Exploring the Feasibility and Acceptability of Acupuncture and Acupressure among Patients with Advanced Cancer Pain and their Primary Family Caregivers

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Abstract

Background: Pain affects an estimated 44.5% patients with cancer, with 30.6% of patients reporting moderate to severe pain. Chemotherapy-induced peripheral neuropathy (CIPN) is one particularly difficult type of cancer-related pain that affects approximately 30-40% of patients and can have a profound effect upon quality of life (QoL). Non-pharmacologic therapies including complementary and alternative medicine (CAM) are used by an estimated 80% of patients with cancer pain. Self-efficacy is associated with decreased cancer pain and symptom burden and can be increased through self-management of symptoms. Acupuncture/pressure is a CAM therapy that is increasing in use for cancer pain and CIPN; however, there is limited research on the feasibility and acceptability of acupuncture/pressure among patients with advanced cancer and their family caregivers.

Specific Aims: The aims of this research are to explore: 1) the feasibility and acceptability of acupuncture/pressure and other non-pharmacologic therapies for pain management reported by patients with advanced cancer and their family caregivers; 2) the association between self-efficacy in cancer pain management and acupuncture/pressure; and 3) demographic and clinical variables that predict use of acupuncture/pressure for pain among patients with advanced cancer.

Study Design: This study is a secondary data analysis using survey data from the parent study *Characterizing the Complexity of Advanced Cancer Pain in the Home Context*. Variables included: 1) reported use and belief in effectiveness of acupuncture/pressure and other non-pharmacologic approaches, such as positioning, being with others, rest/sleep, and guided imagery/hypnosis; 2) self-efficacy in pain management; and 3) demographic and clinical characteristics obtained from both patients and their family caregivers. Feasibility and acceptability were evaluated using: 1) descriptive statistics to evaluate self-reported use of acupuncture/pressure compared to other non-pharmacologic therapies; and 2) independent two-sample t-tests to compare belief in effectiveness of the patient's pain management regimen between patients and caregivers who reported use of acupuncture/pressure and those who did not. Independent two-sample t-tests were used to compare self-efficacy through confidence in pain management between patients and caregivers who reported use of acupuncture/pressure and those who did not. The effect of acupuncture/pressure use on self-efficacy was determined using multiple linear regression. Demographic and clinical variables for patients who used acupuncture/pressure were compared to those who did not using t-tests for continuous variables and chi-square tests for categorical variables.

Results: Feasibility and acceptability were highest for positioning, being with others, and rest/sleep, which all had reported use > 95%. Use of guided imagery/hypnosis and acupuncture/pressure were lowest at 43.8%. Acupuncture/pressure was associated with decreased self-efficacy in pain management, at a significance of p-value= 0.02. Demographic and clinical variables did not predict use of acupuncture/pressure at a significance of p-value < 0.05; educational level was close at p= 0.05.

Conclusions: The relationship between reported use of acupuncture/pressure and decreased self-efficacy may indicate that patients with cancer and the highest symptom management needs are more likely to try acupuncture/pressure. Acupressure can be self-administered and may facilitate access for patients with advanced cancer pain to obtain the benefits of acupuncture/pressure for symptom management. Future research should evaluate acupressure techniques that can be self-managed for advanced cancer pain among patients and their family caregivers.

Acknowledgements and Dedication

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I dedicate this dissertation to my son Henry. May he continue to achieve success in his own academic journey.

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Table of Contents

APPENDICES

CHAPTER ONE

Introduction

Prevalence of Cancer Pain

Pain affects an estimated 44.5% of patients with cancer, including persons currently in treatment and post-treatment survivors, with 30.6% of patients reporting moderate or severe pain (Snijders et al., 2023). The prevalence of pain among cancer survivors related to either cancer or side-effects of treatment is approximately 10% and can persist for years following the initial diagnosis (Gallaway et al., 2020). One particularly difficult type of cancer-related pain is chemotherapy-induced peripheral neuropathy (CIPN), a painful condition affecting an estimated 30-40% of patients with cancer which can have profound effects upon quality of life (QoL) including pain, numbness, altered touch sensation, and risk for falls (Bao et al., 2016; Hershman et al., 2014; Staff et al., 2017; Starbova & Vetter, 2017; Zajackowska et al., 2019). Pharmacologic management of pain related to cancer and treatments for cancer including CIPN may involve multiple approaches including opioids, antidepressants, anticonvulsants, corticosteroids, and bisphosphonates (National Cancer Institute, 2023). For management of chronic pain among patients with cancer and survivors, the benefits of some medications commonly used such as antidepressants and anticonvulsants remain unclear or side-effects may adversely affect overall benefit for QoL (Magnowska et al., 2018; Song et al., 2017; Tofthagen et al., 2020). Complementary and integrative therapies including acupuncture, massage, physical therapy, yoga, tai-chi, guided imagery, hypnosis, cognitive-behavioral therapy, mindfulness, and support groups are increasing in use along pharmacologic management for pain related to cancer

and treatments for cancer including CIPN (Katta et al., 2022; Maindet et al., 2019; National Cancer Institute, 2023; Tofthagen et al., 2020).

An Overview of Acupuncture and Acupressure

Acupuncture is a non-pharmacologic therapy that is increasingly utilized along with standard care in oncology settings and involves stimulation of specific points on the body to promote healing and alleviate symptoms through resolution of imbalances in the body (Kaptchuk, 2002; Lu et al., 2017). A challenge in acupuncture research is inconsistency in the definition of acupuncture in the literature. In our integrative review of acupuncture for CIPN, we incorporated stimulation of acupoints on the body, auricular point stimulation and electroacupuncture (EA) into the definition of "acupuncture" (Kutcher & LeBaron, 2022). While acupuncture techniques involving insertion of needles require facilitation by a licensed acupuncturist or physician, auricular acupressure (APA) is a technique that can be used alone or in conjunction with acupuncture to self-manage symptoms by pressing acupoints on the ear. Prior research has found APA to be feasible and acceptable among patients with cancer (Yang et al., 2020; Yeh et al, 2015).

Although use of acupuncture in the United States is increasing, the available data indicates that acupuncture is used by a relatively small percentage of the population. The most recent available data on acupuncture use is the National Center for Complimentary and Integrative Health (NCCIH) survey on complementary health practices including acupuncture among American adults and children in 2002, 2007 and 2012 (Cui et al., 2017; National Center for Complementary and Integrative Health, 2023). Acupuncture use increased 50% from 4.2% to 6.4% of adults between 2002 and 2012 (National Center for Complementary and Integrative Health, 2022), and the number of licensed acupuncturists more than doubled from 12,000 to

27,835 during the same timeframe (Cui et al., 2017). Pain, most prominently back pain (30.9%), was the most common reason for seeking acupuncture treatment in 2012. The majority of acupuncture users were college-educated women between the ages of 41-65 (Cui et al. 2017). Consistent with use of complementary and alternative medicine (CAM) therapies overall, users of CAM therapies for cancer-related pain are also mainly white women with higher levels of education and financial status, with use of practitioner-facilitated therapies being more frequently used by persons of higher socioeconomic status (Ludwick et al., 2020).

Acupuncture and Acupressure among Patients with Cancer

There is evidence to support the use of acupuncture/pressure for symptoms related to both cancer and treatments for cancer including nausea, vomiting, hot flashes, fatigue, xerostomia, and pain including CIPN (National Cancer Institute, 2023; Lau et al., 2016). Acupuncture is one of the most frequently offered integrative therapies in oncology settings. A systematic review of 45 National Cancer Institute (NCI)-designed cancer center websites indicated that exercise is the integrative health modality featured most frequently on cancer center websites (97.8%), with acupuncture and meditation sharing second place (88.9% each) (Yun et al., 2017). A survey of 116 patients with cancer and 54 informal caregivers found acceptability of acupuncture to be 34.5% and 48.0% respectively (Tack et al., 2021). There is evidence to suggest that among patients with cancer, persons with advanced disease and higher baseline pain levels may have more improvement in their pain with use of acupuncture than patients with lower baseline pain levels (Miller et. al, 2019).

Despite the growing use of acupuncture for patients with cancer, evidence for use of acupuncture and/or acupressure for cancer-related pain among patients with advanced malignancy remains limited (He et al., 2020; Yang et al., 2020). One multicenter study

compared acupuncture to massage as an intervention for pain among 298 patients with advanced

cancer and found that both interventions were associated with reduction in pain and improved

QoL (Epstein et al., 2023). Available studies specific to acupressure for cancer-related pain

among patients with advanced malignancy are even more limited; a recent systematic review of

self-acupressure among patients with cancer did not include any studies of patients with

advanced malignancy and the primary symptoms addressed included nausea, emesis, and fatigue

(Chen et al., 2023). There are no known studies of feasibility and acceptability of acupuncture or

acupressure for pain related to advanced malignancy among both patients and their caregivers.

Study History and Overview

This dissertation research fills an important gap in the literature by evaluating the

feasibility and acceptability of acupuncture and acupressure for cancer-related pain among

patients with advanced malignancy and their caregivers using a secondary data analysis (SDA)

of self-reported survey data. Consistent with recommendations for all cancer-related pain listed

above, non-pharmacologic therapies including exercise interventions, mental health and

integrative therapies including acupuncture and acupressure are recommended in the

management for CIPN (Bao et al., 2016; Tofthagen et al., 2020; Yeh et al., 2019).

The initial proposal for this dissertation study was to evaluate feasibility and acceptability

of self-administered APA for chemotherapy-induced peripheral neuropathy (CIPN) with a

sample of patients with breast cancer. APA as a self-care management strategy for CIPN could

play an important role in reducing symptom burden without the need to access a practitioner as

in the case of acupuncture. However, the initial dissertation study proposal encountered

unforeseen obstacles related to the classification of APA as a medical intervention versus a self-

care management strategy; this classification precluded the execution of the original proposal

given constraints of scope and timeline. Consequently, a related inquiry regarding cancer pain

and the use of acupuncture/acupressure was undertaken with existing data collected through the

Behavioral and Environmental Sensing and Intervention for Cancer (BESI-C) remote health

monitoring system (LeBaron et al., 2022; LeBaron et al. 2023).   This data set, obtained from the

parent National Institutes of Health R01 study, *Characterizing the Complexity of Advanced*

Cancer Pain in the Home Context, includes information on the self-reported use and belief in

effectiveness of acupuncture and acupressure in reducing cancer pain among both patients with

advanced malignancy and their primary family caregiver. Although a pivot from the initial

proposal, this study maintains the spirit of the original concept by expanding what is known

regarding feasibility and acceptability of acupuncture and acupressure among patients with

cancer.

