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Efficacy of non-medicinal approaches in treating side effects associated with cancer treatment

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BOSTON UNIVERSITY
SCHOOL OF MEDICINE

Thesis

**EFFICACY OF NON-MEDICINAL APPROACHES IN TREATING
SIDE EFFECTS ASSOCIATED WITH CANCER TREATMENT**

by

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B.A., Boston University, 2013

Submitted in partial fulfillment of the
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MICHAEL CAPUTO

ABSTRACT

In the United States, the golden standard of treatment for patients afflicted with cancer is adjuvant chemotherapy treatment. Chemotherapy treatment has proven efficacy in eradicating cancer cells, but the treatment itself is associated with a variety of negative side effects. Side effects such as nausea and vomiting have been effectively treated with anti-emetics, but other negative side effects, such as fatigue and reduced quality of life, have no proven pharmacologic agents that effectively treat them. The goal of this paper is to identify alternative approaches to treat the side effects associated with chemotherapy treatment.

This paper reviewed a large collection of literature concerned with determining the efficacy of exercise, music therapy, and spiritual techniques in reducing the magnitude of the negative symptoms associated with chemotherapy treatment. The data showed that exercise was the most effective therapy in reducing fatigue in cancer patients; meanwhile music therapy and spiritual techniques displayed efficacy in improving a patient's overall quality of life. However, further studies are needed in order

to definitively determine the efficacy of exercise, music therapy, and spiritual techniques as adjuncts to chemotherapy treatment.

This paper concluded that exercise, music therapy, and spiritual techniques have the potential to be effective tools that physicians can utilize when helping cancer patients alleviate the side effects associated with chemotherapy treatment. Moreover, exercise has shown the most evidence, through studies, as being an effective adjunct treatment to chemotherapy. Future research should focus on utilizing multiple therapeutic approaches in order to reduce the negative side effects associated with chemotherapy treatment.

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LIST OF ABBREVIATIONS

C-STAI.....	Chinese-STAI
EVAS.....	Emotional Visual Analog Scale
EORTC QLQ-C30.....	European Organization for Research and Treatment of Cancer, quality of life questionnaire
FACT-An-.....	Functional Assessment of Cancer Therapy-Anaemia Questionnaire
HADS.....	Hospital Anxiety and Depression Scale
HRQOL.....	Health-Related Quality of Life
L-PAM.....	L-Phenylalanine Mustard
MBSR.....	Mindfulness-based Stress Reduction
WHO.....	World Health Organization

INTRODUCTION

The use of chemotherapy to treat cancerous cells arose as a byproduct of the Second World War (DeVita & Chu, 2008). While conducting various experiments on potential chemical weapon agents, a compound known as nitrogen mustard was discovered, and the scientists studying this compound soon realized that nitrogen mustard was effective in treating lymphoma. This discovery soon led to the development of alkylating agents, which were compounds capable of destroying the DNA of cancerous cells. Eventually, in the mid-1970s, a researcher named Bernard Fisher completed the L-PAM study, which was concerned with the use of chemotherapy as an adjunct to surgery or radiation therapy (DeVita & Chu, 2008). The study found that treating cancer cells locally with surgery or radiation therapy, and then subsequently treating with chemotherapy to prevent secondary tumor formation was a more effective method of treatment than treating with chemotherapy alone (DeVita & Chu, 2008).

Following the advent of adjuvant chemotherapy treatment as the golden standard for cancer treatment, it was soon discovered that chemotherapeutics had multiple adverse side effects. Some of the major complaints of cancer patients undergoing chemotherapy treatment, besides nausea and vomiting, included fatigue, sleep disturbance, wake disturbance, and emotional disturbance-depression (Erickson et al., 2014). Current pharmacologic approaches focus on utilizing anti-emetic drugs in order to perturb the nausea and vomiting side effects, but there has been a lack of focus within the medical field to help subside the several other adverse side effects (Ropper & Samuels, 2009). However, recently, there has been a significant push within the medical field to look at

the effects of several non-pharmacologic approaches to improve the side effects of fatigue and depression. A study by Chalise (n.d.) demonstrated that alternative treatments such as exercise, spirituality involvement, and listening to music, were effective therapies in reducing the fatigue of cancer patients. However, one major concern from this study was the fact that alternative treatments such as spirituality involvement are more traditional practices, and the extent of their effectiveness on all cancer patients is unclear (Chalise, n.d.).

The literature has provided significantly positive evidence that the alternative practices of exercise and listening to music are effective in subsiding several of the negative side effects of chemotherapy treatment, mainly fatigue. One study conducted by Andersen et al. (2013) found that multimodal exercise intervention could reduce self-reported fatigue in cancer patients. However, a major problem within this study was the fact that its participants were comparatively younger, and better educated than the general cancer population (Andersen et al., 2013). Furthermore, a study conducted by Jacobsen et al. (2013) found that exercise alone fails to improve the depressive side effects associated with chemotherapy treatment. The study demonstrated that only combined intervention of exercise and self-directed stress management training was successful in improving depression, and these results are displayed in figure 1 (Jacobsen et al., 2013). Thus, although an exercise routine was successful in reducing fatigue in cancer patients undergoing chemotherapy, exercise's ability to alleviate depression in cancer patients was dependent on utilization of self-directed stress management techniques.

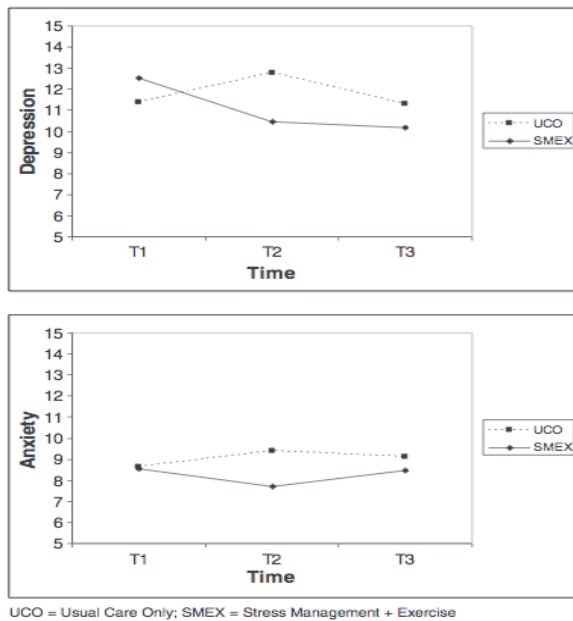


Figure 1. Depression and Anxiety Scores Decrease with Combined Stress Management and Exercise. 286 patients were assessed on depression and anxiety scores at 6 and 12 weeks following either usual care or a combination of stress management and exercise while undergoing chemotherapy. Figure taken from Jacobsen et al., 2013.

Whereas the literature has found that exercise leads to objective improvements in fatigue for cancer patients, studies concerned with listening to music and its effect on cancer patients are divided. O’Callaghan et al., (2012) illustrated that for some cancer patients, music was effective in improving a patient’s quality of life. However, the study also found that some cancer patients found music to induce too many negative emotions (O’Callaghan et al., 2012). A significant problem with this study was the fact that most participants had a musical background, and thus the results may not represent the effect of music on the general cancer population. Another study conducted by Romito et al., (2013) provided a small number of breast cancer patients with a single integration intervention of music therapy during chemotherapy treatment, and the results

demonstrated that music was able to reduce negative emotions felt by these patients, as well as improve depressive side effects.

The current scientific literature on alternative approaches to treating side effects associated with chemotherapy treatment demonstrates that approaches such as exercise and listening to music are two viable options that can subside some of the adverse side effects of chemotherapy treatment. However, the role of these two alternative treatments for treating side effects associated with specific types of chemotherapeutic agents remains ambiguous. Moreover, the use of therapies, mainly spiritual involvement, remains controversial due to the fact that such therapies depend on the individual being treated.

BACKGROUND

What is Cancer?

Cancer arises in individuals, when such individuals experience nonlethal genetic damage to certain genes within their genome (Murray, Jacob, & Varghese, 2012). The four types of genes that can lead to the development of cancer include: proto-oncogenes, tumor suppressor genes, genes involved in DNA repair, and genes involved with the apoptotic process (Murray et al., 2012). When one of these four types of genes undergoes a mutation, there is an increased risk for the damaged gene to start to multiply, eventually resulting in the formation of a malignant tumor (Murray et al., 2012). Figure 1 shows a schematic on how proto-oncogenes and tumor suppressor genes can be altered, eventually resulting in the development of cancer. The growth rate of a malignant tumor is mainly dependent on the specific type of cancer that an individual is afflicted with, and thus, a tumor may take anywhere between months to several years in order to develop (Murray et al., 2012).

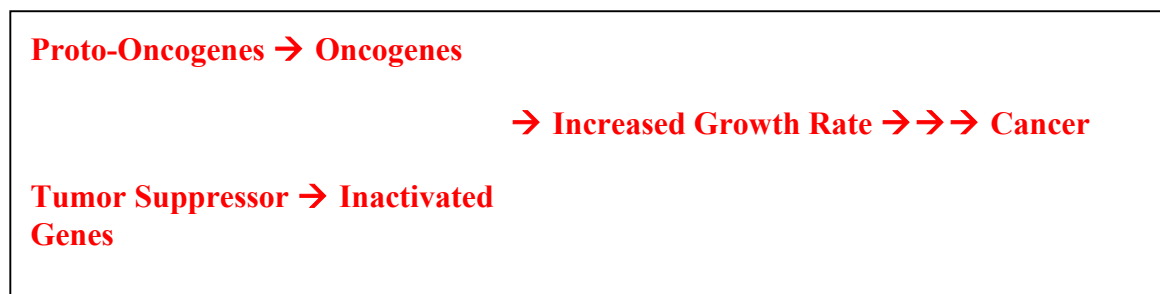


Figure 2. Alterations in either Proto-Oncogenes or Tumor Suppressor Genes Leads to Cancer. Proto-Oncogenes can become activated and subsequently become Oncogenes leading to increased growth rate of cells. Tumor Suppressor genes can become inactivated, releasing inhibition of growth, thus resulting in increased growth rate of cells. Modified from Murray et al.: Harper's Illustrated Biochemistry, 29th edition.

