognize secondary manifestations of pain such as mental illness and fatigue to fully assess a patient's pain level and achieve maximum reduction.

Pharmacological Pain Management in Patients with Cancer

The mainstay in oncologic pain management is opioids (Mestdagh et al., 2023). Opioids with weaker potency, such as codeine and tramadol are used to initiate pain relief, while opioids with stronger potency, such as morphine and oxycodone are used for moderate to severe pain (Mestdagh et al., 2023). While there is research evidence that supports opioids' effectiveness at reducing pain, there is a lot of resistance to the use of opioids for chronic pain management in patients with cancer. Patients often dislike opioids for pain management due to fear of drug addiction, medication tolerance, and the common side effects of these drugs, and over 50% of patients do not report adequate pain relief from pharmacological therapies (Makhlouf et al., 2020; Thota et al., 2011).

Common side effects of opioids include sedation, dizziness, nausea, vomiting, and constipation (Benyamin et al., 2008). More serious side effects include respiratory depression, physical dependence, and addiction (Benyamin et al., 2008). Along with this, a study conducted in 2016 found that from 2006 to 2016 the number of opioid-associated deaths in patients with cancer slightly increased, while the number of opioid-associated hospitalizations for patients with cancer was on a steady rise (Chino et al., 2020). These side effects often discourage patients from keeping to the medication regimen, or refusing to take opioids at all, leading to ineffective pain management (Makhlouf et al., 2020).

There is also research evidence that pharmacological pain management does not achieve adequate pain relief in this population, with 50% of patients reporting that this type of pain management does not achieve adequate pain relief (Thota et al., 2011). A portion of patients with cancer that misuse or overuse opioids do so accidentally, when trying to achieve high pain relief through taking more medication than prescribed (Ganguly et al., 2022). Since cancer pain is very multidimensional and causes a variety of different types of pain, pain management must be flexible and dynamic to meet adequate pain relief (Mestdagh et al., 2023). Opioids do not currently do this and thus this is a topic of research that must be studied.

Nonpharmacological Pain Management in Patients with Cancer

Nonpharmacological cancer pain management includes but is not limited to physical therapy, massage, heat or ice, transcutaneous electrical nerve stimulation (TENS), aromatherapy, and muscle relaxation (Hökkä et al., 2014; Ruano et al., 2022).

Physical modalities include physical therapy, heat or ice, massage, and TENS. Physical therapy is very beneficial for maintaining some muscle strength while treatments decondition patients. This can include range of motion exercises, as well as working on strength and endurance. Having this control over their bodies can help patients feel stronger and more independent, leading to less pain with movement (Menefee & Monti, 2005). Heat and ice has been found to be an effective tool, however heat can sometimes be dangerous for patients with cancer due to different types of cancer sometimes inhibiting a patient's sensory perception of heat, leading to accidentally burning their skin and harming themselves (Menefee & Monti, 2005). A systematic review done in 2023 found that massage therapy was most effective in achieving pain reduction when administered for 10-30 minutes once a week (Y. Zhang et al., 2023). Lastly, TENS has inconclusive results on its effect on pain, mostly due to a lack of

research. TENS includes placing electrodes over painful areas and then those electrodes use low-voltage electrical currents to stimulate nerves and block pain signals (Hurlow et al., 2012).

Nonphysical modalities include aromatherapy and muscle relaxation. Aromatherapy is the therapeutic use of essential oils absorbed through the skin or through inhalation and is becoming increasingly popular for pain relief in adult patients with cancer. It mostly provides short term relief to patients and is often used during procedures and needle sticks (Lakhan et al., 2016). Muscle relaxation is a mindfulness exercise that involves progressive contraction and relaxation of a person's muscles as they are directed through the process through a recorded tape or a live session. It is considered a nonphysical modality as it focuses on the connection between your mind and body, and has been found to be effective reducing longer term pain in adult patients with cancer (Tan et al., 2022).

Music Interventions

In this review, three different music interventions are examined: music therapy, active music, and passive music. Music therapy is defined as the evidence-based use of the interaction between music and therapy, and is administrated by a licensed musical therapist (American Music Therapy Association, n.d.). It is often used to relieve stress, reduce anxiety, promote wellness, increase communication, and encourage physical rehabilitation (American Music Therapy Association, n.d.). Music therapy can include but it not limited to, listening to music, analyzing it, participating in playing the music, talking about it, and creating physical art alongside music (American Music Therapy Association, n.d.). Music therapy has been used in patients with dementia, traumatic brain injuries, substance use disorders, autism spectrum disorder, anxiety, developmental disabilities, and more (Cleveland Clinic, 2023).

Active music intervention is defined as listening to the music as the singular task at hand (CAMMAC, n.d.) The full concentration of the participants in these intervention is on listening

to and focusing on the music. This could be listening to music through headphones, watching a live concert, or playing the radio. In passive music intervention, the music is more of a background stimulation for the participants, with other things going on in the room (CAMMAC, n.d.). The patient could be getting ready for the day with music on or could be sleeping with music on in the background as white noise.

Impact of Music Interventions on Health Outcomes in Patients with Cancer

Music has frequently been used as an intervention for patients with cancer for a multitude of reasons. Most commonly these interventions are put in place to help with psychological symptoms associated with cancer, like stress and distress, and oftentimes music is used in palliative cancer care (Archie et al., 2013; Bradt et al., 2021; Santos et al., 2021). There is a lot of literature that discusses the impact of music on mental health of patients with cancer. A study done in 2021 concluded that music was significantly effective at reducing psychological stress and distress of patients with cancer (Santos et al., 2021). There is also ample evidence that supports the use of music to reduce anxiety and depression in patients with cancer, as well as increase reports of hope and more positive mood (Bradt et al., 2021).

Summary of Music to Treat Cancer Related Pain

Cancer is a highly prevalent health issue and remains one of the top leading causes of death each year, so it is important to investigate how health outcomes can be improved for this vulnerable population. Pain is one of the most commonly reported symptoms by patients with cancer so it is pertinent to examine this outcome and find ways to improve it (Snijders et al., 2023). This review aims to synthesize the existing literature on music's effect on cancer related pain to determine whether or not it is a useful pain management tool that can be successfully

implemented in oncology care. the effect music can have on cancer related pain. The findings could shed light on the impact music can have to guide clinical practice and future research.

Table 1: Definitions Specific to this Review

TERM	DEFINITION
Music Therapy	Interactive form of music exposure administered by a licensed musical therapist (American Music Therapy Association, n.d.)
Active Music	Music intervention where the sole focus is listening to music given to the patient (CAMMAC, n.d.)
Passive Music	Background music, or music intervention given to patients as an option; not the sole task assigned to patients (CAMMAC, n.d.)
Pain (as defined in this review)	Unpleasant physical feeling related to cancer disease process or treatment, causing distress to the patient

Chapter 3: Methods

This chapter goes over the key terms used, inclusion and exclusion criteria, and gives an overview of the quality appraisal tool that was used for each article (results of this quality appraisal will be found in Chapter 4).

Literature Search Process

The search was conducted on March 5, 2025. The databases used for this search were PubMed and CINAHL. The key word search terms were "cancer OR oncology," "music," and "pain OR cancer related pain." The investigator worked with a research librarian to comprise these terms and include any relevant, similar terms. Mesh terms were also used for words that had common definitions, "pain," "cancer pain," and "music" were all used as mesh terms. Keywords were then combined, with the final search being ((cancer OR oncology) AND ((music) OR ("music"[Mesh])) AND ((pain) OR (("pain"[Mesh]) OR "cancer pain"[Mesh])). Before inclusion and exclusion criteria were applied, filter tools provided by the databases were used to set the limits of being published in 2000 to March 2025, adults as the population, and in the English language. PubMed additionally has a filter that can strictly produce randomized controlled trials, so this was used as well, however CINAHL does not include this filter, so the investigator screened titles and abstracts for randomized controlled trials when reviewing the articles from CINAHL. Once articles were identified using these limits, inclusion and exclusion criteria were applied to determine the final set of articles, as described below.

Inclusion and Exclusion Criteria

Inclusion criteria included original interventional research studies published between 2000 to March of 2025, written in English language. This includes the most up to date research in a field that has changed greatly over the last fifty years. Limiting the search to articles published in or after 2000 ensured relevancy of research. Other criteria were that the studies

focused on patients aged 18 years or older diagnosed with any type of cancer. The pain included in this review broadly included any types of pain related to a patient's cancer experience, including but not limited to cancer-related pain and treatment or procedure-related pain. Procedure related pain in this review is defined as pain related to treatment procedures such as mastectomy or chemotherapy. The only pain excluded was pain related to diagnostic cancer procedures to ensure the pain studied was specifically related to a confirmed cancer diagnosis. This includes pain related to biopsies. For research that tested multiple interventions with multiple components, the study must have reported the effect of music alone on pain to be selected. For example, a study that examined both aromatherapy and music therapy must include a music only group in the experiment (Deng et al., 2022). The music intervention could be active or passive music activities, as well as music therapy administered by a music therapist. This review aims to study the effect of music on pain in adult patients with cancer, so all types of music interventions were included. Exclusion criteria were: 1) literature review articles, 2) studies that tested an intervention with multiple components without results on music alone, 3) studies that included patients under the age of 18, 4) studies that investigated pain related to diagnostic procedures, 5) studies that involved palliative care, as this is seen as a separate subset from cancer pain and 6) studies that mentioned COVID-19, as the pandemic could unintentionally produce different results than experiments carried out before or after. These criteria helped guide the search to focus on music's effect on cancer related pain in adult patients with cancer.

Article Selection Process

The article selection process included five steps. First, an initial search using the keywords and mesh terms listed above was conducted in both PubMed and CINAHL. Second, the investigator applied filters on both databases to further screen the results, including the

English language, adult population, and randomized controlled trials (on PubMed only, CINAHL's results were run through by the investigator to determine randomized controlled trials). Third, a screening of the titles and abstracts was then completed and articles that matched the exclusion criteria of diagnostic pain, patients under 18 years old, no separate music intervention, palliative care, and mention of COVID-19. Fourth, duplicates between the two databases were removed. Fifth, the articles went through a full text reading and the investigator eliminated additional articles that did not meet the inclusion and exclusion criteria, including using combination therapies (no stand-alone music intervention), studies with patients younger than 18 years old in their "adult population," studies that involved the COVID-19 pandemic in their results, and studies that involved palliative care. The full breakdown of these criterium can be seen in the PRISMA diagram located on page 24 (Figure 1).