In addition to the primary aim of this study to evaluate feasibility and acceptability of

acupuncture and acupressure for cancer-related pain, secondary aims which were shared by the

initial proposal include evaluation of pain and QoL including functional status and pain

interference in daily activities. An important aspect of this study is the integration of caregivers

(the term "care partner" is also used), who are an integral aspect of the care of patients with

chronic illnesses including cancer and may experience effects on physical and emotional health

and QoL through the caregiver role (Teixeira et al., 2018). In the context of advanced disease,

exploring feasibility and acceptability of acupuncture and acupressure among caregivers in

addition to patients is important as caregivers can take on roles as managers or partners in care

who help facilitate access to treatments and therapies (Wittenberg et al., 2017). Understanding

the relationships among QoL and feasibility of acupuncture and acupressure use among

caregivers in addition to patients is important to understanding best practices for patients with advanced cancer.

Overview of Dissertation Format

This dissertation research is presented in a hybrid format, which includes a traditional five-chapter dissertation incorporating the integrative review of acupuncture for CIPN (Kutcher & LeBaron, 2022). Chapter 1 includes the introduction and background and discusses the prevalence of cancer pain, use of acupuncture/pressure among patients with cancer, and provides an overview of the dissertation study. Chapter 2 is the previously published integrative review of acupuncture for CIPN (Kutcher & LeBaron, 2022). The integrative review remains relevant to the current study as: 1) CIPN is an important aspect of total pain and symptom burden among both patients with cancer who have received treatment with neurotoxic chemotherapy and 2) our findings indicate the need to establish protocols for use of acupuncture/pressure and appropriate measures of evaluation (Kutcher & LeBaron, 2022). Chapter 3 describes the data collection and analysis methods for the SDA including aims, theoretical framework, and analytic approach. Chapter 4 provides the results of the SDA organized by the aims. The discussion and conclusion, which synthesize results, position the study findings in the context of the extant literature, and offer directions for future research, are contained in Chapter 5.

CHAPTER TWO

Integrative Review

Evaluating Acupuncture for Treatment of Chemotherapy-Induced Peripheral Neuropathy: An Integrative Review

Abstract

The purpose of this integrative review of the literature is to synthesize the current evidence and identify gaps in knowledge regarding the effectiveness of acupuncture to treat chemotherapy-induced peripheral neuropathy (CIPN). PubMed, CINAHL, Web of Science, and Cochrane Review databases were searched using inclusion criteria: key words acupuncture, cancer, and peripheral neuropathy, published in English, between 2009 - 2019.   Sixteen articles met the inclusion criteria. The literature indicates that acupuncture is generally well tolerated by patients with cancer and a majority of patients with CIPN reported decreased pain and increased quality of life after receiving acupuncture treatment.   A comprehensive understanding of the ability of acupuncture to treat CIPN is limited by variability of acupuncture techniques and inconsistency in measures of evaluation.

Key words: acupuncture; electro-acupuncture; chemotherapy-induced peripheral neuropathy; integrative oncology; cancer; integrative review

Chemotherapy-induced peripheral neuropathy (CIPN) is a common side-effect of neurotoxic chemotherapy, experienced by an estimated 30-40% of patients with cancer (Staff et al., 2017). Common symptoms of CIPN include burning, pain, tingling, numbness, and altered touch sensation (Hershman et al., 2014; Starbova & Vetter, 2017; Zajaczkowska et al., 2019). Other symptoms may include difficulty with balance and walking, and overall decreased quality of life (Bao et al., 2016; Hammond et al., 2019). The severity of symptoms associated with CIPN is considered to be higher than neuropathy from other causes, such as diabetes, as CIPN is commonly associated with higher pain levels (Zajaczkowska et al., 2019). Additionally, CIPN symptoms often become progressively worse with each additional dose of chemotherapy and cumulative effect of multiple treatments (Hershman et al., 2014; Starbova & Vetter, 2017; Zajaczkowska et al., 2019). Depending on the type of chemotherapy received, onset of CIPN may begin as soon as during treatment, or up to weeks or months following completion of chemotherapy (Starbova & Vetter, 2017; Zajaczkowska et al., 2019). The effects of CIPN may have a profound effect on quality of life for patients with cancer and survivors, lasting up to several years into survivorship (Bao et al., 2016; Song et al., 2017; Tofthagen et al., 2020; Zajaczkowska et al., 2019). Higher levels of CIPN among cancer survivors are associated with increased levels of anxiety, depression, insomnia, obesity and incidence of falls (Bao et al., 2016; Kolb et al., 2016; Song et al., 2017; Starbova & Vetter, 2017).

Integrative oncology has been defined as an area of cancer care which involves the combination of practices from different traditions, including mind-body therapies and natural products, alongside conventional treatments to promote quality of life (Witt et al., 2017). The use of acupuncture is increasing in integrative oncology settings (Li et al., 2019; Lu et al., 2017). Acupuncture is a technique which involves insertion of sterile needles into the skin at

specific locations based on theories of Traditional Chinese Medicine (TCM) that are over 2,000

years old (Kaptchuk, 2002).   The goal of TCM acupuncture therapy is to reduce or alleviate

symptoms based upon a holistic perspective in which stimulation of specific points promotes

healing through resolution of imbalances in the body (Kaptchuk, 2002).   Although not

completely understood, physiological mechanisms of acupuncture may include stimulation of

neurotransmitters and modulation of peripheral and central nervous system pathways (Wu et al.,

2016; Zhou et al., 2014). A survey of acupuncturists working in integrative oncology indicated

that CIPN is the most common condition treated, comprising about a third of patients (Lu et al.,

2017).

Despite the increasing use of acupuncture for CIPN in integrative oncology, prior reviews

have drawn divergent conclusions to support its use.   The earliest systematic review, Franconi et

al. (2013), concluded that there is limited evidence to support use of acupuncture for CIPN, and

that more, higher quality research is needed as many studies have several limitations including

small sample sizes and lack of controls. A recent meta-analysis by Chien et al. (2019) which

included six RCT's (Greenlee et al., 2016; Han et al., 2017; Lu et al., 2019; Molassiotis, Suen,

Cheng, et al., 2019; Rostock et al., 2013; Zhang et al., 2017) found that acupuncture decreased

subjective symptoms of CIPN in four studies (Han et al., 2017; Lu et al., 2019; Molassiotis,

Suen, Cheng, et al., 2019; Zhang et al., 2017), but that there was no correlation in objective

measures including nerve conduction velocity (Han et al., 2017; Molassiotis, Suen, Cheng, et al.,

2019) and immune cytokines (Zhang et al., 2017). Two systematic reviews on the use of

acupuncture for treatment of CIPN were published in 2019. Baviera et al. (2019) determined

that acupuncture is of benefit for symptoms of CIPN while Li et al. (2019) found insufficient

evidence for recommendation in clinical practice. These conclusions were drawn based upon

evaluation of different sets of primary studies. Li et al. (2019) selected randomized controlled trials (RCTs) involving any type of acupuncture, while Baviera et al. (2019) excluded studies if the acupuncture protocol involved electro-acupuncture (EA) or auricular acupuncture.

To address this gap, an integrative review of the literature was performed to evaluate the use and efficacy of acupuncture in the management of CIPN. Integrative reviews of the literature incorporate a wider range of articles and study designs in order to fully assess the state of the science, with aims including enhanced understanding of concepts and methodological issues (Hopia et al., 2016; Whittemore & Knafl, 2005). Acupuncture research has historically focused on experimental studies, which have faced several challenges including the selection of appropriate comparison groups (Zhuang et al., 2013). This integrative review of the literature fills an important gap in knowledge by providing a more complete and comprehensive view of what is currently known about acupuncture for the management of CIPN.

Purpose

The purpose of this integrative review of the literature is to synthesize the current evidence and identify gaps in knowledge regarding the effectiveness of acupuncture to treat chemotherapy-induced peripheral neuropathy (CIPN) through a comprehensive evaluation of the current literature. Additional recommendations for future research involving acupuncture for CIPN are provided.

Methods

Search Strategy

For the purposes of this integrative review, acupuncture is defined as the insertion of a needle into an acupuncture point located on the body, inclusive of auricular acupuncture and

electro-acupuncture (EA) in order to include multiple, common acupuncture styles which involve needle insertion. This distinction is important and impacted the search results. For example, articles that focused on techniques which involve stimulating the location of acupuncture points by methods other than needle insertion, such as non-inserted needles, lasers, press balls, acupressure or reflexology, were excluded. Additionally, neuropathy was limited to CIPN. The search included terms specific to oncology in order to limit results related to neuropathy from other etiologies, such as diabetes or HIV. Additional search criteria included studies published in English. The final search included articles published within the past ten years (2009-2019) in order to capture clinically relevant data that would reflect current practice in integrative oncology settings. The time period of the search was expanded from five to ten years after a prior search for articles within the past 5 years produced only six articles of direct relevance to the research question.

The literature was reviewed using the electronic databases, PubMed, CINAHL, Web of Science and Cochrane Review. These databases include Chinese language journals which have been translated into English. Therefore, Chinese-language databases were not included. The search strategy was completed using key words acupuncture, cancer and peripheral neuropathy. MeSH terms included acupuncture therapy, neoplasm, carcinoma and peripheral nervous system disorders. The search strategy, including selection of terms and relevant databases, was performed in consultation with the health sciences librarian.

Data Management

A total of two hundred twenty articles were identified in the initial search (Figure 1). After duplicates were removed, one hundred five articles remained. Articles were further excluded if titles indicated: 1) the study was not directly related to the research question, e.g.,

including neuropathy from etiology other than chemotherapy, such as diabetic neuropathy; 2) evaluated acupuncture for treatment of a condition unrelated to oncology; 3) available only in a language other than English; and 4), animal studies. Eighty-five abstracts were screened and sixty were excluded if: 1) the article included multiple Complementary and Alternative Medicine (CAM) therapies without presence of an acupuncture specific treatment group or 2) the acupuncture protocol was integrated with another therapy such as reflexology, lasers or injectable medications or vitamins. The remaining twenty-five articles underwent a full text review. Following a full text review, nine articles were removed due to poor fit with the research question, such as focusing on acupuncture for treatment of neuropathic pain in patients with cancer related to cause other than CIPN or if the study was a systematic review or meta-analysis versus a primary study. The final result included sixteen articles, which were organized into a table to summarize key elements of the primary studies.