There are several distinguishing features that characterize cancer cells. The first distinguishing feature is that cancer cells multiply rapidly, and have a diminished ability to control growth (Murray et al., 2012). Cancer cells demonstrate the ability to both control their own growth signals, as well as ignore the growth-inhibiting signals from outside sources within the body. The proliferation of cancer cells is further supplemented by cancer cells' ability to both stimulate angiogenesis, as well as their ability to avoid programmed cell death. Also, cancer cells, when untreated for a long time or after becoming insensitive to treatment, have the ability to invade local tissues and metastasize.

Genetic damage to a person's genome can be attributed to genetic factors, or the mutations can arise from prolonged exposure to carcinogenic substances that pervade within the environment (Murray et al., 2012). Genetic mutations leading to malignant tumors as a result of hereditary factors account for an estimated 5% of reported cancer cases. Specific genes, such as tumor suppressor genes and proto-oncogenes, are the genes that are mainly affected by genetic mutations arising from hereditary factors. Though 5% of cancer cases arise due to hereditary factors, a majority of reported cancer cases are due to exposure to environmental carcinogens, as cited by Murray et al. (2012). Such environmental carcinogens include exposure to radiant energy, such as ultraviolet rays, exposure to carcinogenic chemical compounds, and exposure to tumor viruses, such as the human papilloma virus, which acts by integrating its viral DNA into its host DNA in order to disrupt essential processes that are imperative in preventing the development of

cancerous cells. Table 1, below, displays several examples of types of environmental carcinogens.

Table 1. Examples of Environmental Carcinogens. Current environmental carcinogens that persist in the environment.

Type of Environmental Carcinogen	Examples
Radiant Energy	Ultraviolet Rays, X-Rays, Gamma Rays
Carcinogenic Chemical Compounds	Polycyclic aromatic hydrocarbons, aromatic amines, nitrosamines, various drugs, naturally occurring compounds
Tumor Viruses	Epstein-Barr virus, Hepatitis B, Hepatitis C, Human herpes virus type I, Human papilloma virus, Human T-cell leukemia virus type 1

Of the estimated 95% of cancer cases arising from environmental carcinogens, approximately 80% of those cancer cases are the result of exposure to chemical compounds (Murray et al., 2012). A few examples of chemical compounds that have been implicated in causing cancer in humans include: pesticides, aromatic hydrocarbons, and metals (Boers et al., 2005). In terms of pesticides, an organochlorine compound, referred to as DDT, is a well-known example of a known carcinogenic pesticide. DDT came out in the 1930s, and it was initially used in military operations in World War II because it was extremely important in the control of malaria, as well as the protection of soldiers against acquiring malaria (Carson, 1962). Its toxicity was only really appreciated in response to a text by Rachel Carson entitled *Silent Spring*, which heightened public's awareness of the fact that DDT had a long persistence in the environment. Eventually, DDT was utilized as an insecticide because it had the ability to activate sodium channels in insects, resulting in the paralysis and eventual death of the insects. DDT was eventually banned from use in the US (Carson, 1962). In terms of carcinogenic aromatic

hydrocarbons, benzene and benzopyrene are two examples of aromatic hydrocarbons that have been implicated in increasing one's risk for leukemia and lung cancer, respectively (Murray et al., 2012). These hydrocarbons act by oxidizing either cytochrome P450 enzymes and/or epoxide hydrolase leading to the generation of mutagenic metabolites. Finally, in terms of metal compounds, compounds such as beryllium and nickel subsulfide have been implicated in causing a variety of different types of cancers, most notably, lung cancer. Substances, such as the ones listed above, are tested for carcinogenicity through the Ames Test, which is a powerful tool in testing the mutagenic potential of chemicals.

Based on data collected by the National Cancer Institute (2011), in the United States, there will be an estimated 1,665,540 new cases of cancer in 2014, as well as an estimated 585,720 deaths as a result of cancer. In 2011, the National Cancer Institute found that approximately 13,397,159 people were living with cancer in the United States. Moreover, for both males and females, it is approximated that 40.8 percent of people will be diagnosed with cancer within their lifetime (National Cancer Institute [NIH], 2011). Currently, cancer is the second leading cause of death within the United States, behind heart disease, but it is predicted that cancer will become the predominant form of mortality in the US within the next 15 years. The median age of cancer diagnosis is 66 years old, while the median age of mortality as a result of cancer is 72 years old. Males have a higher incidence of cancer as compared to females. Furthermore, African Americans, Non-Hispanics, and Caucasians have both the highest incidence of cancer amongst ethnic groups, as well as the highest incidence of mortality from cancer amongst

ethnic groups (NIH, 2011). Cancer incidence in the United States has taken center stage within the media in recent years, with many scientific researchers focusing their research on discovering innovative methods to both diagnose, as well as treat certain types of cancers. Figure 3 demonstrates the trends in both the incidence and mortality of cancer within the United States over the last thirty years.

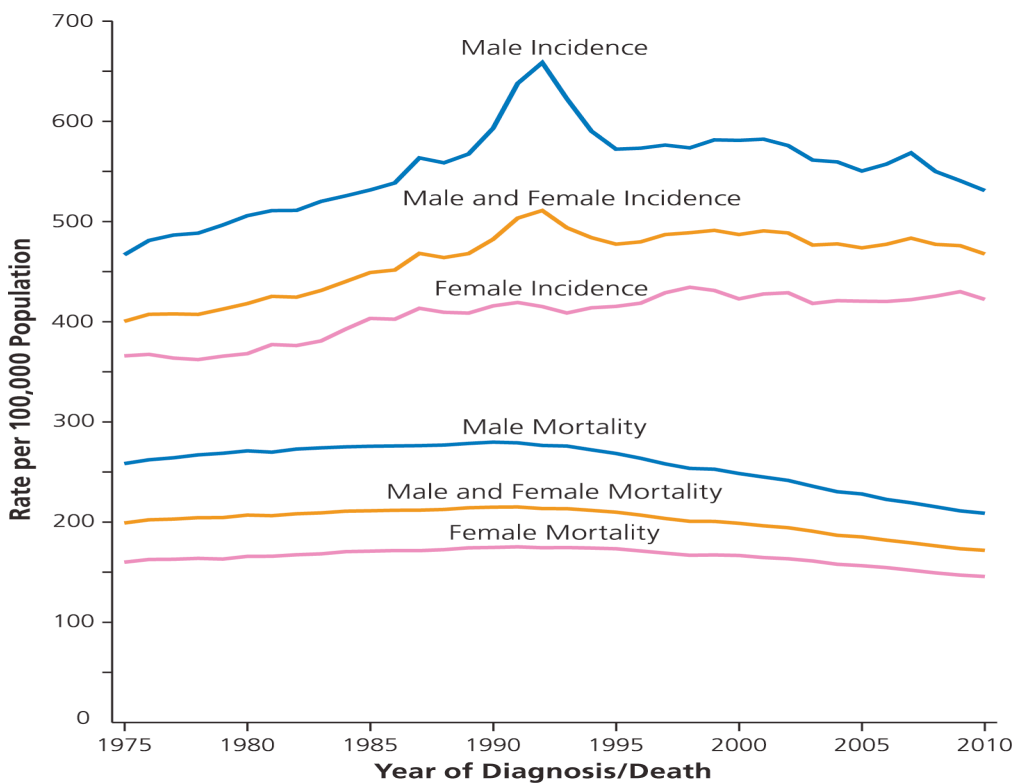


Figure 3. Trends in Cancer Incidence and Mortality in the United States between 1975 and 2010. Incidence of cancer has remained relatively steady from 1975 to 2010, except for a spike in incidence in the early 1990s. Cancer mortality has decreased from 1975 to 2010. Figure taken from Siegel et al., 2014.

Chemotherapy Treatment for Cancer Patients

Presently, the golden standard of treatment for individuals afflicted with locally advanced cancer is adjuvant chemotherapy treatment. Adjuvant chemotherapy treatment

is basically a combined therapeutic approach, consisting of radiation therapy and/or surgery, and then subsequent chemotherapy treatment (Chu & Sartorelli, 2012). Adjuvant chemotherapy is utilized in patients in order to both decrease the likelihood of cancer recurrence, as well increase a patient's overall survival. However, chemotherapy treatment can also be utilized as the primary method of treatment in some patients where the cancer has metastasized and no other methods of treatment are effective, or it can be utilized in patients who have localized cancer, but alternative treatments are not completely efficacious in eradicating the cancer. Utilizing these standardized methods of treatment, it has been estimated that 50% of patients initially diagnosed with cancer will be cured (Chu & Sartorelli, 2012). Furthermore, chemotherapy treatment has a much higher cure rate when combined with surgery and/or radiation therapy, as compared to when it is utilized as the primary method of treatment (Chu & Sartorelli, 2012).

Several chemotherapeutic agents exist today, and the type of chemotherapeutic agent utilized for treatment is dependent on the type and stage of cancer a person has. Types of anticancer agents include: cytotoxic drugs, hormones and antagonists, monoclonal antibodies, and anti-angiogenic agents. Cytotoxic drugs are drugs that will kill any cell, and were the first anticancer agents discovered. Antimetabolites, alkylating agents, antibiotics, such as topoisomerase inhibitors, and plant alkaloids, such as microtubule inhibitors are the four classes of cytotoxic drugs. Antimetabolites were discovered in the 1950s and they are drugs that block the synthesis of purines and pyrimidines. Alkylating agents are drugs that are highly chemically reactive and are capable of alkylating DNA, most commonly at the N7 position of guanine, eventually resulting in cell death.

Topoisomerase inhibitors act on the coiling and uncoiling of DNA, and effectively inhibit cell replication. Microtubule inhibitors are agents that interfere with the actions of microtubules and thus block mitosis, ultimately preventing cell division. Examples of the four types of cytotoxic drugs are listed in Table 2, along with their respective mechanisms of action, as well as their adverse side effects. In terms of hormones and antagonists, there exists tumor cells that are hormone dependent, and thus strategies have been developed in order to block endogenous hormones and prevent the development of tumors (Chu & Sartorelli, 2012). In terms of monoclonal antibodies, there are drugs that act by specifically targeting a site on a protein of a cancer cell, effectively destroying that cell. Lastly, anti-angiogenic agents are drugs that act on a protein critical in solid tumors for promoting the development of blood vessels within the tumor. By preventing the development of new blood vessels, tumors are unable to retrieve the proper nutrients needed for replication, and thus cell replication is inhibited.