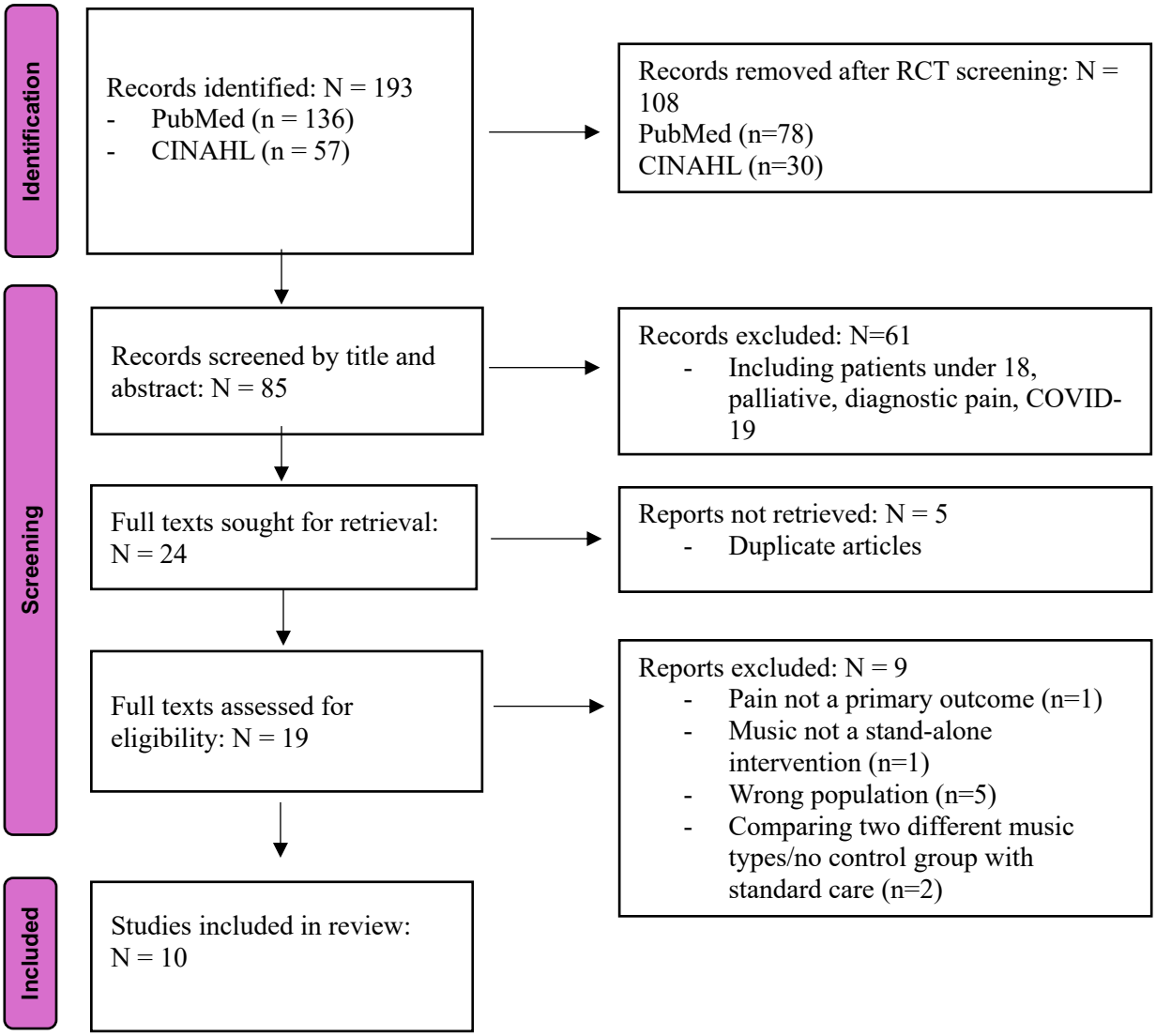
Data Extraction Process

The investigator extracted the study design, sample and setting, intervention and control group information, outcome measures, and results on all studied outcomes across the selected articles. Across all the articles, pain was the primary outcome in this review but results on other parameters were also recorded. These were depression, hope, anxiety, stress, sleep quality, inflammatory cytokines, nausea, narcotic pain medication use, mood level, physiological measures (blood pressure, pulse rate, glycemia, oxygen saturation), fatigue, energy, and cortisol levels. These secondary outcomes were included in this review to accurately depict the results the original researchers were hoping to display in the selected articles. Additionally, as mentioned in Chapter 2 of this review, these secondary outcomes can be indicative of pain or can be a direct result of pain, so it is important to fully synthesize the results for any confounding or contributing factors to pain. Synthesizing all the outcomes together helps to better describe the results on pain.

Quality Appraisal

The Johns Hopkins Nursing Evidence-Based Practice Model for Nursing and Healthcare Professionals (Appendix A) was used to critically appraise each study (Dang & Dearholt, 2012). This tool rates both the level of evidence and the quality of each article. Levels of evidence are ranked from level I to level V, with level I being the highest and level V being the lowest. Level I includes experimental studies like randomized controlled trials, exploratory mixed methods designs, and systematic reviews of randomized controlled trials, with or without meta-analysis. Level II includes quasi-experimental studies and systematic reviews of a combination of RCTs and quasi-experimental studies, or quasi-experimental studies only, with or without meta-analysis. Level III includes nonexperimental studies, systematic reviews of a combination of RCTs, quasi-experimental studies, and nonexperimental studies, or nonexperimental studies only, with or without meta-analysis; exploratory, convergent, or multiphasic mixed methods studies; qualitative studies, and systematic reviews of qualitative studies with or without meta-analysis. Level IV includes clinical practice guidelines and consensus panels or position statements. Level V includes scoping reviews, integrative reviews, literature reviews, quality improvement programs, financial evaluations, case reports, and opinions of nationally recognized experts based on experiential evidence (Dang & Dearholt, 2012). Since all articles examined in this review are randomized controlled trials, all of them are Level I according to this appraisal tool. Quality of articles were rated as grades A to C, with grade A being high quality, and grade C being low quality (Dang & Dearholt, 2012). Criteria used to determine quality grade included generalizability of results, sufficiency of sample sizes, definitive conclusions, and consistency of recommendations based on literature review. Each article was screened and deliberated thoroughly before being appraised using this model to determine the strength of each study. A picture of this quality appraisal tool is located in Appendix A on page 68.

Figure 1: Article Selection Process



Chapter 4: Results

Article Selection

As a systematic review, this paper utilized the PRISMA guidelines (Figure 1 on page 23) to guide the process. A breakdown of the article selection process can be seen on the PRISMA diagram found on page 24. This diagram helped guide the investigator in the search. First, a total of 193 articles were identified in the original search on PubMed and CINAHL. These results included the filters of published in year 2000 and after, in the English language, and including an adult population. Second, the randomized controlled trial filter was applied to PubMed, eliminating 78 articles, and the investigator then removed 30 non-randomized controlled trials from CINAHL's results. This left the investigator with 85 randomized controlled trials to screen by title and abstract. Third, the 85 remaining articles were screened by title and abstract, and 60 articles were removed due to including palliative, diagnostic pain, COVID-19, pediatric population, or not being related to the field of oncology. Fourth, the investigator screened the remaining 24 articles for duplicates and removed 5 duplicate articles. 19 full text articles were then all retrieved, and 9 were removed after further assessment of eligibility using the exclusion criteria. The 9 articles that were removed, matched the exclusion criteria of using combination therapies (no stand-alone music intervention), studies with patients younger than 18 years old in their "adult population," studies that involved the COVID-19 pandemic in their results, and studies that involved palliative care. Two studies also were removed as they studied the difference between two different music interventions with no standard care control group, making it too specific for the purpose of this review, one study was removed due to not specifying the age requirement of their study, and one study was removed due to not having a separate control group in their experiment.

Ten articles ultimately met eligibility criteria (Arruda et al., 2016; Bates et al., 2017; Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Li et al., 2011; Miladinia et al., 2021; Reimnitz & Silverman, 2020; Tang et al., 2021; Tollabzadeh et al., 2023). Details of these ten studies are included in a matrix table in Table 2 located on page 55 (Table 2).

Quality Appraisal Results

As mentioned in Chapter 3, the Johns Hopkins Nursing Evidence-Based Practice Evidence Level and Quality Guide tool was used to determine evidence level and quality of all ten articles. Based on this tool, every article was a level 1, as level 1 articles include randomized controlled trials (Dang & Dearholt, 2012). The grading of the quality of these articles produced varying results, with all ten falling under grade A of high quality or grade B of good quality. These grades were determined based on sample sizes, generalizability of results, consistency of recommendations, and adequacy on control groups. With this criteria, three articles were given grade A, high quality (Arruda et al., 2016; Burrai et al., 2014; Huang et al., 2010, 2010), and seven articles were rated grade B, good quality (Bates et al., 2017; Deng et al., 2022; Li et al., 2011; Miladinia et al., 2021; Reimnitz & Silverman, 2020; Tang et al., 2021; Tollabzadeh et al., 2023). The high-quality articles included a sufficient sample, results that could be generalized to other patients with cancer and had control groups with no other interventions. They also included recommendations that were consistent with the literature reviewed. Six of the good quality articles were ranked the way they were due to ungeneralizable results due to specificity of the sample. This included Bates and colleagues only including multiple myeloma and lymphoma patients undergoing an autologous stem cell transplant (2017), two studies only including women with breast cancer (Deng et al., 2021; Li et al., 2011), Miladinia and colleagues only including leukemia patients (2021), Reimnitz and Silverman only including patients who recently underwent a bone marrow transplant (2020), and Tang and colleagues only including patients

diagnosed with small cell lung cancer undergoing their first dose of platinum-based chemotherapy (2021). All these specificities in the samples makes it difficult to generalize the results to the broader population of adult patients with cancer. The last good quality article was rated grade B due to inadequacy of the control group, as the control group was offered counseling sessions while the intervention group received their music therapy (Tollabzadeh et al., 2023). These counseling sessions could have affected pain scores in the control group. A table of these results can additionally be found in Table 3, located on page 72.