Figure 1
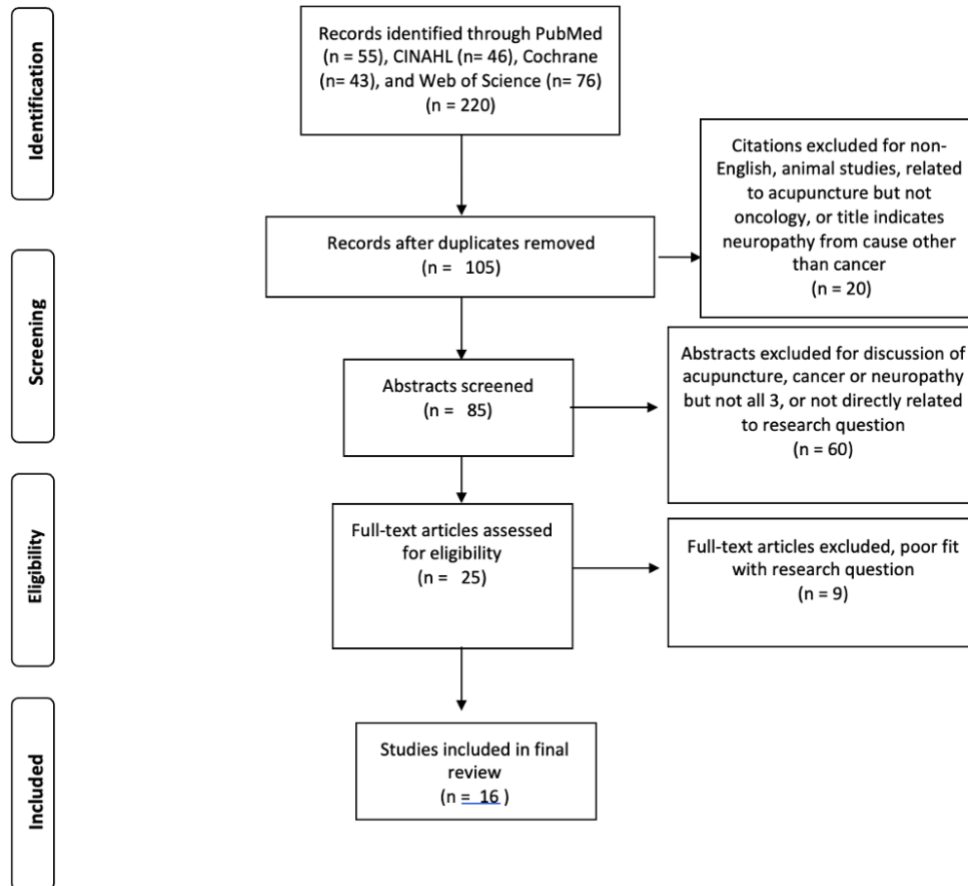
Results

The sixteen studies included in the final review are summarized in Tables 1-3. The studies include thirteen intervention studies, two retrospective chart reviews, and one case report.

Intervention Studies

Non-randomized / Quasi-experimental studies

Six studies involving small, single arm intervention trials are included in this review (Bao et al., 2014; Bao et al., 2018; Ben-Arye et al., 2018; Garcia et al., 2014; Jeong et al., 2018; Zhi et al., 2018). These findings include a diverse set of studies without a clearly consistent theme. Related to patient characteristics, five of the six studies included patients who had completed

treatment (Bao et al., 2014; Ben-Arye et al., 2018; Garcia et al., 2014; Jeong et al., 2018; Zhi et al., 2018), with one study evaluating the effect of acupuncture on patients currently in treatment with chemotherapy (Bao et al., 2018). In all six studies, patients had varying levels of CIPN at study outset from mild to more severe. The aim of the study which involved patients in active treatment (Bao et al., 2018) was to evaluate the effectiveness of acupuncture to limit progression of symptoms from grade II to grade III CIPN.

A variety of acupuncture protocols were utilized, with most investigators using acupuncture without EA on body acupoints (Bao et al., 2014; Bao et al., 2018; Jeong et al., 2018; Zhi et al., 2018) and one study involving EA (Garcia et al., 2014). Also, some investigators included confounding variables making it difficult to ascertain the effect of acupuncture. For example, in Ben-Arye et al. (2018), the acupuncture technique was not defined and only 25% of the participants received an acupuncture-specific intervention that was not combined with another technique, such as touch or other unspecified mind-body therapy. In Garcia et al. (2014), seventeen of nineteen participants used pharmacological therapy to treat CIPN in addition to acupuncture, including anticonvulsants and opioids.

Subjective and objective outcome measures varied among these studies. All six single-arm intervention studies found improvement in patient reported symptoms of CIPN, but no change in objective outcome measures. Subjective measures included Neuropathy Pain Scale (NPS) (Bao et al., 2014; Bao et al., 2018; Zhi et al., 2018), Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx) (Bao et al., 2014; Bao et al., 2018; Garcia et al., 2016; Zhi et al., 2018), Brief Pain Inventory- Short Form (BPI-SF) (Garcia et al., 2014), and Measure Yourself Concerns and Well-being Tool (MYCAW) (Ben-Arye et al., 2018). Objective outcome measures included nerve conduction studies (NCS), also

known as nerve conduction velocity test (NCV), in two studies (Bao et al., 2014; Garcia et al., 2014) and measurement of pro-inflammatory cytokines and neurotrophic factors in one study (Bao et al., 2014).

Schroeder et al. (2012) was a quasi-experimental study which included eleven participants who had developed CIPN following treatment with chemotherapy. This is the first known study in which NCS was utilized as an objective outcome measure. Six received acupuncture without EA. Five patients who refused the intervention provided the control group. Effect of the acupuncture was measured by patient self-report and NCS. Both patient report of symptoms and NCS were improved after six months in five of six patients in the intervention group.

Randomized Studies

Four randomized controlled trials are included in this review: Greenlee et al. (2016), Lu et al. (2019), Molassiotis, Suen, Cheng, et al. (2019), and Rostock et al. (2013). The studies included patients currently in treatment (Greenlee et al., 2016) and post-treatment survivors (Lu et al., 2019; Rostock et al., 2013). Molassiotis, Suen, Cheng, et al. (2019) included both patients actively in treatment and post-treatment survivors. Three studies used EA (Greenlee et al., 2016; Lu et al., 2019; Rostock et al., 2013). Greenlee et al. (2016) evaluated the effects of EA for patients currently in treatment using a variety of acupoints including distal extremity points *bafeng* and *baxie*. Rostock et al. (2013) was a four-arm trial evaluating EA, hydroelectric baths, high doses of vitamin B or a placebo concurrent with other therapies including massage and relaxation therapy in survivors. The acupuncture protocol used in Lu et al. (2019) involved one acupuncture treatment without EA followed by EA in 40 breast cancer survivors.

Subjective outcome measures utilized in the four randomized controlled trials include BPI (Molassiotis, Suen, Cheng, et al., 2019), or BPI-SF (Greenlee et al., 2016; Lu et al., 2019), FACT-Ntx (Greenlee et al., 2016; Lu et al., 2019; Molassiotis, Suen, Cheng, et al., 2019), NPS (Greenlee et al., 2016), Quality of Life Questionnaire (QLQ-C30) (Lu et al., 2019; Rostock et al., 2013) and patient report of symptoms (Rostock et al., 2013). Objective outcome measures assessed included handheld biothesiometer (Greenlee et al., 2016), pegboard test (Greenlee et al., 2016), and NCS (Molassiotis, Suen, Cheng, et al., 2019; Rostock et al., 2013). Greenlee et al. (2016) reported worsening pain at 16 weeks as measured by NPS, with no difference in objective measures. The other three studies (Lu et al., 2019; Molassiotis, Suen, Cheng, et al., 2019; Rostock et al., 2013) indicated improvement in subjective outcome measures. In the study by Rostock et al. (2013), participants in all four arms of the study reported improvement in neuropathy scores and quality of life; there was no improvement in objective outcome measures including NCS, biothesiometer, and pegboard test.

Xiong et al. (2016) randomized 90 women who had developed CIPN following treatment for breast cancer into one of three treatment arms, which included acupuncture, mecobalamin injection without acupuncture, or acupoint injection with mecobalamin. Outcomes assessed included patient symptoms, EMG measurements and changes in hematological indicators. This study found that the outcome measures were improved in all groups, with the greatest improvement in the group that received acupoint injection.

Zhang et al. (2017) randomized 37 male and female participants with baseline CIPN grade I-IV to receive either acupuncture or EA concurrent with treatment with chemotherapy. Only two acupuncture points, LI4 and LV3, were used in both the acupuncture and EA groups. Outcome measures included a diagnosis of neuropathy based on the grading system of Levi,

TCM clinical symptoms, Karnofsky performance status and immune function indicators. The authors note an improvement in all outcome measures with the exception of immune function indicators, with greater improvement in the EA group than the manual acupuncture group.

Retrospective Chart Reviews

Two retrospective studies are included in this review. Donald et al. (2011) reviewed the charts of eighteen patients with neuropathy who had received chemotherapy and acupuncture without EA. The authors note that several of the patients had other medical conditions known to cause neuropathy, including diabetes and spinal metastases. Patient report of symptoms were obtained and revealed fourteen patients (82%) reported improvement in neuropathy symptoms, while three reported no change or worsening symptoms. One patient died prior to completion of the study. However, no baseline measurements of CIPN were available/obtained.

In the study by Valentine-Davis & Altshuler (2015), the charts of ten patients who had received oxaliplatin for colorectal cancer and different combinations of acupuncture treatments were reviewed, including persons currently in treatment and survivors. Not all of the acupuncture treatments are described in detail, however the authors state that the patients received a range of treatments in terms of aggressiveness, which they define by acupuncture points selected and frequency of the treatments. All of the patients had some improvement in symptoms of CIPN, based on healthcare provider report. Two of the patients had a dose reduction in their chemotherapy, the implications of which are not discussed.

Case Report

A case report (Mandıroğlu, et al., 2014) followed a 74-year old patient with CIPN symptoms while receiving bortezomib for multiple myeloma. The patient received fifteen acupuncture treatments. His pain was assessed using NPS, which was 0/10 at the end of the last acupuncture treatment at six months. The authors report that the reduction in patient symptoms supported the patient to continue his chemotherapy.

Discussion

This paper makes an important scientific contribution through a more comprehensive review of the literature on the ability of acupuncture to treat CIPN.   Prior literature reviews by Baviera et al. (2019), Chien et al. (2019), and Li et al. (2019) selected a smaller range of studies based on narrower exclusion criteria such as the definition of acupuncture or the study design. This integrative review reveals that overall the available evidence is limited to studies characterized by small sample sizes, heterogenous design and variable outcome measures. A variety of acupuncture techniques and protocols were used to evaluate the effectiveness of acupuncture to treat CIPN and, with the exception of Greenlee et al. (2016), found at least some improvement in subjective outcome measures without corresponding improvement in objective measurements.   As the evidence demonstrates that patients who receive acupuncture generally report subjective improvement in symptoms of CIPN without improvement in objective measures, the question arises as to whether new objective measures need to be developed, or if the emphasis of evaluation should be patient report of pain and quality of life indicators.