Within the clinical setting, oncologists commonly implement chemotherapy regimens in order to treat a patient diagnosed with cancer. Standard chemotherapy treatment protocols, such as ABVD, are common in identifying combinations of drugs used for treatment in cancer chemotherapy. The goal of combination chemotherapy treatment is to put together drugs with differing target sites, thus improving the efficacy of the treatment, as well as lowering the toxicity of the treatment, ultimately improving the therapeutic index of the treatment. The utilization of several chemotherapeutic agents is also imperative in slowing the development of drug resistance, further increasing the effectiveness of the drug regimen. Selection of specific chemotherapeutic regimens is

based on five principles: efficacy, toxicity, optimum scheduling, mechanism of interaction, and avoidance of arbitrary dose changes (Chu & Sartorelli, 2012). An effective drug is a drug that has high efficaciousness, low toxicity, is utilized at its most advantageous dose and schedule, is well understood mechanistically, and does not need a reduction in dosage in order to incorporate another drug into the regimen.

Upon careful selection of an effective drug regimen, the main limitation that prevents chemotherapeutic agents from achieving cure is dose intensity (Chu & Sartorelli, 2012). Due to the fact that many chemotherapeutic agents are highly toxic, and can result in several adverse effects, it is common practice for clinicians to alter the dose or the dosing regimen in order to reduce the toxicity side effects. However, because the therapeutic window for chemotherapeutic agents is extremely sensitive, as evidenced by animal model studies, a slight reduction in dosage could potentially eliminate the therapeutic effect of the chemotherapeutic agent (Chu & Sartorelli, 2012). In order to avoid the loss of a chemotherapeutic regimen's efficacy, clinicians implement three specific strategies: drug escalation, reducing the interval, and sequential scheduling (Chu & Sartorelli, 2012). Drug escalation deals with escalating the doses of the chemotherapeutic agents. Reducing the interval is associated with decreasing the amount of time between treatment cycles. Sequential scheduling is associated with chronological administration of single chemotherapeutic agents or of chemotherapeutic regimens. Though these strategies have proven to be effective in improving clinical outcomes, the strategies also lead to exacerbation of adverse side effects, due to the fact that the strategies are quite aggressive.

The types of adverse side effects that cancer patients experience as a result of chemotherapy treatment is dependent on the chemotherapeutic agent that is utilized for treatment. For example, cisplatin, which is a platinum analog chemotherapeutic agent that has a similar mechanism of action as compared to alkylating agents, is used to treat several types of cancer, including lung cancer, and it causes a vast array of side effects ranging from nausea and vomiting to nephrotoxicity, peripheral sensory neuropathy, ototoxicity, and nerve dysfunction (Chu & Sartorelli, 2012). However, nearly all-chemotherapeutic agents utilized to destroy neoplastic cells result in nausea, vomiting, myelosuppression, fatigue, and depression. A common feature of many cancer chemotherapeutics is that they are emetics; the chemotherapeutic drugs activate 5HT₃ receptors within the GI tract, which results in excitation of neurons, eventually leading to the induction of nausea and vomiting (Sharkey & Wallace, 2011). Chemotherapeutic agents also are toxic to the bone marrow of patients, resulting in bone marrow suppression, and a subsequent reduction in the creation of leukocytes, erythrocytes, and thrombocytes, which are cells that play important roles in immunity, oxygen transport, and blood clotting, respectively. Furthermore, fatigue and depression side effects develop in many cancer patients as a result of the nausea, vomiting, myelosuppression, and aggressive nature associated with the chemotherapeutic treatment.

Table 2. Examples of Common Cytotoxic Drugs used as Chemotherapeutic Agents.
Table modified from Lange: Basic & Clinical Pharmacology, 12th edition, 2012.

Type of Chemotherapeutic Drug	Generic Name of Drug	Mechanism of Action	Adverse Effects
Alkylating Agent	Cisplatin	Forms intrastrand and interstrand DNA cross-links; binding to nuclear and cytoplasmic proteins	Nausea, vomiting, nephrotoxicity, peripheral sensory neuropathy, ototoxicity, nerve dysfunction
Antimetabolite	Methotrexate	Inhibits Dihydrofolate reductase, inhibits thymidine synthase, inhibits de novo purine nucleotide synthesis	Mucositis, diarrhea, myelosuppression with neutropenia and thrombocytopenia
Antibiotics	Etoposide	Inhibits topoisomerase II	Nausea, vomiting, hypotension, alopecia, myelosuppression
Plant Alkaloids	Docetaxol	Inhibits mitosis	hypersensitivity, neurotoxicity, fluid retention, myelosuppression with neutropenia

Introduction of Palliative Care

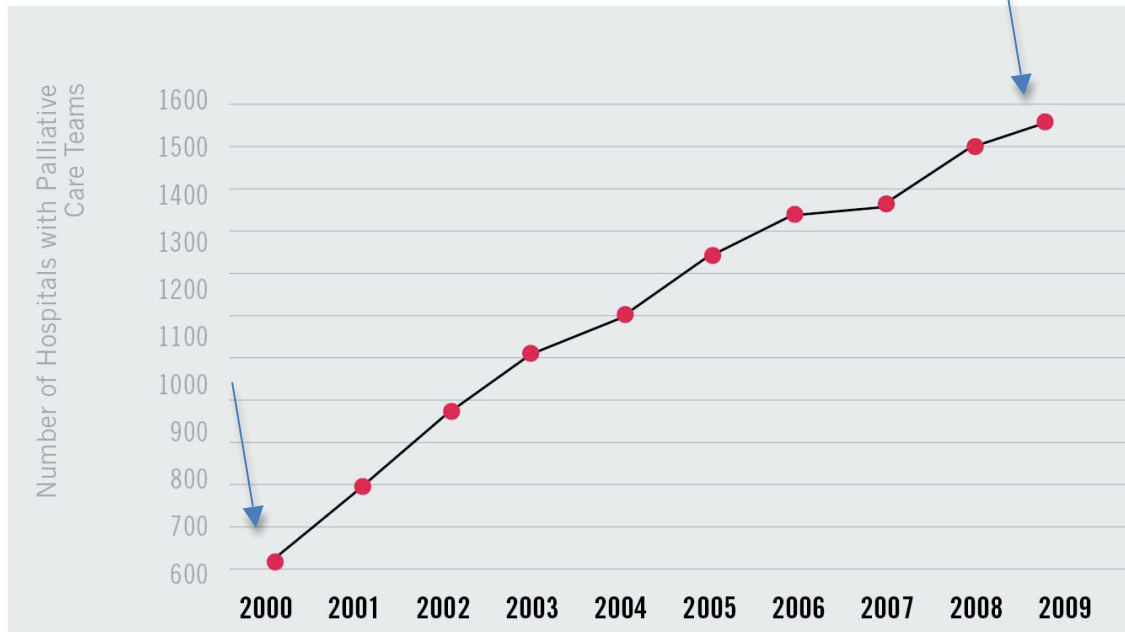
Though chemotherapeutic agents are associated with several debilitating side effects, modern medicine has made it possible to alleviate many of those negative side effects through palliative care. In the early 1950s, medical experts were more focused on finding a cure for patients suffering from cancer, as opposed to both treating the patient's illness, as well as the side effects that were associated with the treatment of the illness (Clark, 2007). In the 1960s, Cicely Saunders, a research fellow at St. Joseph's Hospice in Hackney, London, UK, began interviewing patients about their personal experiences while combating a terminal illness. What soon emerged from her research was a striking pattern of patients reporting extensive physical and mental suffering as a result of the terminal illness. Saunders soon began to push for clinicians to prescribe analgesic agents

in order to help prevent the constant pain that the many patients suffering from terminal diseases felt. At the same time that palliative care began to emerge as a common clinical practice, President Richard Nixon, who declared a “war on cancer” in 1971, thrust cancer into the forefront of the public eye. Soon, in 1982, the World Health Organization enlisted palliative care experts in order to help develop a standardized method for cancer pain relief. Though the attempt by the WHO to develop a program for cancer pain relief was relatively unsuccessful, the WHO managed to initiate the integration of palliative care into oncological curative treatment programs.

Today, palliative care is an integral part of the treatment plan for cancer patients, and those suffering from terminal illnesses. Figure 4 shows how palliative care has been growing steadily within US hospitals. However, as Gaertner et al. (2014) found, there still remains ambiguity in terms of what the specific aims of palliative care are, and it is essential for organizations such as the WHO to clearly define the goals of palliative care. Moreover, Aaist-Cohen et al. (2008) conducted a survey on 37% of medical schools within the United States assessing the extent and manner that palliative care is incorporated in the United States medical school curriculum. These authors found that 30% of responding schools included palliative care within their curriculum, 19% included palliative care as a rotation, 15% offered palliative care as an elective course, 29% offered palliative care as an elective rotation, and 53% of schools integrated palliative care into required courses. These results demonstrate that medical schools in the United States have not fully educated future physicians on palliative care, and thus there is a need for greater attention to provide palliative care education to future healthcare

professionals in order for palliative care to be properly administered to patients when needed.

Prevalence of U.S. Hospital Palliative Care Teams 2000–2009



Source: Center to Advance Palliative Care, March 2011

Figure 4. Prevalence of U.S. Hospital Palliative Care Teams between 2000 – 2009. The number of hospitals with palliative care teams has been increasing since 2000. Figure modified from CAPC Report Card, 2011.