The quality appraisal of the ten articles will be taken into consideration in the Chapter 5 discussion of this review, as different ratings of quality level and grade can impact how generalizable the study results are to the larger population of adult patients with cancer.

Study Characteristics

Study Design

The publication dates range from 2010 to 2023 (Arruda et al., 2016; Bates et al., 2017; Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Li et al., 2011; Miladinia et al., 2021; Reimnitz & Silverman, 2020; Tang et al., 2021; Tollabzadeh et al., 2023). All ten are randomized controlled trials.

Study Sample and Setting

Sample sizes ranged from 35 (Reimnitz & Silverman, 2020) to 160 (Deng et al., 2022), with all samples including the ages 18 and older. Two studies specifically included only women in their sample (Deng et al., 2022; Li et al., 2011), while the rest included both males and females. Two samples studied breast cancer (Deng et al., 2022; Li et al., 2011), one studied small cell lung cancer (Tang et al., 2021), one studied acute leukemia (Miladinia et al., 2021), and one studied multiple myeloma and lymphoma (Bates et al., 2017), while the rest did not focus on a specific type of cancer diagnosis.

Settings included a medical center (Huang et al., 2010), a bone marrow transplant unit of a teaching hospital (Reimnitz & Silverman, 2020), a surgical department in an oncology center (Li et al., 2011), a teaching hospital (Deng et al., 2022), an oncology clinic (Tollabzadeh et al., 2023), a reference hospital (Arruda et al., 2016), a Thoracic Chemotherapy Department (Tang et al., 2021), a medical oncology ward (Burrai et al., 2014), a referral oncology hospital (Miladinia et al., 2021), and one did not specify the clinical setting (Bates et al., 2017). Three took place in China (Deng et al., 2022; Li et al., 2011; Tang et al., 2021), two in Iran (Miladinia et al., 2021; Tollabzadeh et al., 2023), two in the United States (Bates et al., 2017; Reimnitz & Silverman, 2020), one in Taiwan (Huang et al., 2010), one in Brazil (Arruda et al., 2016), and one in Italy (Burrai et al., 2014).

Study Intervention

The three music interventions investigated in this review were active music, passive music, and music therapy. Since the American Music Therapy Association defines music therapy as being performed by a licensed musical therapist, in this review, music therapy was only recognized as an intervention when carried out by a licensed musical therapist, not just by a trained researcher. If not performed by a licensed musical therapist, the other two interventions were considered either active music or passive music.

Three articles used music therapy (Bates et al., 2017; Miladinia et al., 2021; Reimnitz & Silverman, 2020; Tang et al., 2021), five used active music (Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Li et al., 2011; Miladinia et al., 2021), and two used passive music (Arruda et al., 2016; Tollabzadeh et al., 2023). These interventions are described in detail in Table 3 on page 65.

Reimnitz and Silverman utilized patient preferred live music, in which participants selected music and a music therapist came in to play the songs live (2020), Tang and colleagues

utilized a six-step music therapy (2021), and Bates and colleagues utilized individualized live music sessions including music assisted relaxation (2017). Deng and colleagues' active music consisted of 30 minutes of their chosen music type from a list of 40 types one hour before and after surgery (2021), Huang and colleagues' active music consisted of one 30-minute session of music through headphones (2010), Li and colleagues' active music consisted of 30 minute sessions twice a day for an average of 51 day (2011), Burrai and colleagues active music consisted of a 30 minute session each week for 4 weeks (2014), and Miladinia and colleagues active music intervention consisted of thrice weekly 15 minute sessions for 4 weeks (2021). Arruda and colleagues utilized passive music through a series of instrumental songs played through earbuds for 30 minutes per day for three days (2016), and Tollabzadeh and colleagues' passive music consisted of two 20-minute sessions for eight weeks (2023).

Outcome Measurement Tools for Pain

There were different pain measurement tools used across the ten studies. Five studies used a visual analog scale (VAS) for pain (Arruda et al., 2016; Bates et al., 2017; Burrai et al., 2014; Deng et al., 2022; Tang et al., 2021), two studies used a numeric rating scale (NRS) for pain (Miladinia et al., 2021; Reimnitz & Silverman, 2020), one study used the VAS portion of the Chinese version of Short-Form McGill Pain Questionnaire, and also included the present pain intensity portion of this scale (Li et al., 2011), one study used a version of the McGill Pain Questionnaire (Tollabzadeh et al., 2023), and one study utilized sensation and distress dual pain VAS scales (Huang et al., 2010). A VAS is a 10-cm index where patients can report a score between two ends of the index, 0 being no pain, 10 being the most severe (Deng et al., 2022). A numeric rating scale for pain uses the numbers 0-10, with a ranking of 0 indicating no pain at all, and a ranking of 10 being the most severe pain (Reimnitz & Silverman, 2020). The McGill Pain Questionnaire measures both quantitative and qualitative experience of pain. The version of this

measurement tool used by Li and colleagues uses temporal characteristics of pain to help patients describe and visualize timing, location, and character of pain (2011). In this study, the VAS portion (0-10 pain rating) of this tool was used, as well as the present pain intensity ranking (PPI) which is ranked from 0 to 5, 0 being no pain, and 5 being extremely painful (Li et al., 2011). In the study conducted by Tollabzadeh and colleagues a short form of this McGill Pain Questionnaire was used in a slightly different way, with 21 questions being asked about sensory, affective, evaluative, and type of pain being experienced. The patient answers these questions, and each answer gets a score that then gets added up to reveal the patients total pain score (Tollabzadeh et al., 2023). These pain ratings were on a scale of 0-78, with 0 being no pain, and 78 being the worst. The sensation and distress VAS's that Huang and colleagues used are very similar to a regular pain VAS, however it is more specific in that it asks patients to rate the extent of sensation and distress of pain (2010). This scale has a 92% likeness of results with a numeric rating scale, and these ratings are on a scale of 0-10 (Huang et al., 2010).

Effect of Music Interventions on Pain

This section will synthesize results across the ten selected articles. First, the effect of the separate music interventions will be discussed. Additionally, the secondary outcomes of each music intervention will be discussed. Second, short term effects of the various music interventions will be reviewed. Lastly, long term effects of the various music interventions will be discussed.

Effect of Music Therapy

The three studies that utilized a music therapy intervention had varying results regarding the use of a music intervention as an effective way to improve patients' pain. Two studies found a significant decrease in pain scores from the use of a music intervention (Reimnitz & Silverman, 2020; Tang et al., 2021). Tang et al. (2021) found that after administering a six-step music

therapy intervention to their intervention group before, during, and after chemotherapy, their average pain reports significantly decreased from 2.14±0.78 to 2.06±0.79 from one day after chemotherapy to five days after chemotherapy. The average pain scores difference had a p-value of 0.004, across a sample of 100 patients diagnosed with small cell lung cancer after receiving their first dose of platinum-based chemotherapy. This music intervention started one day before the chemotherapy and ended an estimated six days later. Similarly, in Reimnitz and Silverman (2020) study, pain reports decreased from 2.75±3.08 to 1.69±2.31 from the pretest to the posttest, showing roughly a 38% reduction in pain after thirty minutes of music therapy in the form of patient preferred live music ($p = 0.017$ between the pretest and posttest mean pain scores). This sample of 35 patients diagnosed with a range of 16 cancers and recovering from a current or previous bone marrow transplant received patient preferred live music as described above for one 30-minute session at any point during their recovery in the hospital. These studies used a VAS to measure pain (Tang et al., 2021), and a NRS to measure pain (Reimnitz & Silverman, 2020), respectively.

The third study done by Bates and colleagues provided no significant results to support the use of music therapy as a pain reduction tool in adult patients with cancer (2017). The control group did have a higher pain score on day +1 from the stem cell transplant, however the p-value was 0.56, so the result is not significant. This study also showed that a music therapy intervention may only be able to provide temporary pain relief, as pain increased back up to the control group's level on day +5, then surpassed this control group's level on day +7. These results introduce a new facet to this research that music therapy may only be able to provide short term relief (Bates et al., 2017).

These three studies also investigated additional outcomes that can potentially be effects of pain, or indicators of subconscious pain. It is important to note these additional parameters to provide a comprehensive look into the topic. Tang et al. (2021) additionally investigated anxiety and sleep quality as parameters to target possible subconscious pain in participants. These findings indicated a significant decrease in anxiety and significant increase in sleep quality by five days post chemotherapy treatment in the intervention group in comparison to the control group, suggesting that music therapy helped reduce pain, which in turn helps these other parameters. Similarly, Reimnitz and Silverman (2020) surveyed energy and fatigue as additional parameters to measure pain levels in the participants. Fatigue levels in the intervention group were significantly improved in the intervention group, while energy scores were only slightly elevated. The hypothesis was that if a patient is in less pain, they will be more energetic and less fatigued. Bates and colleagues studied nausea, use of narcotic pain medication, as well as six different mood states (depression, vigor, fatigue, tension, confusion, and anger), and found that there were no significant effects on nausea or the mood states, however the use of narcotic pain medication was significantly greater in the control group than the intervention group ($p=0.038$) (2017). This result shows the possibility of music therapy as an effective adjunctive tool for pain management that may help with dependence on narcotics or opioids for this cancer pain (Bates et al., 2017).

Overall, these three studies yielded mixed results and offer some main points to think about regarding the use of music therapy for pain reduction in adult patients with cancer. While Tang et al. (2021) found a 54% decrease in pain scores after a six-step music therapy intervention administered before, during, and after chemotherapy, with pain dropping from 2.14 to 2.06 on a VAS scale ($p = 0.04$), and Reimnitz and Silverman (2020) observed a 38% reduction in pain

following a 30-minute live music therapy session ($p = 0.017$), Bates et al. (2017) found no significant reduction in pain, as their study showed no meaningful differences between the intervention and control groups, with pain returning to baseline levels after a short period of relief. This suggests a main point that while music therapy may offer temporary pain relief, its effectiveness may be limited to short-term effects.