The need to establish consistent and clinically relevant measures to evaluate the impact of acupuncture on quality of life for patients with CIPN is discussed in the review by Baviera et al. (2019). Therefore, evaluating acupuncture through a more pragmatic lens that focuses on

effectiveness, including impact on pain and quality of life, may prove more meaningful than establishing efficacy as measured by improvement in controlled clinical settings (Ang & Kaptchuk, 2011; Kaptchuk et al., 2010). In sum, main themes and recommendations for future research identified by this integrative review of the literature include: 1) the need for a consistent definition of acupuncture as an intervention; 2) the need to develop standardized acupuncture protocols; and 3) the need for consistent outcome measures and comparison treatments to evaluate the benefit of acupuncture for CIPN**.** Each of these themes is discussed in detail below.

Defining Acupuncture

In order to optimally evaluate the effectiveness of acupuncture, consensus is needed on what technique, or group of techniques, is being evaluated when the term "acupuncture" is used. Comparison of the prior reviews by Baviera et al. (2019), Franconi et al. (2013), and Li et al. (2019) demonstrates the need for a consistent definition of acupuncture as a technique. For example, Baviera et al. (2019) included only acupuncture studies which involved manual acupuncture without the use of auricular acupuncture, laser or EA. Franconi et al. (2013) included any studies involving acupuncture needling of humans or animals with the addition of auricular acupuncture and EA. Li et al. (2019) defined acupuncture in even broader terms to include any use of acupuncture, EA or acupressure as a primary or adjunctive therapy.

Excluding studies of acupuncture that involve auricular acupuncture or electro-acupuncture would have eliminated several studies of importance in this review (Bao et al., 2014; Garcia et al., 2016; Greenlee et al., 2016; Lu et al., 2017; Rostock et al., 2013; Xiong et al., 2016; Zhang et al., 2017). EA is used in five of the included studies (Garcia et al. 2016; Greenlee et al., 2016; Lu et al., 2019; Rostock et al., 2013; Zhang et al., 2017), indicating that this technique is considered important and should be evaluated for its effectiveness in clinical

practice for the management of CIPN. This review utilizes a definition of acupuncture similar to that of the search performed in the meta-analysis by Chien et al. (2019), which included studies of true needle acupuncture or EA while excluding techniques that did not involve acupuncture needles such as laser techniques. Defining acupuncture to include studies in which it is used as an adjunctive to other therapies could obscure the effects of the acupuncture intervention. A definition of acupuncture which includes use of true needle acupuncture on the body, auricular acupuncture, and EA provides a comprehensive view of the use of acupuncture in clinical practice while minimizing non-acupuncture techniques such as lasers or injections into acupoints.

Developing Treatment Protocols

Another area for improvement identified by this review of the literature is the need to develop standardized acupuncture treatment protocols. The literature indicates that acupuncture treatment protocols for management of CIPN should be based upon whether patients are currently in treatment or are post-treatment survivors. Patients receiving active treatment with neurotoxic chemotherapy may benefit from a comparatively less aggressive acupuncture treatment approach, as defined by factors including the location of points used, frequency of treatment, and inclusion of EA. Aggressive treatment protocols and EA may have more effectiveness in the management of CIPN for post-therapy survivors.

In addition to consideration of active versus post-therapy treatment status, this integrative review found evidence to support the use of specific treatment points for patients with CIPN. According to diagnostic criteria of TCM, patients with cancer are generally characterized as having what is referred to as "deficiency" in several areas (Lu et al., 2017; Valentine-Davis & Altshuler, 2015).   While TCM practice emphasizes the need to develop individualized patient

treatment plans, the literature suggests that even more tailored and effective point protocols could be developed that reflect TCM principles such as avoidance of more aggressive treatments in deficient patients.   For example, the majority of studies included local treatment points on the hands and feet, and nearly all of these studies were associated with improvement in patient report of CIPN symptoms. Additionally, Chien et al. (2019) suggested that acupuncture may be more effective for CIPN related to the specific type of chemotherapy received, noting a positive effect of acupuncture for patients who developed CIPN following treatment with bortezomib.

Identifying Appropriate Measures of Evaluation

Lack of objective outcome measures of CIPN which correlate with patient report of improved symptoms is also a limitation noted in the systematic review by Baviera et al. (2013) and meta-analysis by Chien et al. (2019).   NCS was used as an outcome measure in several studies (Bao et al., 2014; Garcia et al., 2014; Molassiotis, Suen, Cheng, et al., 2019; Rostock et al., 2013) following Schroeder et al. (2012), a study in which patient report of improvement in symptoms did correlate with results of NCS.   Of note, only six of eleven total patients received the acupuncture intervention in Schroeder et al. (2012). In all of these subsequent studies of acupuncture for CIPN, change in NCS did not correlate with patient report of symptoms.

Ability to determine objective measurements of the effects of acupuncture in the treatment of CIPN is complicated by the fact that recent studies have highlighted inadequacies of current methods of CIPN assessment (Molassiotis, Cheng, Lopez, et al., 2019). NCS has been used as an outcome measure in studies of acupuncture for nerve pain related to other etiologies such as carpal tunnel (Maeda et al., 2017), however NCS may not be an effective measure of effects acupuncture on nerve damage related to other etiologies including neurotoxic chemotherapy. Motor function tests such as timed function tests may be of more benefit to

demonstrate effects of acupuncture on CIPN symptoms. While NCS may not be the most reliable objective measure of acupuncture in the treatment of CIPN, other methods including timed function tests and other assessments of motor symptoms could prove to have more value.

Further work to identify appropriate and consistent measures to evaluate the efficacy of acupuncture for patients with cancer is important to advance symptom science. Different outcome measures may be indicated based upon factors such as the patient's goals of care and whether they are receiving chemotherapy or other potentially neurotoxic therapy. For many patients, subjective improvement in their pain and quality of life, including such factors as mobility or sleep, versus objective measures including NCS, may reflect a more meaningful impact of acupuncture on symptoms of CIPN. In addition to developing appropriate and consistent outcome measurements, future research should seek to more thoroughly explore the potential effects of acupuncture on the overall quality of life of patients coping with CIPN through in-depth qualitative research.

Limitations

The primary limitation of this integrative review is the small number of studies on acupuncture in the management of CIPN published in the past ten years that met inclusion criteria. Risk of bias in the primary studies including lack of random assignment is an additional limitation related to the existing research. Some studies were only available in languages other than English, most notably Chinese; budgetary constraints precluded our ability to translate Chinese language studies into English for consideration, which further limited the sample size. An additional limitation is that the grey literature was not included in the search.

Conclusion

CIPN is a condition associated with both pain and decreased quality of life which affects an estimated 30-40% of patients with cancer or cancer survivors. This integrative review regarding acupuncture for the treatment of CIPN in patients with cancer revealed gaps in the current body of literature that make it difficult to evaluate its impact, including small sample sizes and variability in study design. By evaluating twenty studies in which acupuncture was the primary intervention in the treatment of CIPN, several themes were identified. First, a clear and consistent definition of which technique, or group of techniques, is considered acupuncture is needed for use across the literature. This review proposes a definition of acupuncture which includes needle insertion into body and auricular acupoints, with the addition of EA. A second theme is the need to establish standardized acupuncture protocols for treatment of CIPN, such as those that include local points on the hands and feet. More aggressive point combinations and potentially also EA may be of more benefit for post-treatment survivors than those still in active treatment with neurotoxic chemotherapy. Finally, more research is needed to establish consistent and clinically relevant outcome measures to evaluate the effects of acupuncture on pain and quality of life in patients with CIPN.

Table 1. Quasi-experimental Studies

Author/ Year	Purpose/ Aims	Sample	Intervention Description	Research Design	Outcome Measures	Results and Conclusions
Bao et al. (2018)	Determine efficacy of acupuncture to prevent progression from grade IIA to grade III CIPN in breast cancer patients receiving paclitaxel	27 women, ages 39-53, with stage I-III breast cancer	1-11 (median 3 total) weekly acupuncture treatments Acupuncture with *de qi* sensation per protocol Points used: R ear shenmen & point zero, LI11, SJ5, LI4, St40, bafeng	Single arm intervention study	Primary: progression or absence of progression from grade II to grade III CIPN Multiple secondary outcomes listed, including:CIPN severity, measured by	26/27 patients completed treatment without developing grade III CIPN Stable during continued treatment in all 27 patients No change in vibration test results

				FACT-GOG/Ntx & NPS scores, test of vibration with tuning fork	
Bao et al. (2014)	Evaluate feasibility, safety and efficacy of acupuncture to treat neuropathy in patients who received bortezomib for multiple myeloma Explore possible mechanisms of action of acupuncture	27 patients with history of multiple myeloma who developed grade II or higher neuropathy following treatment with bortezomib	10 acupuncture treatments over 10 weeks including ear points shenmen, point zero and 2 additional points, and LI4, TE5, LI11, St40 & bafeng upper and lower extremities	Single arm intervention study	TNSc, FACT/GOG-NTx and NPS Measurement of pro-inflammatory cytokines and neurotrophic factors NCS	TNSc results invalid Improvement in FACT/GOG-NTx and NPS No significant changes in in cytokines or neurotrophic factors No improvement in NCS
Ben-Arye et al. (2018)	Assess impact of acupuncture and complementary therapies on quality of life and function in women who had received taxanes for breast or gynecologic cancer	59 patient files, women age 18 years or older with breast or gynecologic cancer, who were treated with taxanes and received CIM therapy	All patients received acupuncture, 15 received acupuncture only, technique not described	Single arm intervention study	Patient narratives obtained from file and MYCAW (Measure yourself concerns and wellbeing) tool 4 reviewers asked to assess narratives for impact of CIM on PN symptoms as: no, mild, or moderate benefit, or NA	35 patients received moderate benefit in neuropathy symptoms Effect of acupuncture to reduce symptoms noted by 17 patients
Garcia et al. (2014)	Evaluate safety, feasibility and effective-ness of acupuncture to treat neuropathy in patients who received chemo-therapy for multiple myeloma	19 patients, 14 men and 5 women, mean age 64 years, with grade II-III peripheral neuropathy	20 acupuncture treatments over 9 weeks Points: LI4*, SI3*, baxie, LV3*, Sp6, Gb42*, St36, bafeng, Du20, CV4, CV6 with *de qi* and electrical stimulation on * points	Single arm intervention study	FACT/GOG-NTx, BPI-SF, FACT-G NCS Fall risk Timed function tests (coin test, walking, postural stability, fall and button test)	Scores improved in all patient reported outcome scales, greatest at week 9 No significant change in NCS Some improvement in fall risk Improved time function tests
Jeong et al. (2018)	Assess feasibility and safety of acupuncture for taxane-induced CIPN in Korean women	10 Korean women, ages 45-67, with CIPN grade I-IV following breast cancer treatment	12 acupuncture treatments, 3 times weekly for 4 consecutive weeks Manual acupuncture protocol, with points provided: LI11, LI4, St36, LV3, M-LE	Single arm intervention study	Neuropathy assessed with NPSI and NCS QoL assessed with SF-36 questionnaire	NPSI score reduced for all patients No significant change in NCS Improvement in several areas assessed by SF-36