Though palliative care is still a growing field, there still are several medicinal approaches that palliative care specialists utilize in order to alleviate some of the side effects associated with cancer treatment. For example, patients undergoing chemotherapy treatment are commonly prescribed anti-emetics, which act as 5HT3 receptor antagonists, and subsequently prevent the nausea and vomiting that coincides with chemotherapy treatment (Sharkey & Wallace, 2011). Also, in order to treat the myelosuppression that

many cancer patients experience, physicians administer growth factors for cells made in the bone marrow, such as GM-CSF for neutrophils or erythropoietin for red blood cells, which stimulate replication of precursor cells in the bone marrow (Yuen & Giralt, 2011). Furthermore, depressive side effects are commonly treated with anti-depressive agents, such as Prozac, which is a selective serotonin reuptake inhibitor (DeBattista, 2012). However, in terms of fatigue, there are currently no proven medicinal treatments that effectively alleviate fatigue in cancer patients. Peuckmann-Post et al. (1996) found that even though several drugs exist on the market that have the potential to improve fatigue in patients, such as amantadine and methylphenidate, there is no full consensus within the medical field as to which drugs should be utilized to treat fatigue. There are, however, several non-medicinal approaches currently being investigated by scientific researchers that have shown promising results in improving the quality of life of cancer patients.

Positive Effects of Exercise, Music, and Spirituality

Three of the most common non-medicinal approaches that patients have cited as being helpful in improving their quality of life are exercise, music, and spirituality/religion (Chalise et al., 2012). The positive aspects of exercise on improving quality of life and preventing disease have been extensively studied for many years. In 1996, Dr. Elrick, a medical doctor with an extensive background in understanding the positive effects of exercise, wrote an article concerning how physicians can prescribe exercise therapy in order to treat diseases (Elrick, 1996). In terms of cardiovascular health, exercise could be utilized in order to improve heart function, as well as reduce hypertension, cholesterol levels, and low-density lipoprotein levels (Elrick, 1996).

Moreover, Erlick found that exercise could be utilized to combat both diabetes and obesity. Daily exercise can help reduce weight in obese individuals, as well as both correct abnormal blood lipid patterns that have been implicated in diabetes, and increase an individual's sensitivity to insulin by increasing sugar metabolism within that individual (Erlick, 1996). Exercise has also been cited as a potential therapy for cerebrovascular disease, arthritis, osteoporosis, dyslipidemia, depression, cancer, and COPD (Erlick, 1996).

In terms of music, the positive affects that music offers have been utilized for centuries, dating back all the way to ancient Greece. The true advent of music as a tool for therapy emerged following both World War I and II, when musicians would visit hospitals to play music for the wounded soldiers ("Music Therapy," 2014). Today, there is much research concerned with the potential positive benefits that music offers in order to help treat certain disease states. For example, in children, music therapy has been utilized in autism patients to help improve various social deficits that these patients face (Crowe & Colwell, 2007). Moreover, music has strong implications on the lives of adolescents, particularly in helping adolescents achieve a sense of identity, cope with tough situations, and develop a sense of independence (Laiho, 2004). Most notably, music therapy has been utilized in an array of neurological and psychological disorders. For example, a study conducted by Nayak et al. (2000) found that music therapy could potentially be utilized as a supplemental therapy for patients who suffered a stroke in order to improve social functioning and participation in rehabilitation. Music therapy has also been indicated in depression. Chan et al. (2009) found that music therapy in patients

suffering from depression, led to decreases in both depressive scores and blood pressure in those patients.

Lastly, spirituality, similar to music therapy, has also been a source of healing for centuries. For example, in ancient Greece, society members prayed to Asclepius, known as the Divine Physician, in order to help heal wounded or diseased individuals. A study conducted by Rew and Wong (2006) discovered that spirituality might potentially be an important factor in improving adolescent health and behavior. Furthermore, a second study conducted by Bonelli and Koenig (2013) found further positive correlation between spirituality and improvement in mental health in the areas of depression, substance abuse, suicide, stress-related disorders, and dementia. However, the extent that spirituality provides a positive influence has not been completely corroborated by research studies. The main limitation that prevents attainment of conclusive data on spirituality and its effects on improving disease states is the fact that individuals have differing levels of spirituality. However, current research is beginning to focus on figuring out potential ways to utilize an individual's spirituality as a source of healing within the clinical setting. For example, one paper published by Moreira-Almeida et al. (2014) provided guidelines for assessing a patient's spirituality, and subsequently utilizing a patient's spirituality in order to help treat their disease.

Exercise, Music, and Spirituality as Resources for Palliative Care in Cancer Patients

The role of exercise as a therapy for cancer patients is particularly intriguing. Early epidemiological evidence has suggested that physical training can protect against certain types of cancers. In one prospective study conducted by Holmes et al. (2005) on

approximately 3000 females diagnosed with stage 1, 2 or 3 breast cancer, it was found that women who walked the equivalent of 3 to 5 hours a week reduced their risk of death from the disease. These results are further supported by data published by Segal et al. (2001), which found that 6 months of aerobic training resulted in improvement in both fitness and physical functioning in patients with Breast Cancer. Though exercise has proven positive effects on patients afflicted with cancer, up until recently, studies have been too broad on researching the particular aspects that exercise helps to improve in patients with cancer. Current studies are now focusing on how exercise can be integrated before, during, and after chemotherapy treatment in order to improve both fatigue and quality of life in cancer patients. It is imperative that researchers focus on establishing a method to train physicians on how to successfully integrate a personalized physical training method for patients undergoing a chemotherapy regimen in order to optimize the effects that exercise has to offer for cancer patients.

Music therapy is a second resource that can be utilized as a palliative care option to treat the side effects associated with chemotherapy treatment. Music therapy has been utilized in the clinical setting as a tool for palliative care, and it has demonstrated positive results. In a study conducted by Gutsell et al. (2013) where 200 patients were randomly assigned to either receive standard care or standard care with music therapy, it was found that there was a significant reduction in pain scores for patients who had their care supplemented with music therapy. Though music therapy has demonstrated positive results in helping patients, there still remains a lack of sufficient studies to determine the true efficacy of music therapy, especially music therapy utilized to improve the quality of

life of cancer patients. Korczak et al. (2013) conducted an analysis of the current literature concerned with the use of music therapy for palliative care, and they discovered conflicting results. They concluded that there is a need for higher quality studies on music therapy in order to understand the true effects that music therapy offers to patients. Though research on music therapy for cancer patients undergoing chemotherapy treatment has been lacking in the past, recently, there has been a push to determine the efficacy of music therapy in improving the quality of life of cancer patients.

One last resource that can be utilized in palliative care for cancer patients undergoing chemotherapy treatment is spirituality. As stated previously, the efficacy of spirituality in palliative care is not completely understood. It has been documented that spirituality aids patients in finding meaning in their suffering. Dr. Puchalski (2012), researching the role of spirituality in health care, found that spirituality helps patients with mortality, coping, and recovery. It has been proposed that spirituality possibly increases lifespan through improving stress control (Puchalski, 2012). In terms of coping, one cited study reported that 93% of 108 women claimed that spirituality was a significant factor in helping them cope with gynecological cancer. Interestingly, it was found that 49% of those patients had become more spiritual after their diagnosis (Puchalski, 2012). Furthermore, Young et al. (2014) found that patients who had undergone a significant cardiac event, also found spirituality to provide greater meaning and purpose in their lives, and led to an easier transition in coping with their life-threatening illness. Thus, cancer appears to lead more people to lean on spirituality as a source for coping with their illness, and spirituality can therefore be utilized as an effective tool to improve patients' quality of life. Specifically,

spirituality has the ability to improve the quality of life of patients undergoing chemotherapy treatment.

The positive influences that exercise, music therapy, and spirituality have on improving disease state are well published within the literature. In particular, the positive aspects that exercise offers to patients are well corroborated by published data. The positive effects that both music therapy and spirituality offer are encouraging, but further research is needed in order to definitively determine that music therapy and spirituality should be utilized within the clinic in order to help improve patient outcomes. However, exercise, music therapy, and spirituality all have the ability to be excellent palliative care resources for cancer patients undergoing chemotherapy treatment. Exercise can be utilized to improve fatigue in cancer patients, and both music therapy and spirituality can be utilized to improve the depressive side effects associated with chemotherapy treatment.

Specific Aims/Objectives

Previous studies have demonstrated that alternative treatments, such as exercise and listening to music, are effective treatments for improving fatigue, anxiety, and depression, which are side effects associated with chemotherapy treatment. However, there has not been significant scientific research that has focused on developing specific methods on how to successfully integrate these alternative therapies into the lives of patients undergoing chemotherapy treatment. Specifically,

1. The effectiveness of exercise, music therapy, and spirituality before, during, and after chemotherapy treatment in cancer patients will be examined.
2. The ability for exercise, music therapy, and spirituality to lower fatigue and depression in patients will be examined.
3. The efficacy of certain types of exercises and certain types of music to improve fatigue and depression in cancer patients undergoing chemotherapy will be determined.

It is hypothesized that fatigue and depression scores in cancer patients undergoing chemotherapy treatment will significantly decrease while exercising and listening to music before, during, and after chemotherapy treatment, with the most significant improvement displayed after chemotherapy treatment. The efficacy of spirituality will most probably be dependent on how spiritual a patient is during chemotherapy treatment, so fatigue and depression scores will most likely vary. These results can provide insight into potentially new strategies for combating several of the negative side effects associated with chemotherapy treatment.

PUBLISHED STUDIES

Before discussing the efficacy of exercise, music therapy, and spirituality in treating patients suffering from the adverse side effects of chemotherapy treatment, it is imperative to determine how the adverse side effects of cancer treatment affect the lives of cancer patients. Li et al. (2014) conducted a study where they determined how chemotherapy treatment affected the health-related quality of life of Chinese elderly patients with advanced cancer. The study surveyed 109 elderly patients, who were 60 years of age or older, being treated for advanced cancer with chemotherapy treatment (Li et al., 2014). The survey utilized assessed the HRQOL, anxiety, and depression of the cancer patients (Li et al., 2014). HRQOL was evaluated through the Medical Outcomes 36-Item Short Form Health Survey, as well as the European Organization for Research and Treatment of Cancer, quality of life questionnaire (Li et al., 2014). Both surveys assessed general health, physical functioning, role functioning, emotional health, cognitive functioning, social functioning, and adverse side effects associated with chemotherapy treatment, such as fatigue and pain (Li et al., 2014). Anxiety and depression in the cancer patients was assessed through the Hospital Anxiety and Depression Scale (Li et al., 2014). It was found that both financial impact and fatigue were the most significant factors associated with chemotherapy treatment, as reported by patients. Moreover, anxiety and depression had a strong impact on HRQOL (Li et al., 2014). However, this study may not be completely generalizable to all cancer patients since the study only looked at elderly patients with advanced cancer.