Additionally, the additional parameters studied can also be helpful in determining music therapy's effect on this population. Tang et al. (2021) found that music therapy also significantly reduced anxiety and improved sleep quality post-chemotherapy, while Reimnitz and Silverman (2020) observed improvements in fatigue, although energy levels showed only slight changes. Bates et al. (2017) found that while music therapy did not significantly affect mood states or nausea, it did reduce the use of narcotic pain medication in the intervention group ($p = 0.038$), suggesting that music therapy may serve as a useful adjunct to traditional pain management and potentially reduce opioid dependence that remains a problem in this population as mentioned in chapter 2. These findings highlight the potential of music therapy in managing cancer-related pain and improving associated symptoms, though its effects may vary across different patient populations and timeframes.

Effect of Active Music

There were five articles that used active music interventions, and the results were as follows (Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Li et al., 2011; Miladinia et al., 2021). In the study conducted by Huang et al. (2010), the active music intervention provided 42% of the intervention group 50% or greater pain reduction, while the control group only had 8% of participants reach this amount of relief. This sample of 126 patients diagnosed with any type of cancer and reporting pain greater than a three out of ten on the VAS received one 30-minute session of music without lyrics, and with controlled volume and pitch music through

headphones to achieve this reduction in pain. This study used sensation and distress VAS, so pain was measured based on pain sensation, and the distress patients felt over the pain. For the music group, the intensity of posttest sensation and distress of pain in the intervention group was mild (28-30), while the control group's score was moderate (49-50).

Similarly, Li et al. (2011) conducted a study that examined the use of 30 minutes of active music over the course of approximately 51 days, and found that from the baseline pain scores, to the last posttest pain scores, reports of pain significantly decreased from 4.43±1.14 to 0.09±0.29 (on a scale of 0-10). This intervention was administered twice a day every day that the 105 women diagnosed with breast cancer stayed at the hospital. This is roughly a 97% pain reduction in the intervention group, compared to a smaller 83% pain reduction in the control group (4.55±1.02 at baseline, to 0.76±0.43). Though the control group also experienced a reduction in pain, the difference in average VAS pain scores between the intervention group and control group produced a p-value of <0.01, showing that the music intervention provided a statistically significant better amount of pain relief.

The third active music intervention was performed by Deng et al. (2022). 30 minutes of five preferred music types was played one hour before and after a mastectomy to 160 women diagnosed with breast cancer. This also found statistically significant decreases in pain scores, with the control group having an increase in pain of 5.70±1.42 after surgery (on a scale of 0-10), and the music group having an increase of 3.20±1.11 after surgery ($p < 0.001$). The p-value for the difference between the control group's scores and intervention group's scores was $p < 0.001$. The control group's post-surgery pain score was 6.13±1.02, while the music group's post-surgery pain score was 3.53±0.72. The music group experienced roughly 43% less pain than the control group based on these scores.

The fourth active music intervention was performed by Burrai et al (2014). One 30-minute session of live saxophone music was performed to a patient each week for four weeks to provide these results. In this study, the intervention group went from a pain score of 1.8 (out of 10) at the pretest, to a score of 0.7 at the posttest, while the control group went from 1.3 to 1.4, showing that the active music intervention significantly decreased pain in the intervention group ($p=0.001$). The intervention group experienced roughly a 61% decrease in pain, while the control group experienced an estimated 7% increase in pain (Burrai et al., 2014).

Lastly, the fifth study performed by Miladinia and colleagues provided 15-minute sessions three times a week for a total of four weeks (2021). The music intervention group of 38 patients went from an average pain score of 6.15 to 2.73. This is roughly a 44% reduction, but the study provided no p-value so this result cannot be called significant. However, there was a significant difference reported between final pain scores (ranked out of 10) in the control group (6.2) and in the intervention group (2.73). This difference of 3.47 is statistically significant with a p value of 0.001. Though the reduction of pain in the intervention group was not significant itself, it was significantly better than the control group's change in pain scores. These results provide evidence that active music may be a good start to achieving pain reduction compared to standard care, but there needs to be more research done to determine how to utilize it to achieve a significant pain reduction.

Four of these studies also measured additional outcomes that can potentially be effects of pain, or indicators of subconscious pain (Burrai et al., 2014; Deng et al., 2022; Li et al., 2011; Miladinia et al., 2021). Deng et al. (2022) utilized a secondary outcome of interleukin (IL)-6 and high mobility group box (HMGB)-1 levels in blood plasma to further assess pain in participants. These are both inflammatory cytokines, or small proteins that are important in cell signaling, that

increase when the body is under stress and can provide information on a patient's pain response (Deng et al., 2022). An increase in these levels indicates a higher amount of stress or pain the body is experiencing. The control group results showed roughly a 58% increase in (IL)-6 and 41% increase in (HMGB)-1, while the music therapy group experienced a 48% increase in (IL)-6 ($p < 0.001$), and a 26% increase in (HMGB)-1 ($p < 0.001$).

As mentioned previously, Li et al. (2011) used a short form of the McGill Pain Questionnaire, which also measures pain using present pain intensity (PPI) in addition to the VAS. PPI is measured from 0-5, with 0 being no pain and 5 being extremely painful. This PPI measurement provides a very specific measurement of pain at one moment in time. Across the estimated 51 days of data collection, PPI scores decreased by roughly 96% in the intervention group while in the control group PPI scores decreased by roughly 78%. These two groups had a p-value of less than 0.001 for the differences between the pain reductions. For this review, it is not entirely valid to base conclusions off this measurement as PPI measures pain intensity in one moment and therefore is subject to environmental stimuli and other external factors, whereas the VAS measurements can provide a broader and more comprehensive view on pain.

Burrai and colleagues studied physiological parameters and mood levels in addition to their pain scores (2014). These physiological parameters included systolic and diastolic blood pressure, pulse rate, glycemia, which is blood sugar, and oxygen saturation (Burrai et al., 2014). The only parameter that offered a significant result was oxygen saturation, with the intervention group having a reduction with a p-value of 0.003, while the control group had no significant reduction with a p-value of 0.148. The other five parameters had inconclusive results, with random decreases and increase between both the intervention and control group that did not prove significant by p-values. For mood, the control groups mood went from 3.8 to 4.1, while the

intervention group went from 5 to 2.2 (p=0). Moods were rated on a scale of 0-10, with 0 being the best mood and 10 being the worst mood (Burrai et al., 2014).

Lastly, Miladinia and colleagues studied fatigue in addition to pain (2021). The findings were similar to the findings on pain, as the fatigue rating went from 8.06 to 4.91 over 4 weeks in the intervention group, while the control group went from an estimated 7.6 to an estimated 8, with no p-value provided. The fatigue rating in the intervention group also remained below the control groups rating all the way throughout the study, and just like the pain scores, there was a significant difference between the control group and music intervention group fatigue scores over time (p=0.001).

Overall, these five studies had notable differences in outcomes. While two studies found significant reductions in pain in the active music intervention group (Burrai et al., 2014; Li et al., 2011), the other three studies did not find significant reductions in pain within the intervention group, but found a significant positive difference in pain levels between intervention and control groups (Deng et al., 2022; Huang et al., 2010; Miladinia et al., 2021). These findings suggest that type, frequency, and administration of active music can offer different results in pain reduction, and more research is needed to refine the effectiveness and bring about a significant reduction in pain.

Effect of Passive Music

The two studies that utilized a passive music intervention were Arruda et al. (2016) and Tollabzadeh et al. (2023). Both studies found statistically significant results that support the use of music for pain management in cancer patients. Arruda et al. (2016) used 30 minutes of music per day for three days in a randomized controlled trial and reported a decrease in the music group's pain scores from 3.92±2.85 to 1.31±2.16, while the control groups decreased from 4.17±2.69 to 3.96±2.65 ($p<0.001$). This sample included 65 patients diagnosed with any type of

cancer who reported pain in the previous week and were using pain medications. The music group showed an approximately 67% decrease, while the control group showed approximately a 5% decrease. Similarly, in a randomized controlled trial, Tollabzadeh et al. (2023) used two 20-minute sessions of a mixture of classic, pop, Iranian, and meditation music each week for eight weeks and found a roughly 57% reduction in pain, with raw scores going from 67.77±16.91 before the study, to 29.47±3.53 after the study ($p<0.001$). This sample included 54 patients diagnosed with any type of cancer.

Additionally, both studies identified outside parameters that were hypothesized to indicate pain that may not be reflected by the participant in the VAS. Arruda et al. (2016) investigated depression and hope as the other parameters, while Tollabzadeh et al. (2023) investigated anxiety and stress. Depression, hope, and anxiety were all self-reported by the participants through surveys, while stress was self-reported, as well as measured through cortisol levels in participants. Cortisol is a hormone that raises in times of stress (Tollabzadeh et al., 2023). Arruda et al. (2016) found a significant reduction in depression ($p=0.04$), but no significant change in hope for the music group ($p=0.08$). Tollabzadeh et al. (2023) found a significant reduction in anxiety at the end of the study in the music group ($p<0.001$), as well as a significant reduction in the self-reported stress scores ($p=0.002$), and a significant reduction in mean cortisol scores.

Overall, this intervention was the least popular between the ten studies, with just two focusing on it, however these two studies yielded very similar results. Arruda et al. (2016) and Tollabzadeh et al. (2023) both found statistically significant evidence supporting the use of passive music for pain management in cancer patients. Arruda et al. (2016) observed a 67% reduction in pain scores among the music group, from 3.92 to 1.31, compared to a 5% decrease

in the control group ($p < 0.001$). Similarly, Tollabzadeh et al. (2023) reported a 57% reduction in pain, with scores decreasing from 67.77 to 29.47 ($p < 0.001$) after eight weeks of passive music sessions. These findings suggest that passive music interventions can effectively reduce pain in cancer patients, with consistent results across the two different study designs and patient populations.