			8(bafeng), M-UE 9(baxie)			
Schroeder, Meyer-Hamme & Epplee (2011)	Assess ability of acupuncture to treat CIPN based on objective measures	11 male and female patients, mean age 65 yrs, who developed CIPN during chemotherapy	6 patients received acupuncture, and 5 provided control (based on refusal) 10 weekly acupuncture treatments Points used: St34, qiduan, bafeng, no *de qi* sensation	Quasi-experimental study	NCS Patient report of symptoms	NCS and patient report of symptoms improved after 6 months
Xiong et al. (2016)	Determine ability of acupuncture with injection of mecobalamin to treat symptoms of CIPN in women with breast cancer	90 women with breast cancer, ages 47 to 71, with CIPN following treatment with taxanes or alkaloids	Pts received acupuncture, mecobalamin injection, or acupoint injection once every 3 days x 10 treatments Manual acupuncture protocol: LI 11, LI4, St26, Sp6, Sp10 with manual stimulation	Randomized intervention study	EMG of ulnar and common peroneal nerve Observed changes in hemorrheology indicators	EMG measurements improved in all 3 groups, greatest in acupoint injection group Changes in hemorrheology indicators improved in all 3 groups, greatest in acupoint injection group
Zhang et al. (2017)	Assess effect of electro-acupuncture on QoL and immune status of patients with CIPN	37 male and female patients ages 36-79 with malignancy and CIPN grade I-IV	18 received acupuncture, 19 electro-acupuncture Points: LI4 & LV3 with or without electro-acupuncture	Randomized intervention study	Primary: Peripheral neuropathy diagnosis according to grading system of Levi Secondary: TCM clinical symptoms Karnofsky performance status Immune function (NK cells, CD3, CD4, CD8 & CD4/CD8)	Improved in all categories except for immune function, where there was no effect Electro-acupuncture had a greater effect than acupuncture alone, with exception of immune function

| Zhi et al. (2018) | Evaluate the impact of acupuncture on specific symptoms of CIPN in patients with bortezomib-induced neuropathy | 27 patients with multiple myeloma who developed neuropathy grade 2 or higher following treatment with bortezomib | 10 acupuncture treatments over 10 weeks

Points included: ear points (shen men, point zero, and 2 additional points), LI4, TE5, LI11, St40 bafeng upper and lower extremities with *de qi* | Single arm intervention study | FACT/GOG-Ntx and NPS | FACT/GOG-Ntx scores increased from baseline at week 14, indicating least neuropathy symptoms

NPS scores reduced in all 10 areas, indicating improvement in neuropathic pain |

Table 2. Randomized Studies

Author/ Year	Purpose/ Aims	Sample	Intervention Description	Research Design	Outcome Measures	Results and Conclusions
Greenlee et al. (2016)	Investigate the effect of electro-acupuncture to reduce or prevent CIPN in breast cancer patients treated with taxanes	63 women, ages > 21 years, with stage I-III breast cancer	Patients randomized to receive either sham acupuncture or electro-acupuncture weekly for 12 weeks, within 2 days of weekly chemotherapy infusion Acupuncture protocol points: Gb34*, St36*, LI4*, LI10*, huatoujiaji points (at C5, C7, L3 &L5), bafeng, baxie (* = EA points)	RCT	BPI-SF FACT-NTX NPS-10 FACT-TAX Handheld bio-thesiometer to measure sensory neuropathy and pegboard test to measure motor-neurologic dysfunction	BPI-SF 1.62 greater in EA group vs sham at 16 weeks FACT-NTX trended toward increased pain at 16 weeks, without differences between groups NPS at 16 weeks EA group had worst pain No differences between groups in FACT-TAX, biosthesiometer or grooved pegboard tests
Lu et al. (2019)	Evaluate ability of acupuncture to alleviate CIPN sensory symptoms in women treated with taxanes for breast cancer	40 women who had completed treatment with taxanes for breast cancer. Median time from end of treatment was 14 months.	18 acupuncture treatments over 8 weeks. Manual acupuncture week 1, then EA Points used: yintang, LI11, TW5*, baxie*, Sp9, St36, Sp6*, Kd3, LV3*, qiduan (* = EA points)	RCT	Patient report of symptoms measured by PNQ, FACT-NTX, BPI-SF, QLQ-C30	35/40 patients completed the protocol Significant improvement in CIPN sensory symptoms, pain level, and QOL measures in intervention group
Molassiotis et al. (2019)	Assess efficacy of acupuncture to manage CIPN in cancer patients who had received or	Patients with breast, gynecologic, colorectal,	Patients randomized into wait-list control arm or acupuncture intervention arm	RCT	Primary: BPI to measure pain Secondary:	Pain improved in acupuncture arm vs control arm

					FACT/GOG-Ntx questionnaire to evaluate QoL with neurotoxicity specific module Symptom distress scale NCS	QoL significantly better in acupuncture arm vs control and neurotoxicity score also better in acupuncture arm No significant difference in NCS between groups
	were currently receiving neurotoxic chemotherapy	head or neck cancer or multiple myeloma who had received neurotoxic chemotherapy with symptoms of CIPN	Acupuncture points selected from a standardized pool of points at practitioner discretion: LI4, LI11, PC7, TE5, baxie, Sp6, St36, LV3, St41, bafeng			
Rostock et al. (2013)	Evaluate role of electro-acupuncture in the manage-ment of CIPN	60 male and female patients with history of cancer in remission who developed CIPN following treatment with chemotherapy	Patients received electro-acupuncture, hydroelectric baths, high doses of vitamin B or a placebo Acupuncture treatments were 8 sessions using pts: LV3, Sp9, Gb41, GB34, LI4, LI11, SI3 and Ht3 with electro-acupuncture	RCT	Primary: Patients interviewed on severity of CIPN, level of suffering and to rate severity of symptoms Secondary: CIPN symptoms evaluated by neurologist including NCS QoL measured with EORTC QLQ-C30	Primary: Neuropathy scores improved in all groups Secondary: No significant differences in neurological assessment/NCS QoL moderately improved in all groups

Table 3. Retrospective Chart Reviews and Case Report

Author/ Year	Purpose/ Aims	Sample	Intervention Description	Research Design	Outcome Measures	Results and Conclusions
Donald, Tobin & Stringer (2011)	Assess effectiveness of acupuncture to treat CIPN	18 male and female patients with neuropathy likely related to chemotherapy (comorbidities including DM and spinal metastasis listed for several patients)	17 patients received 6 weekly acupuncture treatments (1 patient died during the study) Most common points used: Sp6, LV3, LI4, Bl60, St36 bafeng/baxie	Retrospective study	Patient report of symptoms	82% reported improvement in neuropathy, 18% no change, no report of worsening symptoms Additional benefits reported: improved sleep, relaxation, stress, improved mood, less medication

Mandiroglu, Cevik & Ayli (2013)	Case study of patient who responded to acupuncture for neuropathy	1 74-year old male patient with multiple myeloma, NPS 8/10	15 acupuncture treatments over 10 weeks Points used: St36, Sp6, LI4 with de qi sensation	Case report	NPS scores during treatment and at 6 months following completion	NPS 0/10 at end of 15th treatment and at 6 months Reduction in symptoms of PN allowed for continued treatment with chemotherapy
Valentine-Davis & Altshuler (2015)	Report experience of the authors to treat and prevent CIPN in colorectal cancer patients who received oxaliplatin	10 patients with stage II-IV colon cancer	Acupuncture points selected based on TCM diagnosis of individual patient Relative aggressiveness of treatment regimen noted in terms of points selected and frequency of treatment	Retrospective study	End CIPN grade according to CTCAE v4.0 and patient response to acupuncture Acupuncture side-effects	Acupuncture resolved, improved or prevented progression in all patients There were no side-effects

CHAPTER THREE

Methods

Overview of Study Design

This dissertation research is a secondary data analysis using survey data from the parent National Institutes of Health R01 study, *Characterizing the Complexity of Advanced Cancer Pain in the Home Context*. Briefly, the parent study deploys and tests the Behavioral and Environmental Sensing and Intervention for Cancer (BESI-C), a remote health monitoring system that aims to understand the experience of cancer pain in the home (LeBaron et al., 2020; LeBaron et al., 2022). The BESI-C study includes both sensing and survey data. Sensing data are collected by a combination of wearable devices (smartwatches) and ambient environmental sensors and includes information on the experience of cancer pain from the perspective of both the patients and their caregivers (LeBaron et al., 2022; LeBaron et al., 2023). Baseline (prior to the deployment of the BESI-C system in the home) RedCap surveys are collected by the clinical research coordinator (CRC) from patient and caregiver dyad participants, including pharmacologic and nonpharmacologic methods used to manage pain and perceptions of the effectiveness of the pain management methods. Although the patients and caregivers were recruited as dyads, the purpose of this analysis was to understand the perspective of patients and caregivers as separate groups.

Data from patient and caregiver demographic and clinical BESI-C baseline surveys were used to evaluate feasibility and acceptability of acupuncture/pressure through self-reported use of nonpharmacologic therapies to manage advanced cancer pain, perceived confidence in pain management, and reported measures of quality of life (QoL). Feasibility can be evaluated using

self-report as a source of data (Teresi et al., 2022). Prior research on feasibility and acceptability

of self-care and self-management interventions among patients with chronic illness has drawn on

patient and caregiver self-report of use and perceived effectiveness (Cossette et al. 2016;

Nightingale et al., 2022). For the purposes of this dissertation research, feasibility and

acceptability of acupuncture for cancer pain are operationalized through self-reported use and

perceived effectiveness from patients and family caregivers as supported by the prior literature

(Cossette et al. 2016; Nightingale et al., 2022; Teresi et al. 2022), Specific details of the items

utilized from the parent study surveys for this secondary data analysis are described in more

detail below in the section, Overview and Rationale for the Selected Variables. The complete

patient and caregiver demographic and baseline BESI-C surveys are available as Appendices A-

D.

Research Questions

The primary research questions addressed by this analysis include:

1) Is acupuncture/pressure feasible and acceptable among patients and caregivers of patients with advanced cancer pain (patients with advanced cancer who have cancer-related pain)?

2) Is self-reported use of acupuncture/pressure associated with higher ratings of self-efficacy in pain management among patients and caregivers of patients with advanced cancer pain?

3) Are demographic and clinical variables associated with self-reported use of acupuncture/pressure for management of advanced cancer pain among both patients and caregivers?