Ancoli-Israel et al. (2014) conducted a similar study that assessed the quality of life of breast cancer patients both before and after chemotherapy treatment. The study enrolled 68 women with stage 1 to stage 3 breast cancer, who were to undergo greater than or equal to four treatments of chemotherapy (Ancoli-Israel et al., 2014). The study matched participants with 60 controls who were cancer-free based on age, ethnicity, and education. Three different scales were assessed: sleep, fatigue, and depression. Sleep was analyzed using both actigraphy and the Pittsburgh Sleep Quality Index, which assessed both nocturnal total sleep time and daytime total naptime. Fatigue was measured through the Fatigue Symptom Inventory-Short Form. Lastly, the researchers measured depression through the Center of Epidemiological Studies-Depression. The study participants were evaluated before chemotherapy treatment, at the end of the fourth cycle of chemotherapy treatment, and then 1 year post-chemotherapy (Ancoli-Israel et al., 2014). It was found that compared to controls, patients with breast cancer displayed worse sleep quality, greater fatigue, increased depressive symptoms, increased disrupted circadian rhythms, and worse quality of life at baseline. When patients were evaluated at the fourth cycle of chemotherapy treatment, the cancer patients all displayed worse ratings for all factors assessed as compared to baseline (Ancoli-Israel et al., 2014). One year after chemotherapy treatment, fatigue, depression, and quality of life levels for breast cancer patients all returned to baseline, but the levels were still worse as compared to controls (Ancoli-Israel et al., 2014). Figure 5 shows the changes in sleep, fatigue, and depressive symptoms that breast cancer patients experienced as a result of chemotherapy treatment. The study conducted by Ancoli-Israel et al. (2014) was still limited in terms of its

generalizability due to the fact that the participants were only females with stage 1 to stage 3 breast cancer from a single geographic region. The results provide some evidence for the need to address the side effects associated with both cancer and chemotherapy treatment, but broader studies are needed for more definitive proof.

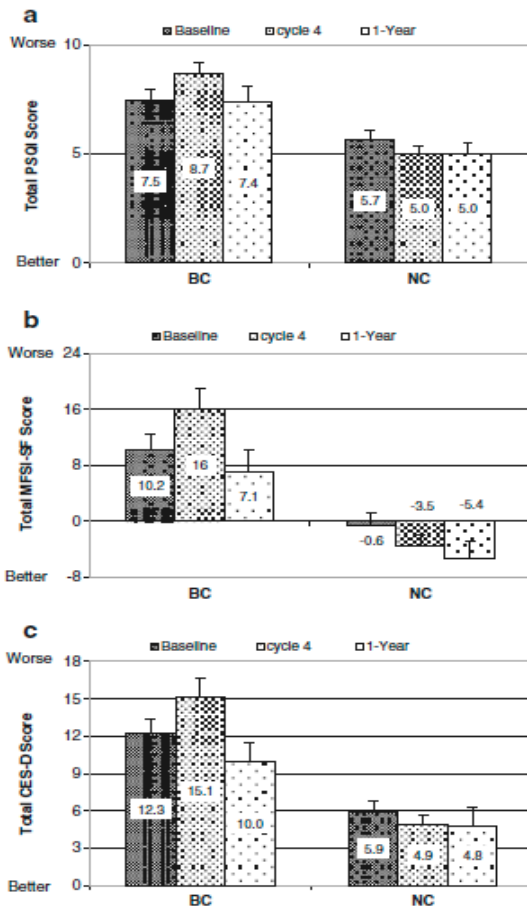


Figure 5. Changes in Sleep (a), Fatigue (b), & Depressive Symptoms (c) as a Result of Chemotherapy Treatment for Breast Cancer Patients (BC) as Compared to Cancer-free Controls (NC). Sleep, fatigue, and depressive symptoms all worsen as compared to baseline after cycle 4 of chemotherapy treatment for breast cancer patients. Figure taken from Ancoli-Israel et al., 2014.

To determine how debilitating chemotherapy treatment was to cancer patients, Wang et al. (2014) conducted a study that aimed to discover the extent of how severe fatigue was to cancer patients. They enrolled 3123 patients who suffered from breast,

prostate, colorectal, or lung cancer, and were either undergoing chemotherapy treatment or were following up with a physician at an outpatient setting. Fatigue was measured using the M.D. Anderson Symptom Inventory, which rated fatigue on a scale of zero to ten, with zero representing no fatigue, and ten representing severe fatigue. Study participants also were asked to rate their overall quality of life as excellent, good, fair, poor, or very poor. Wang et al. (2014) found that for the 2177 patients actively undergoing treatment, 55% responded to having no or mild fatigue and 45% responded to having moderate to severe fatigue. The authors also found that for the 515 patients labeled as cancer survivors, and not undergoing cancer treatment, 71% responded to having no or mild fatigue and 29% responded to having moderate to severe fatigue. In terms of type of cancer, Wang et al. (2014) found that fatigue affected patients regardless of the specific type of cancer the patients had. Due to the fact that fatigue has large implications on the daily activity of patients undergoing chemotherapy treatment, the study demonstrates a strong need for clinicians to have the necessary tools to assess and evaluate the extent of fatigue in cancer patients. Moreover, the study also substantiates the need for finding effective treatments for subsiding fatigue in cancer patients in order to improve the quality of life of such patients. The main limitation for this study was the fact that the scale used to rate fatigue was objective in nature, and a more subjective rating system would be needed in order to determine the actual extent of fatigue in cancer patients (Wang et al., 2014). However, the study still illustrates a need to both assess and treat the adverse effects associated with cancer treatment due to the fact that there was a high prevalence of moderate to severe fatigue in cancer patients undergoing treatment.

To demonstrate a need for managing fatigue and pain associated with chemotherapy treatment, Ediebah et al. (2014) analyzed data from a lung cancer trial study that had enrolled 391 patients afflicted with non-small-cell lung cancer in order to compare chemotherapy regimens. Patients in this lung cancer trial had advanced stage non-small-cell lung cancer, and were between the ages of 18 and 76. Patients were administered different regimens of chemotherapeutic drugs every 3 weeks. The chemotherapeutic drugs that were utilized in the trial were paclitaxel, cisplatin, and gemcitabine. Health-related quality of life was recorded in the patients through the EORTC QLQ-C30 and QLQ-LC13, which are questionnaires that assess the quality of life in the generalizable cancer population and also the lung cancer population, respectively. Higher scores in the questionnaire represented an increased functioning level. Patients were assessed pretreatment, as well as following each chemotherapy regimen (Ediebah et al., 2014). It was found that every 10-point increase from baseline levels in pain and dysphagia was correlated with an 11% and 12% greater risk of death, respectively. Moreover, a 10-point increase in physical function from baseline was associated with a 7% decrease in mortality (Ediebah et al., 2014). For specific chemotherapy cycles, a 10-point increase in pain in cycle 1 was positively correlated with an 8% increased mortality risk, and every 10-point increase in social function in cycle 2 decreased the risk of mortality by 9%. Thus, the study demonstrated that the pain and fatigue associated with chemotherapy treatment could lead to decreased survival rates in cancer patients. Though this study was limited by the fact that it only looked at cancer patients with stage 3 or stage 4 non-small-cell lung cancer, their findings still lend

significant credence to the fact that clinicians should focus on improving the quality of life of patients during chemotherapy treatment, in order to help increase survival in such patients.

Andersen et al. (2013) carried out a study where the relationship between exercise and cancer-related fatigue was analyzed. The goal of their study was to determine the efficacy of exercise as an adjunct to chemotherapy treatment (Andersen et al., 2013). The researchers utilized data collected from a prospective randomized control trial known as “The Body & Cancer Trial” (Andersen et al., 2013). The trial enrolled 213 cancer patients with varying types of cancers currently undergoing chemotherapy treatment, and subsequently divided those patients into either a treatment group or control group. Investigators determined a patient’s fatigue level through the Functional Assessment of Cancer Therapy-Anaemia Questionnaire. The training regimen for the treatment group took place over the course of 6 weeks, 9 hours per week, and in the morning hours. The training regimen was comprised of “high-intensity cardiovascular workouts, relaxation training, body-awareness training, and massage” (Andersen et al., 2013). Following the 6-week training regimen, the treatment group showed significantly lower fatigue scores as compared to the control group. However, no statistically significant effect of exercise on quality of life, as well as physical, emotional, social, and function scores was found. Table 3, below, illustrates the effect of a 6-week exercise intervention as an adjunct to chemotherapy treatment on several different parameters, such as fatigue and quality of life. The main limitation of the study was the fact that many of the participants in the study showed increased motivation to participate, and most participants were younger

and better educated as compared to the general population (Andersen et al., 2013). This limitation, as well as the fact that exercise showed no significant improvement in the quality of life of patients proves that further studies are needed in order to gain a better understanding on the full range of beneficial effects that exercise offers to patients undergoing chemotherapy treatment.

Table 3. Changes in Fatigue, FACT-An score, FACT-G score, FACT-An Toi score, ANS Score, Physical Function, Emotional Function, Social Function, & Quality of Life after 6-week Exercise Intervention. Fatigue, FACT-An score, FACT-An Toi score, and ANS score all show statistically significant improvements as compared to baseline after 6-week exercise intervention. Table modified from Andersen et al., 2013.

FACT-An outcome variables and intervention effect estimates.