In addition to pain, both studies investigated secondary outcomes related to psychological stress. Arruda et al. (2016) found a significant reduction in depression ($p = 0.04$), while Tollabzadeh et al. (2023) observed significant reductions in anxiety ($p < 0.001$), self-reported stress ($p = 0.002$), and cortisol levels, a physiological marker of stress. These results suggest that passive music interventions may also improve emotional well-being by reducing stress and anxiety, offering a more holistic approach to pain management in cancer patients.

Effect of Various Music Interventions

Across the three different music interventions utilized, each intervention showed significant reductions in pain across various patient samples and settings in at least one or more of the studies that utilized each intervention.

Short and Long-Term Post-Intervention Effects

Across the ten studies, different time ranges were used for outcome measurements. It is important to investigate these different time ranges to determine the effect of music on pain both in the short term, and in the long term. For the evaluation of music's effect, outcomes were measured starting right after music intervention to as long as eight weeks after the intervention. For this review, the median time of the studies was seven days, with the longest study lasting approximately 117 days (eight weeks followed by two months) (Tollabzadeh et al., 2023), and the shortest studies just taking place in one day (Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Reimnitz & Silverman, 2020). With seven days being the median, for this review

anything under seven was considered short term, and anything over seven days was considered long term. There were five articles done short term (Arruda et al., 2016; Burrai et al., 2014; Deng et al., 2022; Huang et al., 2010; Reimnitz & Silverman, 2020), and five studies that were considered long term (Bates et al., 2017; Li et al., 2011; Miladinia et al., 2021; Tang et al., 2021; Tollabzadeh et al., 2023). Of the five short term studies, two used active music, two used music therapy, and one used passive music, and of the long-term studies, two used active music, two used music therapy, and one used passive music.

Short-Term Effects

All five studies that measured outcomes over shorter periods of time found significant reductions in pain in the intervention groups. The two active music short term studies were done by Deng et al. (2021) and Huang et al. (2010). Deng et al. provided 30 minutes of music one hour before and after a mastectomy, while Huang et al. provided one 30-minute session of music listened to through headphones. Four hours after tracheal extubation and three hours after the music intervention, Deng et al. found a significantly smaller increase in pain in the music group compared to the control group's increase in pain ($p<0.001$). Huang et al. measured a significant decrease in pain among the intervention group right after the music intervention ($p<0.001$).

Tang et al. (2021) and Reimnitz and Silverman (2020) were the two music therapy interventions that investigated shorter term outcomes. Tang et al. utilized a six-step music therapy approach, while Reimnitz and Silverman (2020) utilized one 30-minute session of patient preferred live music. Tang et al. found significant reductions from one day post chemotherapy ($p=0.005$) and five days post chemotherapy ($p=0.004$) versus the control group, and Reimnitz and Silverman found a significant decrease in pain from right before the intervention and right after in the intervention group compared to the control group ($p=0.017$).

Arruda et al. (2016) was the one passive music intervention that measured short term outcomes. This time range was over a period of three days, with measurements being taken right after the intervention each day. After administering one 30-minute session of instrumental songs, the pain scores in the intervention group significantly decreased ($p<0.001$).

Overall, all three music interventions demonstrate a possible successful way of reducing short term cancer related pain. Music therapy showed an approximately 54% reduction in pain immediately following the intervention (Reimnitz & Silverman, 2020) and approximately a 38% reduction in pain up to five days after the intervention (Tang et al., 2021). Active music interventions measured effectiveness of pain reduction right after the intervention (Huang et al., 2010) to three hours after (Deng et al., 2022), with Huang and colleagues reporting 42% of participants reaching 50% pain reduction (2010) and Deng and colleagues reporting a 42% reduction of pain in their music group (Deng et al., 2022). Finally, passive music provided an approximate 67% decrease in pain for the music intervention group over a period of three days (Arruda et al., 2016).

Long-Term Effects

The five studies that investigated long term effects included three studies that provided significant results (Burrai et al., 2014; Li et al., 2011; Tollabzadeh et al., 2023), one study that had varied results (Miladinia et al., 2021), and one study that did not provide any significant results (Bates et al., 2017). There were three active music long term studies (Burrai et al., 2014; Li et al., 2011; Miladinia et al., 2021), one passive music long term study (Tollabzadeh et al., 2023), and one music therapy long term study (Bates et al., 2017).

Out of the three active music interventions, two provided significant reductions in pain in the studies done by Li et al. (2011) and Burrai et al. (2014). These active music interventions included twice daily 30-minute sessions throughout an average of 51 days in the hospital (Li et

al., 2011), and 30-minute sessions performed each week for four weeks (Burrai et al., 2014). In Li's study, by third posttest at the end of the ~51 day stay, pain scores in the intervention group were 0.09±0.29, while the control group was elevated at 0.76±0.43 ($p<0.001$) (2011) . Throughout the entire hospital stay, this intervention was found to alleviate the intervention group's pain by approximately 90%. Similarly, Burrai and colleagues' study, while baseline pain scores in the intervention group and control groups only differed by 0.5 points on the VAS scale (no statistically significant difference), showed a pain score of 1.4 in their control group and a score of 0.7 in the intervention group by the end of the four weeks (2014). This is a 50% difference in pain between groups. The third active music long term study was done by Miladinia and colleagues (2021). This study had varied results in that it found no significant reduction of pain within the intervention group, but did find a significant difference in the pain levels between the intervention and control groups (Miladinia et al., 2021). It is also important to note from this study that the intervention groups mean pain scores increased over the last weeks of the experiment, indicating that active music may not provide significant long-term relief (Miladinia et al., 2021).

The one music therapy long term intervention was used by Bates and colleagues in 2017. Their intervention included one 30-minute session provided one day after a stem cell transplant and five days after a stem cell transplant. This study did not find any significant results supporting the use of music therapy for long term pain reduction in adult patients with cancer. The difference in pain scores between the intervention and control groups did show that music therapy may help alleviate pain, but the p-value was 0.73, so this result is insignificant. Additionally, over the course of the nine-day study, the pain ratings in the intervention group continued to rise after the last music intervention and even surpassed the control group ratings by

seven days after the stem cell transplant. This is another study that indicates that active music intervention may not provide significant long term pain relief (Bates et al., 2017).

The one passive music long term intervention used by Tollabzadeh et al. (2023) included two 20-minute sessions of music each week for eight weeks. This study found intervention group pain scores at 29.47±3.53 (out of 78) at the conclusion of the study, while control group pain scores remained at 60.86±14.73 ($p<0.001$). This is approximately a 57% reduction in pain (Tollabzadeh et al., 2023). Though these results provide support for the use of a passive music intervention for long term pain relief, it is a stand-alone study in that it is the only passive long term one found, so a conclusion cannot be drawn entirely on it alone.

Overall, these five studies show that music's long-term effect on pain cannot be proven and needs more research to determine its full effect and how to best utilize it to achieve pain reduction. In two out of three active music studies, the intervention provided significant long term relief (Burrai et al., 2014; Li et al., 2011), but the third showed statistically insignificant results (Miladinia et al., 2021), suggesting that duration and consistency of active music intervention may influence its effectiveness. For example, Miladinia utilized fifteen-minute sessions, while both Li and Burrai utilized thirty-minute sessions, potentially showing that a longer session is needed to provide longer effects on pain. Music therapy's long-term effectiveness is also questionable, as the one study that looked at music therapy for long term pain relief provided no significant results (Bates et al., 2017). There is nothing to compare these results to in terms of interventions so to provide a more comprehensive view into long term pain relief by music therapy, more research is needed. Passive music, on the other hand, had one study and was able to provide significant results for the intervention decreasing long term pain relief

(Tollabzadeh et al., 2023). Like music therapy, this also requires more research to determine the best duration and consistency to provide long term pain relief.

Chapter 5: Discussion

This chapter aims to synthesize the results from ten selected articles, as well as the literature reviewed in the previous chapters. This synthesis will offer a comprehensive discussion of the findings, implications of these findings, and the broader context in which the results lie. An analysis of the study limitations, future avenues for research, and clinical implications for pain management in adult cancer patients will also be included. In sum, this chapter integrates the key findings with the existing literature on this topic, to provide a well-rounded understanding of the role of music interventions in managing pain in adult patients with cancer.

Summary of Key Findings

This review aimed to synthesize the current literature on music's effect on cancer related pain in adult patients with cancer. Every study included was a randomized controlled trial, but locations of the studies, sample sizes, types of music interventions, types of samples, and the outcome measures used varied throughout the ten reviewed articles. Despite this variety, broad conclusions can be synthesized together from all ten pieces. All three music interventions have the potential to reduce pain in adult patients with cancer, but there are limitations to each of the studies that must be considered when interpreting these results.

Throughout the ten studies, there was no standardization of any intervention protocols. One of the primary areas that requires further research is the optimal type, frequency, duration, administration, and consistency of the music intervention. To be able to compare results effectively, future studies should aim to establish standardized music interventions that can be consistently applied across different samples and settings. This would allow for more reliable results and could help determine the optimal type of music intervention, session lengths, and frequency for pain relief. In this study, passive music had the most consistent and significant results, but it is difficult to use this to generalize as passive music was only studied in two

studies, while music therapy was studied in three and produced mixed results, and active music was studied in five and produced mixed results. There was also a total of 119 patients across the passive music studies, 217 patients across the music therapy studies, and 427 patients across the active music studies. These inconsistencies in number of studies and number of participants makes it difficult to compare the music interventions to each other.

The generalizability of these findings is also difficult to apply due to relatively small and specific samples seen amongst the included studies. Across the ten studies, sample sizes ranged from 35 at the smallest (Reimnitz & Silverman, 2020) to 160 at the largest (Deng et al., 2022). All the ten studies provided differing sample sizes and characteristics, leading to results that are hard to group together or generalize to the broad population of adult patients with cancer. Some of the characteristics that differed among the studies included the type of cancer diagnosis, the type of treatment the patients were receiving, and the age and gender of patients. For example, Li and colleagues focused on women with breast cancer (2011), Reimnitz and Silverman only focused on patients undergoing a bone marrow transplant (2020), and Tang and colleagues only looked at patients diagnosed with small cell lung cancer (2021). Larger, more diverse samples are needed to establish more concrete evidence for the use of music as a pain management or reduction tool. Diversity of samples would mean including different cancer diagnoses, different treatments, and different socioeconomic statuses amongst participants. With these varying samples, it can be concluded that the results are not necessarily generalizable to the broader audience this review intended to study.