These research questions address a gap in the literature as there is limited available

research on use of acupuncture or acupuncture for management of advanced cancer pain, or

feasibility and acceptability of acupuncture/pressure among both patients and their

primary/family caregivers. A systematic review of the literature on acupuncture for cancer pain published in 2020 included only one study specific to acupuncture for advanced cancer pain (He, 2020). One additional study was identified involving acupuncture for pain among patients with advanced malignancy in which acupuncture was compared to massage (Epstein et al., 2020). Regarding feasibility and acceptability of acupuncture/pressure among both patients with cancer and their informal caregivers, one article was found which evaluated acceptability of acupuncture among patients with cancer and their caregivers in Belgium, however this study was not specific to pain (Tack et al., 2020).

Overview of Study Aims

Analysis Procedures Used to Evaluate the Feasibility and Acceptability of Acupuncture (Aim 1).

Aim 1: To evaluate the feasibility and acceptability of acupuncture/pressure among patients and caregivers of patients with pain related to advanced cancer using baseline surveys collected as part of the BESI-C parent study. **Hypothesis 1:** Acupuncture/pressure is feasible and acceptable among patients and caregivers of patients with cancer pain. Feasibility was evaluated using univariate analysis to obtain the percentage of patients and caregivers who have tried acupuncture/pressure to manage their pain. Use of acupuncture/pressure among patients and caregivers was compared with the use of 12 other non-pharmacological methods for pain management including: positioning, being with other people, rest/sleep, listening to music/watching TV, exercise/activity, massage, ice/heat, over-the-counter creams and ointments, guided imagery/hypnosis, prayer/meditation, progressive muscle relaxation, and distraction. Comparisons of use of the non-pharmacologic therapies were made using relative frequencies,

consistent with prior research on use of nonpharmacologic therapies for management of chronic pain (Almutairi et al., 2019; Eaton et al., 2017).

Acceptability was evaluated through patient and caregiver responses regarding perceptions of whether acupuncture is helpful to relieve the patient's pain and belief in the overall effectiveness of the current pain regimen. Patients and caregivers who indicated that they believe acupuncture/pressure is effective to manage the patients' pain were compared to those who do not using descriptive statistics. Belief in the effectiveness of the current pain regimen among both patients and caregivers of patients who have used acupuncture/pressure was compared to responses of the patients and caregivers of patients who have not tried acupuncture/pressure using an independent two sample t-test for comparison between groups. A p-value of less than 0.05 was considered statistically significant.

Analysis Procedures Used to Evaluate Use of Acupuncture/pressure on Self-Efficacy and Relationship to QoL (Aim 2).

Aim 2: To evaluate if use of acupuncture/pressure among patients and caregivers of patients with cancer pain is associated with higher self-efficacy, measured by confidence in pain management. **Hypothesis 2:** Use of acupuncture/pressure is associated with higher self-efficacy in pain management among patients and caregivers of patients with cancer pain. The baseline patient and caregiver survey data evaluate the degree of confidence in managing the patient's pain from "not at all" to "very" with a Likert-style scale.   Numeric values were assigned to the Likert-style responses for degree of confidence in pain management from 1 indicating "not at all" to 5 indicating "very confident." The degree of confidence in managing pain was compared between the patients and caregivers of patients who have tried acupuncture/pressure and those who have not using an independent two sample t-test for comparison. Multiple linear regression was used to determine if acupuncture/pressure predicts confidence in pain management

controlling for functional status and pain interference in daily activities among both patients and caregivers. Statistical significance was considered at a p-value of less than 0.05.

Analysis Procedures Used to Evaluate the Relationship of Demographic and Clinical Variables to Use of Acupuncture/pressure for Cancer Pain (Aim 3).

Aim 3: To evaluate demographic and clinical factors associated with the use of acupuncture/pressure and other non-pharmacological therapies among patients with cancer pain and their caregivers. **Hypothesis 3:** Demographic and clinical variables including age, self-reported gender, work status, level of education, primary cancer diagnosis and stage, pain characteristics, and use of medications for pain management are associated with use of acupuncture/pressure. The data were analyzed using independent two sample t-tests for continuous data and chi-squared tests for categorical data. Significance was determined at a p-value of less than 0.05.

Conceptual Frameworks to Support the Analysis

Three theories support the aims of this research study, including Bandura's Theory of Self-Efficacy, the Whole-Person Model of Chronic Pain, and the Theory of Self-Care Management in Cancer. In addition to these frameworks, the concept of holism deserves a brief review in order to understand what is meant when describing acupuncture/pressure as a holistic health intervention. The concept of holism in health care emphasizes synergy and interaction among aspects of the individual including physical, social, and emotional realms and how these interplay with external health determinants and influences (Michaelson et al., 2018). Holism could be conceptualized as a foundation which unifies the theories of self-efficacy, Self-Care Management in Cancer, and the Whole-Person Model of Chronic Pain.

Bandura's Theory of Self-Efficacy describes the extent to which individuals are able to influence the events affecting their lives (Bandura, 1994). This belief in personal ability to influence events also includes knowledge of the skills that are needed to affect outcomes and when to use them (White et al., 2019). The relevance of self-efficacy for diverse populations is indicated by international studies using self-efficacy (Eller et al., 2016). Self-efficacy questionnaires related to pain and chronic condition management have been used with diverse populations including Arab, Hispanic, and non-Hispanic Black (Almutairi et al., 2023; Nephew at al. 2022; Philip et al., 2022). In patients with cancer, self-efficacy has been identified as a positive outcome in itself related to an increased sense of control and self-management skills (Foster et al., 2015; Merluzzi et al., 2019) and a decrease in frequency and severity of symptoms (White et al., 2019). Positive clinical outcomes associated with increased self-efficacy include decreased pain, emotional distress, and fatigue (Merluzzi et al., 2019). Self-efficacy is relevant to this dissertation research in order to contextualize the relationships among pain, self-management of symptoms, and QoL.

The Theory of Self-Care Management in Cancer is a middle-range nursing theory that emphasizes active patient involvement and self-care management of symptoms in patients with cancer (Beydoun et al., 2018). Middle range nursing theories are developed through integration of theories from multiple sources including other disciplines to guide concepts for nursing practice and research (Liehr & Smith, 2017). In this model, self-efficacy and self-regulation skills, such as the ability to establish goals, self-monitoring and self-regulation and reflective thinking, are conceptualized as moderators of the relationship between self-care behaviors and symptoms. Additionally, this theory emphasizes understanding cancer as a chronic illness, increasing the need for patients to develop symptom self-management skills (Baydoun et al.,

2018). The Theory of Self-Care Management in Cancer supports this dissertation research by conceptualizing cancer as a chronic illness and highlighting the importance of symptom self-management among patients with cancer pain.

In the Whole-Person Model of Chronic Pain, management of pain should involve the patient partnering with health care providers to choose the most appropriate strategies to address symptoms. These strategies can be divided into five components: biological (including medical interventions), nutrition, personal story (described as the mind-body psychodynamic), and thoughts and actions, which together are called cognitive-behavioral interventions (Hayes & Hodson, 2011). This model supports the dissertation research as acupuncture/pressure is both a biological and cognitive-behavioral intervention that affects the whole person in the context of managing cancer pain.

In the absence of a theory specifically conceptualized to support research on acupuncture/pressure, the three theories above were selected related to their ability to create a synthesis that demonstrates the effects of a complementary health intervention on the whole person. Figure 1 demonstrates the synthesis of these theories and how they relate to the aims of this study. The five aspects of the whole-person model were derived from the Whole-Person Model of Chronic Pain, which includes environment, relationships, body, mind and spirit (Hayes & Hodson, 2011).

The ability of self-care management behaviors to affect symptom experience and QoL was taken from the Theory of Self-Care Management in Cancer. Self-efficacy is an integral aspect of this model throughout and will be evaluated through patient and caregiver report of confidence in pain management. Through use of self-care behaviors to successfully address symptoms and improve quality of life, feelings of self-efficacy are increased. As self-efficacy is

also a moderator of the relationship between self-care management and symptoms, increasing

self-efficacy continually strengthens the effect of self-care interventions including
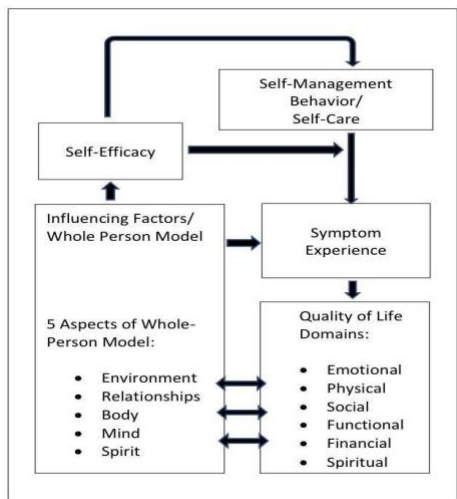
acupuncture/pressure.

Figure 2. The relationship among self-efficacy, self-care, symptoms and QoL in a whole-person model of care.

Conceptual Frameworks and Relationship to the BESI-C System

The BESI-C system assesses the holistic home context through environmental sensors in

the home used to collect environmental data (LeBaron et al., 2022). Both patients and caregivers

use technology delivered over smart watches to provide real-time data on interventions they use

for pain (LeBaron et al., 2023). The smart watches obtain data on emotional distress among

patients and caregivers, and interventions for pain include activities such as meditation and

prayer, integrating mind and spirit. Within this greater framework of the BESI-C system, this

secondary data analysis will utilize survey data that highlights functional aspects of QoL by

measuring pain interference with daily activities, and functional status including ability to

participate in self-care.

**Table 4. Conceptual Frameworks and Relationship to Data Sources from BESI-C Remote
Health Monitoring System**

Conceptual	Domain	Data Obtained from BESI-C System

Framework		
Quality of Life Domains	Emotional	Emotional distress and mood self-reports obtained from on-demand and scheduled Ecological Momentary Assessments (EMAs) recorded by smart watches worn by participants
	Physical	Self-symptom reports of pain, fatigue, sleep obtained from on-demand and scheduled Ecological Momentary Assessments (EMAs) recorded by smart watches worn by participants Physiological data (heartrate; stepcount) passively recorded by smart watches worn by participants
	Social	Caregiver report of patient symptoms via on-demand and scheduled EMAs; measurement of patient-caregiver proximity and time spent outside the home; time spent together, and time spent with others via EMAs and passive localization sensing.
	Functional	Physiological data (heartrate; stepcount) passively recorded by smart watches worn by participants
	Spiritual	Self-reported use of meditation and prayer as interventions for pain obtained from scheduled Ecological Momentary Assessments (EMAs) recorded by smart watches worn by participants
Whole Person Model	Environment	Environmental data from ambient sensors placed in dyad homes that passively collect data regarding noise, temperature, light, barometric pressure, humidity, and location within home
	Relationships	Caregiver report of patient symptoms via on-demand and scheduled EMAs; measurement of patient-caregiver proximity and time spent outside the home; time spent together, and time spent with others via EMAs and passive localization sensing.
	Body	Patient and caregivers report of patient symptoms including pain, fatigue, sleep recorded via on-demand and scheduled EMAs; smart watches passively obtain physiological data such as heart rate from participants
	Mind	Self-reported use of mind-body interventions for pain including hypnosis, guided imagery as interventions for pain obtained from scheduled Ecological Momentary Assessments (EMAs) recorded by smart watches worn by participants
	Spirit	Self-reported use of meditation and prayer as interventions for pain obtained from scheduled Ecological Momentary Assessments (EMAs) recorded by smart watches worn by participants

Overview and Rationale for Selected Variables from the BESI-C Baseline Surveys

Demographic and clinical data for patient and caregiver participants were utilized to characterize the sample. Feasibility and acceptability of the use of non-pharmacologic therapies to manage cancer pain were assessed through: 1) self-reported use of the nonpharmacologic

therapies including acupuncture/pressure; 2) self-reported effectiveness of nonpharmacologic therapies for pain management; and 3) self-reported overall effectiveness of the current pain regimen. As self-efficacy is associated with an increased sense of control and self-management skills, survey items measuring perceived confidence in pain management were used as a proxy measure of self-efficacy. Self-efficacy has been defined as confidence in pain management (Fisher et al., 2023) and is linked to belief in personal ability to manage pain (Raman & Sharma, 2022). QoL is an important and complex variable as QoL captures multiple aspects of the symptom experience: emotional, physical, social, functional, financial and spiritual. QoL was evaluated through patient and caregiver report of the degree to which pain interferes with daily activities and functional status.