Outcome	Mean (SD)		Test (reference: control) mean difference (95% CI)	P value ^a
	Baseline	6 Weeks		
Fatigue score (0–52) ^b				
Control	35.34 (9.88)	36.34 (9.27)	3.04 (1.17–4.91)	0.002
Intervention	36.86 (9.54)	40.24 (7.94)		
FACT-An score (0–188) ^c				
Control	135.27 (25.07)	139.14 (24.08)	5.40 (1.09–9.73)	0.015
Intervention	140.43 (24.16)	147.60 (21.28)		
FACT-G score (0–108)				
Control	78.84 (13.97)	81.45 (13.33)	1.55 (–0.90–4.01)	0.21
Intervention	81.14 (14.51)	84.41 (12.88)		
FACT-An Toi score (0–136) ^d				
Control	93.81 (21.70)	97.11 (20.51)	5.22 (1.34–9.11)	0.009
Intervention	98.80 (20.31)	105.08 (17.51)		
Anaemia – ANS score (0–80) ^e				
Control	56.42 (12.76)	57.69 (12.28)	3.76 (1.42–6.10)	0.002
Intervention	59.07 (12.06)	63.02 (10.09)		
PWB score physical well-being (0–28)				
Control	19.77 (5.44)	20.59 (5.19)	0.91 (–0.27–2.10)	0.13
Intervention	20.64 (5.41)	21.92 (4.59)		
EWB score emotional well-being (0–24)				
Control	17.69 (4.32)	18.91 (3.73)	0.06 (–0.67–0.80)	0.87
Intervention	18.14 (4.01)	19.25 (3.76)		
SWB score social well-being (0–28)				
Control	23.53 (3.77)	23.27 (3.73)	0.08 (–0.63–0.78)	0.83
Intervention	23.38 (4.20)	23.25 (3.84)		
FWB score functional well-being (0–28)				
Control	17.85 (5.81)	18.67 (5.10)	0.57 (–0.42–1.56)	0.26
Intervention	18.93 (4.97)	19.92 (4.88)		

A study conducted by Jacobsen et al. (2013) investigated the efficacy of both exercise and stress-management training in improving the quality of life of cancer patients. Investigators first assessed each patients bodily functioning, psychological functioning, anxiety levels, depression levels, exercise regimens, and stress reduction

behavior (Jacobsen et al., 2013). Participants were then randomized into four groups: “stress-management intervention, exercise intervention, combined stress-management and exercise intervention, or control group” (Jacobsen et al., 2013). Of the 460 participants who were enrolled in the study, 286 participants completed the study. Intervention treatments were administered concurrently with chemotherapy treatment, and the patients were evaluated at both 6 and 12 weeks after chemotherapy started. The 150 patients that did not complete the study were found to have an increased likelihood of having received both chemotherapy and radiotherapy treatment (Jacobsen et al., 2013). The participants of the study were mainly female, white, and non-Hispanic. Moreover, the majority of participants were diagnosed with either breast or lung cancer. Researchers utilized several different scales to assess the quality of life of cancer patients who completed the study. It was found that combined stress-management and exercise intervention led to increased overall quality of life in patients, as compared to patients who were only administered standard care. Moreover, coinciding with the findings of Andersen et al., this study found that exercise or stress-management alone did not lead to substantial changes in quality of life (Andersen et al., 2013, Jacobsen et al., 2013). The study conducted by Jacobsen et al. had several limitations. The main limitation was the high attrition rate, but investigators cited the fact that patients with lower baseline physical functioning levels due to combined chemotherapy and radiotherapy treatment were the main participants to not complete the study (Jacobsen et al., 2013). Also, participants in the study were not supervised in order to ensure that they adhered to the interventions they were designated to undergo (Jacobsen et al., 2013). Lastly, the effect

that combined stress-management and exercise had on quality of life was relatively small, but the authors explained that the study was conducted within a limited timeframe, and with inadequate resources, suggesting that increased intervention time may lead to a greater effect on quality of life. Overall, the study by Jacobsen et al., along with the study by Andersen et al. demonstrate the potential for exercise and stress-management intervention in improving fatigue and quality of life in cancer patients, but larger trials are needed to fully determine the efficacy of the interventions (Andersen et al., 2013; Jacobsen et al., 2013).

In order to get a better representation of the effects of exercise intervention on cancer patients undergoing chemotherapy treatment, Mishra et al. (2012) conducted a meta-analysis that integrated 56 different clinical trials encompassing 4826 patients. 2286 of those patients received exercise intervention, and 1985 of the 4826 patients were part of the control group. 36 of the 56 trials were conducted while patients were undergoing chemotherapy treatment. 10 of the 56 trials were conducted while patients were undergoing chemotherapy treatment, as well as post-treatment. The remaining 10 trials were conducted before patients were to begin a chemotherapy regimen. The types of exercises utilized in each of the trials, the types of cancers the patients were diagnosed with, and the types of scales utilized to measure health-related quality of life all varied between trials. Researchers concluded that “exercise intervention resulted in improvements in health-related quality of life, physical functioning, role functioning, social functioning, and fatigue” (Mishra et al., 2012). Researchers also discovered that breast cancer patients saw a greater reduction in anxiety as compared to other types of

cancers. Moreover, patients with cancers other than breast cancer experienced a greater reduction in depression, fatigue, and sleep disturbances, as well as greater enhancement in health-related quality of life, emotional well being, bodily functioning, and role function (Mishra et al., 2012). In terms of the training regimen that was most effective, investigators found that a moderate/vigorous exercise routine resulted in better outcomes as compared to a mild exercise routine. The researchers noted that all the trials might have been influenced by performance and selection bias. Moreover, the researchers noted that most of the trials might have been limited by detection and attrition.

Exercise intervention has proven efficacy in reducing fatigue, yet its effect on improving quality of life has not been fully determined. Music therapy is an alternative non-medicinal approach that has been studied in order to determine its efficacy in improving quality of life, anxiety, and depression in cancer patients undergoing chemotherapy treatment. One study by O’Callaghan et al. (2012) delved into determining the effects of music-based therapy on cancer patients. The study focused on young adolescents afflicted with cancer due to the fact that music listening is a widespread phenomenon amongst teenagers, with “adolescents listening to or watching music for an estimated 56.6 hours per week” (O’Callaghan et al., 2012). The study enrolled 12 adolescents between the ages of 15 and 25 years old. Investigators collected data on the effects of music therapy on improving quality of life of cancer patients through both a music demographic questionnaire, as well as an interview session (O’Callaghan et al., 2012). The study participants mainly cited music as having a soothing, caring, and relaxing effect, which helped in subsiding suffering associated with cancer diagnoses.

The study participants also reported that music listening helped in enduring both the cancer treatment phase, as well as the post-treatment phase (O’Callaghan et al., 2012). The participants explained that music had the ability to express messages, as well as aid in dealing with emotional responses. In terms of having sessions with music therapists, participants were divided. Some of the participants sought out music therapists and cited them as a viable option to help with symptom reduction strategies, while other participants felt the music therapy sessions were uncomfortable. Overall, investigators determined that music had the potential to “enable endurance, identity development, and adjustment while cancer patients were either undergoing treatment, or in the post-treatment phase” (O’Callaghan et al., 2012). However, this study was limited due to its small sample size.. Moreover, the study could also potentially be affected by sources of bias.. While the study offers hopeful results for the integration of music therapy as an adjunct to chemotherapy treatment, larger, more detailed studies are needed in order to definitively determine music therapy’s role in the lives of cancer patients.

Lin et al., (2011) conducted one larger study looking into the efficacy of music therapy. The authors conducted a randomized control trial that enrolled 98 patients that were about to undergo chemotherapy treatment, and divided those patients amongst three different treatment interventions: 1 hour of music therapy treatment, 30 minutes of verbal relaxation treatment, and standard care. Investigators measured anxiety levels through the Chinese-STAI, which is a 40-item questionnaire that measures anxiety on a four-point scale (Lin et al., 2011). Immediate anxiety in cancer patients was measured through the Emotional Visual Analog Scale. The C-STAI was administered to participants before the

administration of cancer treatment, and the EVAS was administered after initiation of chemotherapy treatment. It was found that music therapy was more effective in reducing anxiety post-chemotherapy treatment as compared to either verbal relaxation treatment or standard care. Table 4 shows the changes in anxiety and EVAS scores following music therapy, verbal relaxation, or standard care treatment in cancer patients undergoing chemotherapy. Moreover, patients that were identified as having high state anxiety saw the greatest decrease in anxiety due to music therapy intervention as compared to patients identified as having normal state anxiety (Lin et al., 2011). It was also observed that music therapy utilized in cancer patients undergoing chemotherapy treatment led to a decrease in anxiety after thirty minutes of intervention. The main limitation of the study, as cited by the researchers, was the fact that the patients were not provided with their ideal type of music, even though previous studies had demonstrated that administration of preferred music resulted in better outcomes in patients (Lin et al., 2011). Though patients did not receive their preferred type of music, the study still resulted in anxiety reduction in patients. Thus, this study conducted by Lin et al. demonstrates that music therapy can be utilized as a potential tool to reduce anxiety in patients undergoing chemotherapy. Moreover, music therapy as an adjunct to chemotherapy treatment is potentially pertinent in both reducing anxiety in patients with high state anxiety, as well as in reducing anxiety in patients suffering acute anxiety symptoms post-chemotherapy treatment.

Table 4. Changes in Anxiety & EVAS Scores Before and After Music Therapy, Verbal Relaxation, or Standard Care. Anxiety and EVAS scores in cancer patients had greatest improvements following music therapy, as compared to verbal relaxation and standard care treatments. Figure modified from Lin et al., 2011.

Variable	Pretest	Post-test	Paired <i>T</i>	<i>F</i>
	\bar{X} (SD)	\bar{X} (SD)		
State anxiety (20–80)				
Music therapy	39.18 (12.26)	29.76 (8.76)	5.644***	5.580**
Verbal relaxation	41.07 (13.71)	31.63 (10.76)	5.363***	
Control	39.53 (13.10)	35.15 (10.96)	3.898***	
EVAS (0–20)				
Music therapy	12.79 (4.50)	17.08 (2.91)	–6.188***	7.197***
Verbal relaxation	11.53 (4.33)	15.73 (3.65)	–6.114***	
Control	12.76 (4.83)	14.69 (3.80)	–4.373***	

EVAS, Emotional Visual Analog Scale.

p* < 0.01, *p* < 0.001.