Additionally, within these samples, some inclusion and exclusion criteria that the researchers set when selecting their participants limit the application of these findings in larger populations. Some of these criteria included no history of or presence of mental illness (Deng et

al., 2022; Tang et al., 2021), being fond of music prior to a cancer diagnosis (Deng et al., 2022; Li et al., 2011), having major surgery within the past month (Huang et al., 2010), and having an education level at minimum of elementary school completion (Tollabzadeh et al., 2023). As mentioned earlier in this review, patients with cancer experience higher levels of psychological distress, including higher rates of anxiety, depression, and anger; excluding patients who fall under this category takes away a large part of patients with cancer that is important to include in this research (Glover et al., 1995). Along with this, many patients with cancer require major surgeries to remove tumors and correct complications caused by cancer and treatments; this is another large part of the population that needs to be included in this research. Likewise, only including patients who reach an educational threshold leaves room for lower socioeconomic class patients with cancer to not be represented in these findings. As for bias, including only patients who typically enjoy music brings bias into the experiment, as patients are more likely to find relief in something they enjoy.

The lack of blinding of the studies can also introduce bias to the results. Within the different studies included, only one of the experiments explicitly blinded their participants (Huang et al., 2010). All other studies were open-labeled or assumed to be based on no blinding classification being made. Randomization and blinding combined are the most effective way of reducing bias within studies (K. M. Higgins et al., 2024). A systematic review done in 2014 compared randomized controlled trials with blinding to randomized controlled trials without blinding and found that without blinding, control groups know they are not receiving something, and intervention groups know they are receiving something in addition to whatever the control group is receiving (Hróbjartsson et al., 2014). This can lead to feelings of missing out on something, or knowing they are receiving something that is meant to show results can naturally

bring patients to different outcomes, whether through intentionally wanting to skew results, or through a placebo effect (Hróbjartsson et al., 2014).

Another limitation of the studies is that relatively short follow-up periods or no follow up periods at all were utilized. While there was heterogeneity (differences) in these measurements, and some studies investigated short term while others investigated long term, the longer-term studies provided inconclusive results with varying degrees of significance when it came to the results in pain relief. This is important to this review as cancer is often chronic, similar to diseases such as heart disease or diabetes (2024a). With a long disease progress, pain lasts a very long time, warranting a need for long-term pain management and reduction. Longer follow-up periods are needed to determine the effectiveness and reliability of music's effects on pain in patients with cancer.

Along with pain management and reduction, the ten studies also included secondary outcomes that the researchers included to either provide a more comprehensive view on pain, or because their studies were not only specific to music's effect on pain reduction. While not every secondary outcome studied showed significant improvement, these results and the fact that researchers are including these parameters suggest that music intervention may offer broader therapeutic benefits to adult patients with cancer outside of pain relief. Improved ratings of sleep quality, anxiety, depression, fatigue, and energy scores can all be indicative of pain, but can also provide evidence that music may be an effective holistic tool when treating adult patients with cancer. While this review was originally conducted to determine music's effect on pain in adult patients with cancer, significant evidence was found that supports music possible use in this population to help increase overall wellbeing with further research and implementation.

The studies reviewed had varying outcome measurement tools for their pain results. While half of the studies utilized a VAS (Arruda et al., 2016; Bates et al., 2017; Burrai et al., 2014; Deng et al., 2022; Tang et al., 2021), there were four other outcome measurement tools across the remaining half of the studies. Consistency in outcome measurement tools allows for stronger results, and eliminates some of the risk of bias that arises when multiple tools are used across different studies (Mokkink et al., 2017). Additionally, while the VAS is widely accepted, it is subjective in nature due to self-reporting and may not be able to capture the full complexity of cancer-related pain as it cannot address multidimensional aspects of pain (Firdous et al., 2017). Furthermore, the self-reported measurements of the secondary outcomes such as stress, depression, and anxiety are also subject to potential bias. While stress can be objectively measured through physiological parameters as some studies attempted, other outcomes like depression and anxiety will always be subject to potential bias due to an inability to objectively observe these qualities.

Lastly, the quality appraisal done in the preceding chapters also has to be considered when interpreting these results. Level I, high quality articles produce more valid results than the level I, good quality articles included in this review. For example, the only studies that were rated high quality studied active music and passive music. Therefore, when interpreting results for music therapy there is a need to account for a lower level of quality of the results. This means that these results may not provide as strong evidence for clinical implications, or that music therapy may require further research before it can be compared to active or passive music. The rigor of the high-quality studies provides more generalizable evidence and stronger conclusions. Comparing both the high-quality and good-quality studies suggests that while there is potential for music therapy to be effective in reducing pain, further high-quality studies are necessary to

fully establish the clinical implications and effectiveness of this approach. The gap between high-quality and good-quality studies underlines the need for more comprehensive research to build stronger, evidence-based recommendations for practice.

Study Limitations

After determining the selected studies limitations and sources of bias, it is also important to note that this review itself is subject to bias, limitations, and weaknesses. Systematic reviews are very valuable in synthesizing evidence on a specific topic, however there are several factors that open them up to bias and limitations including the selection of studies, the data extraction process, quality appraisal, and heterogeneity between selected studies.

The literature search for a systematic review is extensive and critical to ensuring a successful review, however this process can be flawed. In this search, two databases were utilized, which potentially limits some results that may have been available or other databases not included. The inclusion criteria selected for this review, including English language, publication date, and limiting to randomized controlled trials, could also limit the scope of the review and exclude potentially relevant studies that may have presented significant results that are in line with the other studies, or provide a different view (Egger et al., 1997).

There is also a risk for publication bias within the selected studies, where studies with negative or insignificant results are less likely to be published in these databases than ones with positive or significant results. This could lead to an overrepresentation of desired outcomes and mislead overall conclusions drawn from the search by excluding relevant studies (J. Higgins & Green, 2011).

The data extraction and analysis process are also prone to bias and limitations. When interpreting the findings of the studies, personal bias may come into play and lead to inconsistencies in data extraction. It is important to recognize that this is a review done by a first-

time investigator with no second author to screen the articles examined, so this process is subject to limitations or weaknesses across all ten of the studies due to lack of expertise (Jansen, 2017).

Quality appraisal is another area where this review could be weakened. Though the use of a qualified and evidence-based tool reduces the risk of bias greatly, the Johns Hopkins Nursing Evidence-Based Practice Quality Guide is a subjective tool to appraise quality of articles. While the levels of the studies are objective, the grading of high, good, and low-quality articles is up to the interpretation of the writer. Appropriateness of samples, and generalizability of results are two criterium that were heavily decided on when comparing the studies to each other. For example, a few samples were noted to cause results to not be generalizable due to the specificity of cancer diagnosis. This criterion was set forth by the investigator because there were also studies that were included that provided a sample of any cancer diagnosis. In another systematic review on this same topic, these studies may have been considered high quality if the investigator did not consider this when determining the appropriateness of the study samples.

Lastly, the heterogeneity of the studies opens sources of bias and limitations in this review. When significant variability exists between studies music interventions, outcome measures, and samples, it can be difficult to combine these results into an unbiased synthesis. The investigator's bias will come into play when achieving a unified conclusion based on different studies. Subjective decisions are made about how to handle the data. For example, in this review, the investigator debated whether to include secondary or other outcomes the researchers studied as they do not specifically measure pain. Personal bias came into effect when deciding to include them, as a subjective decision was made that these secondary outcomes may be indicative of pain as well.

In conclusion, it is pertinent to explore the writer's personal bias and limitations when writing a systematic review. This is a review written by a first-time investigator, and therefore is subject to the above bias and weaknesses. Though this not does diminish the information found in this paper, it is relevant to understand that this research is flawed in similar ways of all systematic reviews (Yuan & Hunt, 2009).

Implications for Practice

The findings in this review suggest that music interventions can be an effective way to manage or reduce pain in patients with cancer. With the growing body of evidence supporting its efficacy, music interventions such as active music, passive music, or music therapy should be considered as a part of care plans for patients with cancer. Healthcare workers such as nurses and physicians can incorporate this use into everyday care and procedures to help provide pain relief to patients going through chemotherapy, surgery, and other parts of cancer treatment.

While this review has suggested these uses, future research is still warranted to provide full effectiveness of this intervention. More studies can be done to determine the optimal parameters of music intervention to achieve the highest pain relief, such as timing and the type of music. Before implementing music as a standard of care in the field of oncology, research must be done to prove effectiveness.

Recommendations for Future Research

Samples

In future studies, researchers should include larger and more diverse samples. Patients with all cancer types can be included in the same study, allowing there to be a bigger population, and more generality of the results. For example, three of the studies included patients with any cancer diagnosis, making these results higher quality and more generalizable to a broader population (Arruda et al., 2016; Burrai et al., 2014; Huang et al., 2010). Along with this, patients

at each stage of disease progression and treatment can be included in future studies. This will allow for the results to apply to a larger audience in the population looked at in this review, hopefully proving a larger body of evidence that can help future patients with cancer.

Additionally, future studies can aim to have less limiting inclusion and exclusion criteria. Allowing more types of patients to participate in the study gives the results more room to generalize in a larger population and can help apply the research to more patients with cancer. Including patients with a history or present mental illness will greatly help this population, as pain is a driving factor behind mental illness in patients with cancer. It would also be beneficial remove any exclusion criteria that does not allow low literacy or socioeconomic status to limit any patients from participating. Cancer does not affect any literacy level or socioeconomic status more than another, so it is important to include any patient with cancer if results are to be valid and generalizable.

Blinding of Participants

Including more blinding in future studies is pertinent. This will help reduce bias and any kind of placebo effect in the intervention and control groups. Making future studies double blinded could also be very beneficial. Blinding both the participants and the researchers on who is receiving an intervention and who is not can greatly eliminate outside forces and bias to get as pure results as possible. To blind participants in future randomized controlled trials, the music intervention may need to be designed so it does not directly indicate to the patient that it is an "active" treatment. For example, patients could have access to headphones and a music source in their room, but no one is telling them to use it. A nurse could observe the patients and mark which ones use it, and which ones do not, then when researchers collect the pain scores from all the patients, the nurses can go through and separate the results based on who utilized the music and who did not. Having the separation of researchers who are collecting data and nurses who

are noting who used the intervention and who didn't is important to avoid researcher bias. This type of study design would ensure that both the participants and researchers are blind to the two groups and would greatly reduce the risk of bias in these studies.