Table 5. Variables and Rationale

Variable	Purpose/ Construct of Interest	Rationale
Demographic and clinical data	Feasibility	Relationship of patient and caregiver characteristics to use of non-pharmacologic therapies including acupuncture/pressure
Reported use of non-pharmacologic therapies including acupuncture/pressure	Feasibility	Feasibility of non-pharmacologic therapies including acupuncture/pressure
Belief in the effectiveness of the non-pharmacologic therapies including acupuncture/pressure for pain management	Acceptability	Acceptability of non-pharmacologic therapies including acupuncture/pressure
Belief in effectiveness of the current pain regimen	Acceptability	Acceptability of non-pharmacologic therapies including acupuncture/pressure
Functional status (ECOG*)	QoL	Relationship of QoL to acupuncture/pressure use and self-efficacy

Degree of pain interference in daily activities	QoL	Relationship of QoL to acupuncture/pressure use and self-efficacy
Confidence in pain management	Self-efficacy	Effect of acupuncture/pressure use on self-efficacy

* ECOG Performance Status Scale measures patient functional status on a scale from 0 indicating fully active without restrictions to 5 or dead (ECOG-ACRIN, 2022).

Tables 6a-b indicate which variables are present in the patient surveys, the caregiver surveys, or both.

Table 6a-b. Self-Reported Demographic and Clinical Variables Used in Analysis, by Patient and Caregiver Participants

6a. Demographic Variables by Patient and Caregiver		
Variable	**Patient**	**Caregiver**
Age	x	x
Gender	x	x
Racial Identity	x	x
Ethnic Identity	x	x
Occupational Status	x	x
Former Occupation	x	x
Educational Level	x	x
Caregiver Relationship to the Patient		x
Length of Time as Patient's Primary Caregiver		x

6b. Clinical Variables by Patient and Caregiver		
Variable	**Patient**	**Caregiver**
Diagnoses of Other Medical Problems (Self-Reported Comorbidities)	x	x
Patient's Primary Cancer Diagnosis	x	
Cancer Stage	x	
Presence of Constant Cancer-Related Pain	x	

Average Constant Pain Level	x	
Frequency of Acute Cancer Pain Events	x	
Average Acute Pain Level	x	
Current Pain Level	x	
Location of Most Cancer Pain	x	
Use of Long-Acting/Sustained Release Medications for Cancer Pain	x	
Belief in Effectiveness of Non-Pharmacologic Therapies for Management of Cancer Pain	x	x
Belief in Effectiveness of Current Pain Regimen	x	x
Confidence in Pain Management	x	x
Patient/Caregiver Report of Degree of Patient's Pain Interference in Daily Activities	x	x
Patient/Caregiver Report of Patient's Functional Status	x	x

Study Participants and Clinical Site

The study participants for the parent study and this SDA included dyads of patients with cancer and their primary family ("family" defined broadly) caregiver recruited from a palliative care clinic at an academic medical center and a community hospice, both located in Central Virginia. This SDA utilized data from all participants recruited for the parent study between October 2021 – September 2023.

Inclusion and Exclusion Criteria

Inclusion criteria for the patients and their caregivers included age greater than 18, fluent in English, ability to interact with the wearable devices (smart watches), and willingness to comply with study procedures. The patients must have taken prescribed opioids for cancer-related pain with a Numerical Rating Scale (NRS) of 6 (on a 0-10 scale) or greater within the past 6 months, had a diagnosis of locally advanced or metastatic malignancy with a prognosis of

> 1 month but less than 1 year, and lived in the same home with an informal/unpaid caregiver. Exclusion criteria for both patients and caregivers included serious cognitive and/or visual impairment or serious mental illness that would limit ability to participate in study procedures.

Data Collection and Analysis

This study received approval from the University of Virginia Health System Institutional Review Board (HSR IRB #21017) and all participants signed consent prior to any data collection.

Details of the Survey Instrument and Items Utilized

Patient and caregiver demographic and clinical data were obtained from Demographic and Baseline surveys administered pre-deployment of the BESI-C system. Surveys were administered by the CRC and responses entered into RedCap, a secure, HIPAA compliant database system. The patient demographic and clinical pre-deployment survey tools are included as Appendix A and B, and the caregiver demographic and clinical survey tools are Appendix C and D.   The patient clinical pre-deployment survey tool consists of 53 items; the caregiver clinical survey tool includes 47 items.

The BESI-C RedCap surveys were informed by the literature, consultation with clinical partners, expert oncology nurse scientists, and researchers from the UVA Center for Survey Research. Final surveys included a combination of standardized and validated items, such as the System Usability Scale (Usability.gov, 2024) and PROMIS pain interference measures (HealthMeasures, 2024), as well as custom items designed to understand baseline patient and caregiver health status, self-efficacy in cancer pain management, and to help contextualize findings during deployments.

Items present in the BESI-C demographic and baseline surveys that were utilized in this SDA include are included in Tables 6a-b. Table 6a includes the demographic information for both patients and caregivers. Clinical variables including presence of acute and chronic pain measured using the Numeric Rating Scale (NRS), self-efficacy in pain management, and measures of QoL are in Table 6b. The NRS measures pain level from 0 (no pain) to 10 (worst pain) and has established validity to measure pain in patients with cancer (Kim & Jung, 2020). Self-efficacy is evaluated through confidence in cancer pain management among both patients and caregivers, supporting self-efficacy as a measure of the extent to which individuals have the ability and skills to control events in their lives (Bandura 1994; White et al., 2019), and sense of control and self-management skills (Foster et al., 2015; Merluzzi et al., 2019). Self-efficacy was measured through confidence in pain management. QoL was evaluated using reported pain interference in daily activities and functional status.

Data Analysis

Preparing the Data for Analysis

De-identified patient and caregiver baseline surveys were downloaded from RedCap into SPSS (v 29.0) for analysis. Copies of the patient and caregiver files were merged into one combined master file. Minimal data cleaning was required to prepare data for analysis. In the combined master file, variables present in both the patient and caregiver data were relabeled to create new variables for clarity and to indicate that they are representative of both patient and caregiver data. Data cleaning involved removing "cg" or "pt" from the beginning of each item that represented both patient and caregiver data and creation of more specific labels to facilitate the analysis - for example, "pt_nonpharm_1" became "creams."

A variable was created to indicate if patients and caregivers were currently working, with 1 indicating employed full or part-time and 0 indicating unemployed, retired, or disabled from the survey responses. As there was not a variable in the primary data set to indicate use of non-pharmacologic therapies separate from belief in efficacy, new variables were created for each non-pharmacologic therapy by separating the response "I haven't tried this" from responses indicating belief in efficacy. For the non-pharmacologic therapies, "I haven't tried this" was coded as "0" and the others were coded as "1" to indicate that the therapy was tried. Several baseline variables, for example confidence in pain management, used Likert-style scales with responses from 1-5 indicating "not at all" to "very" and 9 for "I don't know." For the variables with Likert-style scales, there were two total responses of "I don't know" originally coded as "9" which were recoded as missing or "." in SPSS as the values of 9 would create false outliers in the data. Missing data were not imputed as the percentage was less than 5% for both patient and caregiver data, which is often considered a cut-off point to consider imputation for missing data (Heymans & Twisk, 2022).

Summary of Research Questions and Analytic Approach

Table 7 provides a summary of: 1) study research questions, 2) variables of interest, 3) descriptions of the survey items which were the sources for the variables of interest, and 4) the analytic approach.

Table 7. Research Questions and Analytic Approach

Research Questions	Variables of Interest	Description of Survey Items	Analytic Approach

Is acupuncture/ pressure feasible and acceptable among patients and caregivers of patients with cancer pain?	Use of non-pharmacologic therapies to manage cancer pain, including acupuncture/ pressure Belief in the effectiveness of non-pharmacologic therapies including acupuncture/ pressure Belief in effectiveness of the current pain regimen	<u>Belief in the effectiveness of the non-pharmacologic therapies including acupuncture/pressure and use of non-pharmacologic therapies including acupuncture/pressure</u> were obtained from baseline patient and caregiver surveys including responses to the following questions: Do the following help relieve your pain? (patient survey item) In your opinion, do you think the following help relieve the patient's pain? (caregiver survey item) Response options: Patients and caregivers indicate "yes," "no," or "I haven't tried this" to each type of therapy. Users of acupuncture/pressure vs. non-users were determined by separating the patients and caregivers who responded "I haven't tried this" from those who were able to report belief in the effectiveness of acupuncture/pressure. <u>Belief in effectiveness of the current pain regimen</u> was determined using responses to the questions: How effective, overall, do you think your current pain regimen is at controlling your pain? How effective, overall, do you think the patient's current pain regimen is at controlling their pain? Reponses range from "somewhat" to "very" or "I don't know" using a Likert-style scale.	Feasibility was evaluated using descriptive statistics to obtain the percentage of patients and caregivers who have tried acupuncture/pressure. Use of non-pharmacologic therapies were listed by frequency to determine more commonly used therapies, including use of acupuncture/pressure relative to other non-pharmacologic therapies. Acceptability was assessed using descriptive statistics to compare patients and caregivers who indicated that acupuncture/pressure is effective to relieve pain to those who do not. Belief in the effectiveness of the current pain regimen to manage the patient's pain among patients and caregivers who have tried acupuncture/pressure was compared to those who have not. The values were compared with an independent 2 sample t-test using SPSS. Significance was determined at a p-value of less than 0.05.
Is use of acupuncture/ pressure associated with higher self-efficacy in pain management among patients and caregivers of	Self-efficacy Acupuncture/ pressure use	<u>Self-efficacy</u> was assessed using responses to the following questions from the baseline patient and caregiver surveys: How confident are you in managing your pain?	The effect of acupuncture/pressure use on self-efficacy was determined through use of an independent 2 sample t-test using SPSS to compare degree of confidence in pain management between patients and caregivers who have tried