Similar to the study described above (Lin et al., 2011), Romito et al. (2013) conducted a study on breast cancer patients that aimed to determine the effectiveness of music therapy intervention on reducing stress, anxiety, depression, and anger. The study enrolled 62 breast cancer patients receiving chemotherapy treatment. Half of the patients were placed in the experimental group, which received a 2.5-hour session of music therapy within a group format while undergoing chemotherapy treatment, while the other half of the patients were placed in the control group, which received the standard care. A patient’s stress, anxiety, depression, and anger was measured through the “Emotion Thermometers Tool,” which is an established oncologic tool utilized to measure the efficacy of a specific treatment, in this case music therapy (Romito et al., 2013). The authors found that patients who received music therapy intervention saw considerable reductions in stress, anxiety, depression, and anger levels. They also noted that anxiety

and stress were reduced in the control group after standard care treatment, but the effect size was negligible. Moreover, the perceived efficacy of treatment was greater in cancer patients receiving music therapy treatment versus the control group (Romito et al., 2013). One significant limitation of this study is that the music therapy intervention only consisted of one session. Another limitation of the study was that the sample size was relatively small. The limitations of this study elucidate the need for significantly larger, as well as lengthier well-controlled studies. However, the results concerning the effect of music therapy on anxiety still corroborate with the results discovered by Lin et al. (Lin et al., 2011; Romito et al., 2013).

As described above, several studies have produced results that demonstrate music therapy can potentially be an effective palliative care tool in the clinical setting in order to improve the quality of life of patients suffering from cancer and consequently undergoing chemotherapy treatment. Mesquita et al. (2013) conducted a study where they aimed to learn the role of spirituality/religion on people with cancer undergoing chemotherapy treatment. The study enrolled 101 patients undergoing chemotherapy treatment, 21 years and older. Data was collected during chemotherapy sessions and was assessed through the Brief-SRCOPE, which is a questionnaire that measures the extent that religious and spiritual strategies are utilized by patients in order to deal with difficult situations in life. The three main types of cancer amongst the study participants were colorectal, breast, and prostate cancer. Also, 37% of the study participants stated they had not experienced any adverse side effects of chemotherapy treatment, meanwhile 54% reported having mild to severe side effects from chemotherapy treatment (Mesquita et al.,

2013). It was found that all 101 patients undergoing chemotherapy treatment reported that they had utilized spirituality for managing their side effects. Moreover, younger study participants, participants who reported having no religion, and participants that reported spirituality as being unimportant were more likely to utilize spiritual coping in a negative manner, meanwhile participants that were eager to utilize spiritual support and who actively participated in cancer support groups utilized spiritual coping in a positive manner (Mesquita et al., 2013). Furthermore, study participants that reported having severe side effects from chemotherapy treatment utilized spiritual coping to the greatest extent, as compared to the other study participants. However, when the side effects of chemotherapy treatment failed to subside, the patient tended to utilize negative coping strategies. The main limitation of this study was the fact that it took place in a single geographic area, and thus, the study results may not be completely generalizable to the general population (Mesquita et al., 2013). The authors concluded that spirituality can be potentially beneficial for patients suffering from the adverse side effects of chemotherapy treatment, but the benefit of spirituality appears to be reliant on the individual patients themselves.

One common practice that many spiritual individuals undertake in order to establish a connection with their spirituality is yoga. Dhruva et al. (2012) conducted a study where they evaluated the effects of pranayama, or yoga breathing, on improving the side effects associated with chemotherapy treatment in cancer patients. Study participants were randomized into two different treatment groups: the pranayama group, which received pranayama while undergoing chemotherapy treatment, and the control group,

which received the standard care for chemotherapy treatment after the first cycle, and then received pranayama while undergoing chemotherapy treatment during the second cycle (Dhruva et al., 2012). A total of 16 study participants completed the study, and thus were utilized for the final analysis of the data. Fatigue, sleep disturbance, anxiety, depression, and stress were evaluated using a variety of clinically verified scales. Investigators collected data between the first and second cycles of chemotherapy, as well as after the completion of the study (Dhruva et al., 2012). It was found that the more the patients practiced pranayama, the greater the improvement in quality of life and symptom scores in those patients.. Moreover, the parameters of sleep disturbance, anxiety, and mental quality of life all attained or neared statistical significance. The main limitation of this study was the small sample size and, the study also may have been affected by selection bias, as well as dependence on self-reported results (Dhruva et al., 2012). This study provides a meaningful pilot study that delves into the therapeutic effects of yoga on improving side effects associated with chemotherapy treatment in cancer patients. However, due to the small sample size, larger studies are needed in order to garner more meaningful, as well as clinically relevant results. Overall, this study demonstrates that spiritual techniques, such as yoga, have the potential to be utilized in the clinical setting as an adjunct to chemotherapy treatment.

Mindfulness-based stress reduction is another spiritual technique being analyzed by researchers in order to determine its efficacy in reducing the adverse quality of life side effects associated with chemotherapy treatment. Hoffman et al. (2012) conducted a study that assessed a total of 229 women with stage 0 to stage 3 breast cancer following

surgery, chemotherapy, and radiotherapy treatment. The study participants were randomized to either an eight-week MBSR program or standard care. Patients enrolled in the MBSR program received instruction on how to perform several mindfulness-body techniques, such as yoga-based stretches, sitting meditation, and group discussions. Profile of Mood States and WHO five-item well-being questionnaire were both utilized to assess the study participants' mood and well-being, respectively. Researchers collected data at three separate time periods during the study: week 0, week 8, and week 12. The authors observed that the group in the MBSR program demonstrated statistically significant improvements in both mood and well-being as compared to the control group. Moreover, the study participants in the MBSR program also showed improvements in anxiety, depression, anger, and fatigue, which are all side effects associated with chemotherapy treatment (Hoffman et al., 2012). This study was limited in several aspects. The main limitation of the study was the fact that following the eight-week MBSR program, the investigators did not follow-up with the study participants to ensure that they continually utilized MBSR techniques. Moreover, the study was potentially limited by its dependence on self-reported outcomes. Also, due to the fact that the study only enrolled patients with breast cancer, the generalizability of the data to patients with other types of cancers may not be relevant (Hoffman et al., 2012). It is also worth noting that patients were less likely to enroll in the study if they either had stage 3 breast cancer or received more chemotherapy, as compared to the study participants (Hoffman et al., 2012). Overall, this study provides insight into the potential use of MBSR techniques within the hospital setting. However, further studies are needed in order to determine the

full efficacy of MBSR on improving the side effects associated with chemotherapy.

Studies that focus on determining the efficacy of MBSR techniques on other types of cancer are needed in order to garner more relevant data.

DISCUSSION

Exercise, music therapy, and spirituality have each been shown to have significant potential as tools of palliative care for physicians to utilize when treating cancer patients receiving chemotherapy treatment. In terms of exercise, Andersen et al. (2013), Jacobsen et al. (2013), and Mishra et al. (2012) all discovered that exercise intervention, as an adjunct to chemotherapy treatment, led to a reduction in fatigue scores in cancer patients. Furthermore, the first two studies both found that exercise intervention alone was not sufficient in improving the quality of life of cancer patients receiving chemotherapy treatment (Andersen et al., 2013; Jacobsen et al., 2013). The results on how exercise intervention affects quality of life discovered by Mishra et al. contradict the results found in the other two studies. Andersen et al. (2013) and Jacobsen et al. (2013) both found that exercise intervention alone had no significant effect on quality of life of patients, yet Mishra et al. (2012) found that exercise intervention had a significant positive effect on quality of life. However, as compared to the studies conducted by both Andersen et al. and Jacobsen et al., the study conducted by Mishra et al. analyzed a greater number of patients, and thus may be more relevant to the general population. It is very likely that the limited number of participants that took part in the studies administered by both Andersen et al. (2013) and Jacobsen et al. (2013) resulted in a failure to find statistically significant results in terms of the correlation between exercise intervention and quality of life.

With regard to the most effective training regimen, the meta-analysis conducted by Mishra et al. (2012) found that high-intensity exercise resulted in greater

improvements in both fatigue and quality of life as compared to mild- to moderate-intensity exercises. It is also worth noting that the study conducted by Andersen et al. (2013) also utilized high-intensity cardiovascular works as part of the training regimen administered to study participants, but the efficaciousness of high-intensity cardiovascular workouts versus mild- to moderate- intensity cardiovascular workouts was not analyzed. In terms of the length of time that exercise intervention should be utilized, it appears that the longer the length of the training regimen, the better the outcome. Jacobsen et al. (2013) observed that fatigue scores continued to improve from both baseline, as well as 6 weeks into a chemotherapy cycle, as measured at 12 weeks after chemotherapy had started. It is possible that fatigue scores improve to a greater extent over 12 weeks as compared to 6 weeks due to the fact that the longer time period allows for the cancer patients to better acclimate to the chemotherapy treatment, thus resulting in reduced fatigue over time. Moreover, the physiological changes that the body undergoes following a period of continual exercise might also play a contributing role to greater improvement in fatigue scores at 12 weeks as compared to 6 weeks.

Though exercise intervention has demonstrated an ability to improve both fatigue and quality of life in cancer patients undergoing chemotherapy treatment, its efficacy may not be the same in all cancer patients. The studies administered by Andersen et al. (2013), Jacobsen et al. (2013), and Mishra et al. (2012) each analyzed patients with varying types of cancers, but only the study by Mishra et al. explored which type of cancer benefited the most from exercise intervention as an adjunct to chemotherapy treatment. Further studies that focus on the effect of exercise intervention on patients with

a specific type of cancer undergoing chemotherapy treatment are needed in order to determine the full extent that exercise intervention produces its effects. Furthermore, the study conducted by Jacobsen et al. (2013) found that patients who underwent concurrent chemotherapy and radiation therapy treatment were less likely to enroll in their study. This discovery demonstrates that a patient's willingness to utilize exercise intervention as an adjunct to chemotherapy treatment may be limited by the aggressiveness of the treatment that they must undergo. It is likely that more aggressive cancer treatments lead to both a greater extent of fatigue, as well as a greater reduction in quality of life scores in cancer patients resulting in both decreased motivation, as well as strength to integrate exercise into their daily lives. Further studies on advanced cancer patients undergoing aggressive cancer treatment are needed in order to determine how to incorporate a successful exercise regimen in the lives of advanced cancer patients.