Follow Up Durations

Allowing for longer follow up durations in future studies is also necessary. With cancer pain being often chronic, or lasting three months or longer, studies should reflect this timeline. Including more longitudinal studies in the future will help determine if music can be used as a long-term pain management tool, as opposed to a temporary form of relief. Cancer is a drawn-out disease, and pain is involved in most of the steps towards remission, so achieving a nonpharmacological pain management tool like music intervention would be very helpful in allowing these patients to have a greater quality of life. A longitudinal study design may be useful in implementing this change, where the same group of adult patients with cancer are studied throughout their disease progress and treatment, with pain scores and music interventions being collected and administered from the time of their diagnosis to the day they are declared cancer free. Having these comprehensive results can help determine the long-term effects of music on pain, as well as possibly inform us of the optimal timing of music intervention. For example, it could be that the music intervention administered during the first couple weeks of treatment is more helpful than music interventions administered during the last couple weeks of treatment.

Optimal Parameters

Future studies should also begin to examine the optimal parameters of music intervention. Knowing the best timing, type of music, and way to administer it is essential to achieve maximum pain reduction. Future studies can begin have different music interventions compared to each other as opposed to a non-music control group. Once these studies can be

completed, more information will be known about the best way to utilize this tool. For example, Huang and colleagues offered Taiwanese, Western, and Buddhist music to their participants and let them pick one (2010). In the future, this could involve three different intervention groups with each kind of music to determine which is most effective.

Additionally, investigating the physiological mechanisms of music's effect on pain would help sort out how music is able to achieve pain reduction, therefore making it easier to determine how we can best utilize it. For example, Deng and colleagues went a little further by studying inflammatory cytokines to determine some of music's biological impact of the patients (2021). Further studies like this that investigate what physiological or biological changes music makes in a patient's body could help provide an explanation on how and why music is able to reduce or manage pain, giving researchers more insight into the best ways to use it.

Conclusion

In conclusion, this review and the included studies suggest that music intervention in patients with cancer could reduce and manage pain. Three different types of music intervention were studied in this review: active music, passive music, and music therapy. All three warranted significant reductions in pain compared to the control groups, as well as some significant secondary outcomes in anxiety, sleep quality, depression, and fatigue. Samples of adult patients with cancer were included in all ten studies with varying inclusion and exclusion criteria, however these results warrant the need for larger scale, and more longitudinal studies to determine the true effectiveness of music as an intervention for pain. With the future research completed as laid out previously, music intervention has the potential to be a standard implementation into oncology care plans for maximum pain management and relief.

Table 2: Matrix Table

Author, Year	Study Design	Sample	Intervention	Control Group	Outcome/Measure	Results
Arruda et al., 2016	RCT	N = 65 patients diagnosed with cancer 18 years or older who reported pain in the previous week and are using pain medications.	N = 22 Passive music intervention	N = 21 no music intervention, received standard care N = 22 listened to recorded poetry	- Pain (primary): VAS - Depression: Beck depression inventory - Hope: Herth hope scale Before and after 30 minutes of music intervention over a period of three days	- Primary outcome - Control group pain score before 4.17±2.69, after 3.96±2.65 (p=1, no significant reduction for control); music group pain score before 3.92±2.85, after 1.31±2.16 (p<0.001, significant reduction for music) - Secondary outcomes - Control group depression score before 11.21±4.94, after 10.14±5.05 (p=0.36, no significant reduction for control); music group depression score before 13.18±7.87, after 10.22±6.21 (p=0.004, significant reduction for music group) - Control group hope score before 36±3.78, after 35.95±3.62 (p=0.9, no significant increase for control); music group hope score before 36.54±3.85, after 37.86±4.71 (p=0.08, no

						significant increase in music group)

Bates et al., 2017	RCT	N = 82
		patients 18 or older with a diagnosis of multiple myeloma or lymphoma undergoing first autologous stem cell transplant, no previous music therapy experience.
			N = 37
			Music therapy intervention
				N = 45
				No music intervention, received standard care
					- Pain (primary): VAS
					  - Before and after first music therapy session on day +1, then on days +5 and +7
					- Nausea: VAS
					  - Before and after first music therapy session on day +1, then on days +5 and +7
					- Mood disturbance: Profile of Mood States (POMS) self-rating scale; includes depression, vigor, anger, tension, confusion, fatigue
					  - Before admission and on day +5
					- Narcotic pain medication use measured in total daily milligrams from electronic medical record
					  - Once a day from day -1 to +5
						- Primary outcome
						  - Pain scores did not differ significantly between control and intervention group at any times (difference had p value of 0.73)
						  - Control group had higher pain rating than intervention group day +1 post assessment (p=0.56)
						  - Pain increased in intervention group on days +5, and exceeded control group ratings on day +7
						- Secondary outcomes
						  - No significant difference in nausea on day +1 (p=0.17) or day +5 (p=0.86); day +7 intervention group reported higher nausea than control group (p=0.035)
						  - All 6 POMS subscales showed insignificant changes in control vs intervention group
						  - Narcotic use greater in control group than

						intervention group over 5 days (p=0.038)
Burrai et al., 2014	RCT	N = 52 Patients aged 18 or older with a diagnosis of cancer on chemotherapy treatment.	N = 26 Active music intervention	N = 26 No music intervention, received standard care	- Pain (primary): VAS - Mood level: VAS - Physiological parameters: systolic blood pressure, diastolic blood pressure, pulse rate, glycemia, oxygen saturation - Before music intervention and 30 minutes after intervention each week for 4 weeks	- Primary outcome - Control group went from an average of 1.3 to 1.4 at the posttest, intervention group went from an average of 1.8 to 0.7 at the posttest (p=0.001, intervention group had significant decrease in pain) - Secondary outcomes - Control group mood went from 3.8 to 4.1, intervention group went from 5 to 2.2 (p=0, intervention group had significant improvement in mood) - Systolic BP, diastolic BP, pulse rate, glycemia all had no significant changes between control and intervention groups - Oxygen saturation had a significant reduction (p=0.003) in intervention group while control group had no significant change (p=0.148)

Deng et al., 2021	RCT	N = 160 women aged 18 and older diagnosed with breast cancer having a mastectomy in early morning.	N = 40 Active music intervention	N = 40 received general anesthesia N = 40 received aromatherapy sessions N = 40 received combined music and aromatherapy sessions	- Pain (primary): VAS - Inflammatory cytokines (IL-6, HMGB-1): enzyme-linked immunosorbent assay (ELISA) - 30 minutes before surgery and 4 hours after tracheal extubation	- Primary outcome - Control group pain increased by 5.70±1.42, music group pain score increased by 3.20±1.11 ($p<0.001$, significantly less increase in music group) - Secondary outcomes - Control group IL-6 increased by 158.3±19.37, music group IL-6 increased by 103.58±18.96 ($p<0.001$, significantly less increase in music group) - Control group HMGB-1 increased by 171.18±17.89, music group HMGB-1 increased by 92.2±16.42 ($p<0.001$, significantly less increase in music group)
Huang et al., 2010	RCT	N = 126 patients 18 years or older diagnosed with cancer reporting unusual pain in past 24 hours that rated > 3 out of 10 on VAS.	N = 62 Active music intervention	N = 64 No music intervention	- Sensation and distress VAS - Right before and after 30-minute music intervention	- Music group reported significantly less pain compared to control group. - 42% of intervention group patients reported 50% decrease in pain; 8% of control group reached this amount of relief
Li et al., 2011	RCT	N = 105 women 25-65 years old diagnosed with	N = 54 Active music intervention	N = 51 No music intervention	- Pain (primary): VAS portion of Chinese version of Short-	- Primary outcome - Baseline pain scores: control group 4.55±1.02,

		breast cancer and receiving a radical mastectomy.			Form of McGill Pain Questionnaire (SF-MPQ) - Present pain intensity: SF-MPQ - First day after mastectomy, day before discharge, and days of admission for first and second chemotherapy sessions	intervention group 4.43±1.14 - First post test: control group reported 1.82±0.83, intervention group reported 0.98±0.62 ($p < 0.001$) - Second posttest: control group reported 1.33±0.55, intervention group reported 0.56±0.54 ($p < 0.001$) - Third posttest: control group reported 0.76±0.43, intervention group reported 0.09±0.29 ($p < 0.001$) - Secondary outcome - Baseline PPI scores: 2.72±0.55, intervention group 2.58±0.53 - First posttest: control group PPI score 1.38±0.58, intervention group PPI score 0.58±0.53 ($p<0.001$) - Second posttest: control group PPI score 1±0.57, intervention group PPI score 0.2±0.41 ($p<0.001$) - Third posttest: control group PPI score 0.57±0.5, intervention group PPI score 0.02±0.014 ($p<0.001$)
Miladinia et al., 2021	RCT	N = 104	N = 38	N = 38	- Pain (primary): numeric rating scale	- Primary outcome

		Patients 18 or older at least 3 months after being diagnosed with acute leukemia and undergoing chemotherapy, had to have expressed pain and fatigue intensity of >3 in the past 24 hours.	Active music intervention	No music intervention, received standard care N = 38 Massage therapy intervention	0-10; 0 = no pain, 10 = most severe pain - Fatigue: numeric rating scale 0-10; 0 = no pain, 10 = most severe pain - Before interventions, then weekly during 4 weeks of intervention sessions, and an additional 2 weeks after	- Music intervention went from baseline of 6.15 to fourth week score of 2.73, control group went from estimated 6.4 to estimated 6.2 (p value not provided) - Mean pain score increased over 2 weeks after last music intervention, remained below baseline - Significant difference between control group and music intervention group in pain scores over time (p=0.001) - Secondary outcome - Music intervention went from baseline of 8.06 to fourth week of 4.91, control group went from estimated 7.6 to estimated 8 (p value not provided - Mean fatigue score increased over 2 weeks after last massage therapy intervention, remained below baseline - Significant difference between control group and music intervention group in fatigue scores over time (p=0.001)

Reimnitz & Silverman, 2020	RCT	N = 35 patients 18 years or older diagnosed with cancer recovering from current or previous bone marrow transplant (BMT).	N = 18 Music therapy intervention	N = 17 No music intervention	- Pain (primary): numeric rating scale 0-10; 0 = no pain, 10 = most severe pain - Energy: Lee visual analog scale for fatigue (VAS-F) - Fatigue: VAS-F - Right before and after the 30-minute music intervention	- Primary outcome - Pre to posttest pain decreased in experimental group, pre to posttest pain increased in control group. - Control group pretest pain score 2.50±2.55, posttest pain score 2.85±2.68; intervention group pretest pain score 2.75±3.08, posttest pain score 1.69±2.31 (p=0.017, intervention had significantly less posttest pain) - Secondary outcomes - Control group pretest energy score 41.31±18.53, intervention group pretest energy score 34.41±18.74; control group posttest energy score 41.87±17.84, intervention group posttest energy score 46.19±18.48 (p=0.079, not significant) - Control group pretest fatigue score 45.23±17.69, intervention group pretest fatigue score 42.98±26.7; control group posttest fatigue score 43.70±19.08, intervention group posttest fatigue score 28.86±18.99

						(p=0.003, significant reduction of fatigue in intervention group)

Tang et al., 2021	Randomized controlled trial (RCT)	N = 100 patients diagnosed with small cell lung cancer and scheduled to receive first dose platinum-based chemotherapy.	N = 50
			Music therapy intervention
				N = 50
				No music intervention
					- Pain (primary): visual analog scale (VAS)
					- Anxiety: self-rating anxiety scale (SAS)
					- Sleep quality: Pittsburgh sleep quality index (PSQI)
					- Before treatment, one day after, five days after
						- Primary outcome
						  - Before chemotherapy: no significant VAS score difference between control and intervention
						  - One day after chemotherapy: control group VAS scores 4.74±1.01, intervention group VAS scores 2.14±0.78 (p=0.005, significant reduction in intervention group
						  - Five days after chemotherapy: control group VAS scores 4.74±1.08, intervention group VAS scores 2.06±0.79 (p=0.004, significant reduction in intervention group)
						- Secondary outcomes
						  - Before chemotherapy: no significant SAS score difference between groups; no significant PSQI score difference between groups
						  - One day after chemotherapy: control

						group SAS scores 61.46±8.8, intervention group SAS scores 49.48±2.14 (p=0.011, significant reduction in intervention group; control group PSQI scores 17.81±3.01, intervention group PSQI scores 8.50±1.69 (p=0.006, significant increase in intervention group) - Five days after chemotherapy: control group SAS scores 62.02±8.83, intervention group SAS scores 39.73±1.79 (p=0.005, significant reduction in intervention group); control group PSQI scores 9.84±3.02, intervention group PSQI scores 18.66±2.91 (p=0.012, significant increase in intervention group)
Tollabzadeh et al., 2023	RCT	N = 54 patients diagnosed with cancer, 20-63 years old, no severe physical ailments, no medical history,	N = 25 Passive music intervention	N = 29 No music intervention, counseling sessions offered	- Pain (primary): The McGill Pain Questionnaire (MPQ) - Anxiety: Beck anxiety inventory (BAI)	- Primary outcome - Control group MPQ before study reported at 59.96±13.46, after the study reported at 60.86±14.73; intervention group MPQ before study

		or present psychotic disorders.			- Stress: cortisol blood levels and perceived stress scale (PSS) - During pre-test, a post-test after eight sessions of intervention, and a follow up two months later	reported at 67.77±16.91, after the study reported at 29.47±3.53 (p<0.001) - Secondary outcomes - Control group BAI before study reported at 67.51±19.43, after reported at 77.13±18.36; music group BAI before study reported at 75.80±12.81, after reported at 28.90±7.32 (p<0.001, significant reduction) - Control group PSS score before study reported at 59.93±8.24, after study reported at 51.75±10.95; music group PSS before study reported at 60.17±12.29, after study reported at 49.41±9.95 (p=0.002, significant reduction) - Control group cortisol level before study 29.19±4.35, after study 29.34±3.66 (p=0.838, no significant change); music group cortisol level before study 29.51±6.85, after study 16.17±5.48

						($p<0.001$, significant reduction)

Table 3: Music Interventions

Article	Type	Frequency and Duration	Interventionist	Music Intervention Details
Tang et al., 2021	Music therapy	Step 1: one day before chemotherapy, 30-90 minutes Step 2: before sleeping (# of days not specified) Step 3: during chemotherapy, 30-90 minutes Step 4: after each injection Step 5: during chemotherapy Step 6: twice daily for 25 minutes (# of days not specified)	Licensed music therapist	Step 1: patient chose one piece to listen to followed by music discussion (grouped) Step 2: music assisted progressive muscle relaxation (individualized) Step 3: music imagery (individualized) Step 4: music breathing exercises (grouped) Step 5: playing musical instruments (grouped) Step 6: rhythmic music (grouped)
Reimnitz & Silverman, 2020	Music therapy	One 30-minute session	Licensed music therapist	Participants received patient-preferred live music (PPLM) music therapy, a practice where participants select preferred music for a licensed music therapist to play live.
Bates et al., 2017	Music therapy	One 30-minute session provided on day +1 and day +5	Licensed musical therapist	Sessions were individualized to each patient. Broadly, songs were usually performed live and sung by the music therapist. The therapist used a piano or guitar for accompaniment and singing along and instrument playing was encouraged. Music assisted relaxation was also provided through verbal prompts by the therapist.
Burrai et al., 2014	Active music	One 30-minute session each week for 4 weeks	Trained nurse	Participants selected 5-6 musical pieces of different styles (including relaxing, cheerful, and lively pieces), and genres (pop, classical, film scores, folk, and jazz) to be performed by a trained nurse on the saxophone.

Deng et al., 2021	Active music	30 minutes of music one hour before and after surgery	Trained researcher	Received general anesthesia for pain relief then chose five of their preferred music types from a list of 40 types.
Huang et al., 2010	Active music	One 30-minute session	Trained researcher	Participants chose between Taiwanese, Western, and Buddhist music. Music was sedative at 60-80 beats per minute, without lyrics, and with controlled volume and pitch, administered through headphones.
Li et al., 2011	Active music	Twice a day for 30 minutes each session throughout a 51-day hospital stay (on average)	Trained researcher	Given a choice of 202 music names and four types of music stored on an MP3 player, told to listen through headphones.
Miladinia et al., 2021	Active music	15-minute sessions provided 3 times weekly for 4 weeks for a total of 12 sessions	Trained nurse	Patients first focused on their breathing for 1 minute, then listened to self-selected music without lyrics using headphones. Music pieces were simple, with a rhythm of 60-80 bpm, low pitch, and controlled volume. Pieces included Persian traditional music, Iranian religious music, and nature-based sounds.
Arruda et al., 2016	Passive music	30 minutes per day for 3 days	Trained researcher	A series of instrumental songs were provided on an MP3 player and played through earbuds.
Tollabzadeh et al., 2023	Passive music	Two 20 minutes session each week for eight weeks	Trained Researcher	Participants selected their list of music from a mixture of classic, pop, Iranian, and meditation music.

Table 4: Quality Appraisal Results

Article	Appropriate Sample	Adequate Control	Generalizable Results	Consistent Recommendations	Quality Grade
Arruda et al., 2016	✓	✓	✓	✓	A, High Quality
Bates et al., 2017		✓		✓	B, Good Quality
Burrai et al., 2014	✓	✓	✓	✓	A, High Quality
Deng et al., 2021		✓		✓	B, Good Quality
Huang et al., 2010	✓	✓	✓	✓	A, High Quality
Li et al., 2011		✓		✓	B, Good Quality
Miladinia et al., 2021		✓		✓	B, Good Quality
Reimnitz & Silverman, 2020		✓		✓	B, Good Quality
Tang et al., 2021		✓		✓	B, Good Quality
Tollabzadeh et al., 2023	✓		✓	✓	B, Good Quality

Appendix A

Johns Hopkins Nursing Evidence-Based Practice Evidence Level and Quality Guide

Evidence Levels	Quality Guides
Level I Experimental study, randomized controlled trial (RCT) Systematic review of RCTs, with or without meta-analysis	A **High quality:** Consistent, generalizable results; sufficient sample size for the study design; adequate control; definitive conclusions; consistent recommendations based on comprehensive literature review that includes thorough reference to scientific evidence B **Good quality:** Reasonably consistent results; sufficient sample size for the study design; some control, fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence C **Low quality or major flaws:** Little evidence with inconsistent results; insufficient sample size for the study design; conclusions cannot be drawn
Level II Quasi-experimental study Systematic review of a combination of RCTs and quasi-experimental, or quasi-experimental studies only, with or without meta-analysis	
Level III Non-experimental study Systematic review of a combination of RCTs, quasi-experimental and non-experimental studies, or non-experimental studies only, with or without meta-analysis Qualitative study or systematic review with or without a meta-synthesis	
Level IV Opinion of respected authorities and/or nationally recognized expert committees/consensus panels based on scientific evidence Includes: • Clinical practice guidelines • Consensus panels	A **High quality:** Material officially sponsored by a professional, public, private organization, or government agency; documentation of a systematic literature search strategy; consistent results with sufficient numbers of well-designed studies; criteria-based evaluation of overall scientific strength and quality of included studies and definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years B **Good quality:** Material officially sponsored by a professional, public, private organization, or government agency; reasonably thorough and appropriate systematic literature search strategy; reasonably consistent results, sufficient numbers of well-designed studies; evaluation of strengths and limitations of included studies with fairly definitive conclusions; national expertise is clearly evident; developed or revised within the last 5 years C **Low quality or major flaws:** Material not sponsored by an official organization or agency; undefined, poorly defined, or limited literature search strategy; no evaluation of strengths and limitations of included studies, insufficient evidence with inconsistent results, conclusions cannot be drawn; not revised within the last 5 years

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