While the effects of exercise as an adjunct to chemotherapy treatment have shown marked potential in improving the side effects associated with chemotherapy treatment in cancer patients, the efficacy of music therapy is less well documented in the scientific literature. Unlike the exercise intervention studies, the studies concerning music therapy utilized in this paper did not indicate any statistically significant change in fatigue score as a result of music therapy as an adjunct to chemotherapy treatment. However, the cited studies each demonstrated that music therapy could be used as a potential tool to reduce both anxiety and stress in cancer patients receiving chemotherapy (Lin et al., 2011; O'Callaghan et al., 2012; Romito et al., 2013). Music therapy appears to have perceived efficacy in aiding cancer patients in the reduction of fear, subsiding of depression, and

attainment of an identity. The role that music therapy plays in the lives of cancer patients is a critical one because it helps cancer patients cope with both their disease, as well as the difficult treatment associated with that disease. Moreover, as illustrated by Lin et al. (2011), music therapy appears to have marked efficacy in reducing anxiety in cancer patients that suffer from acute anxiety attacks. Further research that compares music therapy to other potential therapies would be needed in order to study the true efficacy of music therapy in reducing spontaneous anxiety attacks in cancer patients undergoing chemotherapy treatment. Overall, however, music therapy appears to have evident potential as a multi-use therapy treatment in cancer patients receiving chemotherapy treatment.

The manner in which music therapy should be administered to cancer patients as an adjunct to chemotherapy treatment is still up for debate. As cited by O'Callaghan et al. (2012), some of the patients receiving music therapy sessions found them uncomfortable. It is possible that if this study was conducted over a larger time span, the perceived discomfort with music therapy sessions would decrease as patients become more acclimated to the sessions, but further research is needed in order to determine how to properly administer music therapy sessions to cancer patients. Furthermore, both the length of the music therapy sessions, as well as the types of music utilized for music therapy have not been fully investigated. It is possible that music therapy could be utilized on a spontaneous basis whenever cancer patients start to feel either depressed or anxious. Moreover, as previous studies have demonstrated, preferred music, versus non-preferred music, appears to have the greatest efficacy in reducing the side effects

associated with chemotherapy treatment. Thus, the integration of music therapy into the lives of cancer patients receiving chemotherapy treatment seems to be a matter of personal preference, and it would be essential for a patient's clinician to determine the ideal manner in administering music therapy.

The main issue concerning the effectiveness of music therapy as a palliative care tool for cancer patients receiving chemotherapy treatment is that there is a lack of focus on the topic within the scientific community. One reason why many researchers may not be interested in investigating the effects of music therapy on cancer patients is because its desired effect on patients is subjective in nature, and thus it is difficult to ascertain the full extent that music therapy imposes on both anxiety and depression in patients. Secondly, most scientific research is focused on finding new ways to treat a patient's cancer, in hopes of developing a cure. Yet, it is still imperative that both the healthcare, as well as the scientific communities, concentrate on finding ways to treat patients holistically, so that clinicians can effectively treat a patient's disease, as well as the side effects that are procured due to having that disease. Music therapy offers a potential avenue for physicians to utilize when treating patients who either prefer alternative medicines over pharmacologic compounds, or are seeking novel approaches to treat the side effects associated with chemotherapy treatment.

Similar to how music therapy could be utilized to improve the quality of life and well-being of patients, spirituality has also been studied as a potential tool to help patients improve their quality of life while undergoing chemotherapy treatment. Spirituality, in the context of the studies explored in this paper, is concerned with utilizing an array of

different techniques in order to reduce stress and anxiety. This paper looked at studies that investigated the effects of religion, yoga, and MBSR on improving a patient's quality of life. The study conducted by Mesquita et al. (2013) explored how religion can reduce stress and anxiety in cancer patients receiving chemotherapy treatment. The most significant finding of the study was that the effect of religion on patients was dependent upon the role that spirituality played in the patients' lives. The more religious or spiritual a person was, the more that person tended to utilize spirituality in a positive way in order to improve their quality of life. Interestingly, even if a person was spiritual or religious, and utilized spirituality in a positive manner, it was found that if the side effects of chemotherapy treatment did not subside, that person tended to start to utilize spirituality in a negative manner (Mesquita et al., 2013). The most likely explanation for this effect is that if a patient fails to see improvement in quality of life after relying upon spirituality to help cope with their disease, the patient most likely begins to become more pessimistic towards their beliefs. Though religion appears to play a role in improving the lives of patients afflicted by cancer and undergoing treatment, its efficacy is limited, and its potential as a viable option as a palliative care tool is reliant on the individual receiving treatment. Thus, it is important that studies focus on helping physicians develop guidelines that allow them to take a patient's spirituality history in order to determine if spirituality can be utilized as a potential treatment option for the adverse side effects associated with chemotherapy treatment.

Unlike the questionable efficacy of religion on improving the quality of life of cancer patients, the efficacy that yoga and MBSR offer to patients afflicted with cancer

and undergoing chemotherapy treatment is much more definitive. Both Dhruva et al. (2012) and Hoffman et al. (2012) discovered that utilizing either yoga or MBSR, respectively, while patients underwent chemotherapy treatment, resulted in significant improvements in quality of life for those patients. Moreover, Hoffman et al. (2012) found statistically significant improvements in fatigue scores as well, after patients utilized MBSR techniques. The effectiveness of both yoga and MBSR most likely stems from the fact that both can be utilized in order to relax a person both mentally and physically. Compared to exercise, which also demonstrated significant improvements in fatigue scores in cancer patients undergoing chemotherapy treatment, MBSR offers less strenuous exercises that can be utilized in order to help improve the quality of life of patients.

Similar to music therapy, however, there are only a limited number of scientific papers concerned with the effects of spirituality on cancer patients undergoing chemotherapy treatment. Moreover, the studies investigated within this paper were relatively small, and did not encompass all of the various types of cancers, so the data from these studies may not be completely relevant. Larger studies that delve into how to properly utilize spirituality to treat cancer patients receiving chemotherapy, how to properly incorporate spirituality into a patient's treatment regimen, and how to definitively determine its effectiveness as an adjunct to chemotherapy treatment are needed in order to fully understand the role that spirituality can potentially play as a palliative care tool.

Overall, exercise, music therapy, and spirituality offer promise in aiding the fight against cancer. Exercise, music therapy, and spirituality have each demonstrated, to some extent, potential in improving fatigue, quality of life, or both fatigue and quality of life in cancer patients undergoing chemotherapy treatment. One of the main issues that is preventing the utilization of exercise, music therapy, and spirituality in treating cancer patients receiving chemotherapy treatment is the fact that the scientific community is more focused on finding a cure for cancer, as opposed to finding ways to help improve the side effects associated with chemotherapy treatment. As treatment options for cancer improve, there will be a shift in focus on finding ways to help patients improve their quality of life. Clinically, it is imperative that physicians attempt to treat both a patient's disease, as well as the side effects associated with either the disease itself or the treatment of that disease due to the fact that sometimes the side effects of chemotherapy treatment can be as detrimental as the disease itself. Finding ways to allow patients to still maintain their daily lives is essential to the general well-being of the patients. As noted above, further research is needed in order to gain a better understanding on the use of exercise intervention, music therapy, and spirituality as an adjunct to chemotherapy treatment. It would be interesting for further studies to delve into the integration of all three interventions in order to figure out the most effective treatment plan for cancer patients undergoing chemotherapy treatment. The future of cancer research is promising, and over the next decade further research will allow for cancer patients to better cope with their disease.

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CURRICULUM VITAE

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Education

- M.S. in Medical Sciences, Boston University School of Medicine, September 2014 (expected)
- B.A. in Biology, Boston University, May 2013
 - o GPA: 3.65/4.0
 - o Magna Cum Laude

Awards & Honors

- Patriot League Honor Roll (Fall 2013)
- Senior Scholar-Athlete Award (Spring 2013)
- America East Commissioner's Honor Roll (Fall 2009 to May 2013)
- America East All-Academic Team (Fall 2012)
- Boston University Dean's List (Fall 2009 to May 2012)
- National Honor Society of Collegiate Scholars

Work Experience

- Excel Elevators: Administrative Assistant (May 2011 to August 2011, July 2013 to August 2013)
 - o Organize new clients into easily accessible and understandable excel file.
 - o Dispatched jobs to elevator mechanics.
 - o Developed program that was responsible for keeping track of elevator jobs that were not completed.
 - o Created excel spreadsheet for invoices, as well as elevator violations that needed attention.
- NYC Parks Department: Maintenance Worker (July 2010 to August 2010)
 - o Maintained cleanliness of Wolfe's Pond Park.
 - o Assisted parks department employees in improving quality of park.

Volunteer Experience

- Shadowing Experience at Staten Island University Hospital (May 2011 to August 2011)
 - o Shadowed several emergency room physicians at SIUH.
 - o Assisted nurses with retrieval of necessary medical equipment.
- Brigham & Women's Hospital (MCEP) (November 2010 to May 2011)
 - o Transferred blood and plasma samples to the correct locations within hospital.

- Assisted security guards in making sure that the correct people were gaining access to the maternity ward.
- Richmond University Medical Center Volunteer (June 2008 to August 2008)
 - Assisted physical therapists while treating their patients.

Research Experience

- Cervical Cancer Research – Volunteer Research Assistant, CSI Banerjee Lab (May 2012 to September 2012)
 - Performed western blot analyses, focusing on the ability for curcumin-based vaginal cream to decrease expression of pro-cancer protein EGFR.
 - Performed tissue cultures of HeLa cell line (cervical cancer cell line).
 - Treated HeLa cell line with differing doses of curcumin-based vaginal cream to study dose-dependent effect of cream.
 - Performed PCR analysis, as well as cell counting.

Presentations

- CSI Biochemistry Conference, Staten Island, NY (July 2012)
 - Explained classification system of Papillomavirus.

Leadership and Activities

- Cross Country/Track & Field (Division 1) (Fall 2009 to Fall 2013)
 - Co-captain of the track & field distance group for Fall 2013 Cross Country Season.
 - Member of the 2010 America East Cross Country Championship team.
- BU Premedical Society (Fall 2009 to May 2013)