patients with cancer pain?		How confident are you in managing the patient's pain? Responses range from "a little" to "very" or "I don't know" using 5-point Likert-style scale. Acupuncture/pressure use was obtained from baseline patient and caregiver surveys.	acupuncture/pressure and those who have not. Significance was determined at a p-value of less than 0.05.
Does use of acupuncture/ pressure predict increased self-efficacy in pain management, controlling for measures of QoL	QoL Self-efficacy Acupuncture/ pressure use	QoL was evaluated through patient and caregiver report of pain interference in activities and functional status: How much does pain interfere with your daily activities? (patient survey item) How much does the patient's pain interfere with your day-to-day activities? (caregiver survey item) Responses are provided on both patient and caregiver surveys from "not at all" to "very" or "I don't know" using a Likert-style scale. Functional status is evaluated on patient and caregiver surveys from "I am fully active" or "The patient is fully active" to "I need much help caring for myself and spend nearly all day in a bed or chair" or "The patient needs much help caring for themselves and spends nearly all day in a bed or chair" from 1-5 using a Likert-style scale. Self-efficacy was assessed though patient and caregiver report of confidence in pain management. Acupuncture/pressure use was obtained from baseline patient and caregiver surveys.	The effect of acupuncture/pressure use on self-efficacy in pain management, controlling for reported pain interference in daily activities and functional status, was evaluated with multiple linear regression. Due to the limited sample size, there were 2 regression equations, each with 2 regressors. Significance was determined at a p-value of less than 0.05. IVs: Acupuncture/pressure use, QoL (pain interference and functional status) DV: Self-efficacy
Are demographic and clinical variables associated with use of acupuncture/	Demographic and clinical data Acupuncture/	Demographic variables including: patient age, gender, race/ethnicity? education, and employment status.	A table was created to compare patient demographic and clinical variables by use of acupuncture/pressure. Data was analyzed using t-tests for

| pressure for management of cancer pain among both patients and caregivers? | pressure use | <u>Clinical variables</u> include patient primary cancer diagnosis and stage, pain characteristics (including advanced localized and advanced metastatic disease, and pain level using NRS from 0-10) and use of medications for pain (including opioid and non-opioid medications).

<u>Acupuncture/pressure use</u> was obtained from baseline patient and caregiver surveys. | continuous variables and chi-squared tests for categorical data. Significance was determined at a p-value of less than 0.05. |

CHAPTER FOUR

Results of the Analysis

Demographic Variables

Sixteen patient and caregiver dyads were included in the analysis, for a total of 32 participants. The mean age of the patients and caregivers was 62.25 years, with a range of 28 to 75 years. The patients were 56.3% male, and their caregivers were 68.8% female. Level of education among both patients and caregivers ranged from less than high school (9.4%, n=3) and high school graduates (37.5%, n=12) to 4-year degree (18.8%, n=6) and graduate or doctoral level degree (9.4%, n=3). Seventy-five percent (n=12) of the caregivers were married to the patient, and 62.5% (n= 10) of caregivers reported being the patient's primary caregiver for 2 years or longer. Complete demographic data for both patients and caregivers are summarized in Table 8.

Table 8. Demographic Variables – Self-Reported by Patients and Caregivers			
Variable	**Total (N=32)**	**Patient (n=16)**	**Caregiver (n=16)**
Age (Mean [SD)]; range)	62.25 (10.64); 28-75	63.81 (9.28); 41-75	60.69 (11.95); 28-74
Preferred gender			
Male	43.8% (14)	56.3% (9)	31.3% (5)
Female	56.3% (18)	43.8% (7)	68.8% (11)
Racial identity			
White	90.6% (29)	93.8% (15)	87.5% (14)
African-American/Black	6.3% (2)	6.3% (1)	6.3% (1)
Other	3.1% (1)		6.3% (1)
Ethnic identity			
Hispanic	3.1% (1)	0.0%	6.3% (1)
Non-Hispanic	96.9% (31)	100.0% (16)	93.8% (15)

Current occupational status			
Employed, full time	21.9% (7)	6.3% (1)	37.5% (6)
Employed, part time	15.6% (5)	6.3% (1)	25.0% (4)
Retired	50.0% (16)	68.8% (11)	31.3% (5)
Disabled	9.4% (3)	18.8% (3)	
Other	3.1% (1)		6.3% (1)
Current occupation			
Education	3.1% (1)	0.0%	6.3% (1)
Business/finance	12.5% (4)	12.5% (2)	12.5% (2)
Service/sales	3.1% (1)	0.0%	6.3% (1)
Social/community services	6.3% (2)	0.0%	12.5% (2)
Agriculture/farming	3.1% (1)	0.0%	6.3% (1)
Other	9.4% (3)	0.0%	18.8% (3)
Prior/former occupation			
Education	3.1% (1)	6.3% (1)	0.0%
Healthcare	6.3% (2)	0.0%	12.5% (2)
Business/finance	9.4% (3)	18.8% (3)	0.0%
Service/sales	3.1% (1)	6.3% (1)	0.0%
Construction/building	6.3% (2)	6.3% (1)	6.3% (1)
Other	34.4% (11)	50.0% (8)	18.8% (3)
Education level			
Less than high school	9.4% (3)	6.3% (1)	12.5% (2)
High school graduate	37.5% (12)	50.0% (8)	25.0% (4)
Some college	15.6% (5)	18.8% (3)	12.5% (2)
2-year degree	9.4% (3)	6.3% (1)	12.5% (2)
4-year degree	18.8% (6)	12.5% (2)	25.0% (4)
Graduate/doctorate	9.4% (3)	6.3% (1)	12.5% (2)
Caregiver's relationship to the patient			
Spouse			75% (12)
Significant other			6.3% (1)
Child			12.5% (2)
Other			6.3% (1)

Length of time as patient's primary caregiver			
< 6 months			6.3% (1)
6 months - < 2 years			18.8% (3)
2 - < 5 years			31.3% (5)
5 + years			31.3% (5)

Clinical Variables

Clinical data for the patients included information on cancer diagnosis, cancer-related pain level and frequency, and medications used for pain (Tables 9a-c). The most frequent primary cancer diagnosis sites for the patients as listed in the electronic health record included: genital-urinary (18.8%, n=3), lymphoma or leukemia (18.8%, n=3) and gynecological (12.5%, n=2). Cancer stage was categorized as metastatic in 87.5% (n=14) of cases and advanced, localized in 12.5% of cases (n= 2). Seventy-five percent (n=12) of patients indicated that they have some amount of constant pain, and 81.3% (n=13) indicated that they experience acute pain events. All of the participants (n=12; 100%) who reported constant pain also indicated acute pain events. Data were collected on where (i.e., body location) patients experience most of their pain, with 25.0% (n= 4) reporting "all over" and 18.8% (n=3) indicating chest. All patients reported use of opiate pain medications for pain; 100% (n=16) of patients reported use of short-acting opiates and 56.3% (n=9) reported use of long-acting opiates. Patients also reported use of non-opioid medications for pain, including 50.0% (n=8) reporting use of anticonvulsants, 43.7% (n=7) reporting use of acetaminophen, and 31.3% (n=5) reporting use of antidepressants.

Clinical data available for both patients and caregivers included presence of comorbid conditions and additional baseline survey data including functional status (Tables 9d-e). Depression and anxiety were self-reported as current health conditions by 43.8% (n=14) of both patients and caregivers, including 75.0% (n=12) of patients, and 12.5% (n=2) of caregivers.

Chronic pain other than cancer-related pain was self-reported by 28.1% (n= 9) of patients and caregivers, 31.3% (n= 5) of patients, and 25.0% (n=4) of caregivers. Mean confidence in pain management among patients and caregivers was 4, indicating "quite" confident. Patient pain interference in daily activities reported by both patients and caregivers was a mean value of 3 or "somewhat." Patient functional status using ECOG score as reported by both patients and caregivers was close to 3 at 2.9, indicating that the patient cannot do any work but can still care for themselves.

Table 9a. Primary Cancer Diagnosis and Stage Obtained from the Electronic Health Record (EHR) – Patient Only

Variable	Patient (n=16)
Patient's primary cancer diagnosis (as listed in the EHR)	
Breast	6.3% (1)
CNS (includes brain)	6.3% (1)
GI (other, non-pancreatic)	6.3% (1)
GI (pancreatic)	6.3% (1)
Genital-urinary (bladder, kidney)	18.8% (3)
Gynecological (ovarian, uterine)	12.5% (2)
Liquid/blood (lymphoma/leukemia/other heme)	18.8% (3)
Prostate	6.3% (1)
Skin (melanoma)	6.3% (1)
Skin (other than melanoma)	6.3% (1)
Other	6.3% (1)
Stage of cancer	
Advanced, localized	12.5% (2)
Advanced, metastatic	87.5% (14)

Table 9b. Self-Reported Pain Characteristics – Patient Only

Variable	Patient (n=16)
Presence of constant cancer-related pain	
Yes	75.0% (12)
No	12.5% (2)
Unsure	6.3% (1)
Average constant pain level*	
2	6.3% (1)
3	6.3% (1)
4	18.8% (3)
5	25.0% (4)
6	12.5% (2)
9	6.3% (1)
Frequency of acute/sudden cancer pain events	
Never	6.3% (1)
1-4 times/day	50.0% (8)
5-8 times/day	18.8% (3)
More than 8 times/day	12.5% (2)
Unsure	18.8% (3)
Average acute pain level*	
3	6.3% (1)
4	6.3% (1)
5	12.5% (2)
6	6.3% (1)
7	12.5% (2)
8	12.5% (2)
9	18.8% (3)
10	6.3% (1)
Current pain level*	
1	6.3% (1)
2	12.5% (2)

3	12.5% (2)
4	25.0% (4)
5	12.5% (2)
6	12.5% (2)
7	6.3% (1)
9	6.3% (1)
Location of most cancer-related pain	
All over	25.0% (4)
Chest	18.8% (3)
Back	12.5% (2)
Leg(s)	12.5% (2)
Other	12.5% (2)
Arms	6.3% (1)
Stomach	6.3% (1)

All pain levels were recorded using the 0-10 Numeric Rating Scale

Table 9c. Medications Used for Cancer-Related Pain – Patient Only	
Variable	**Patient (n=16)**
Use of long-acting/sustained release opioid for cancer-related pain	
Yes	56.3% (9)
No	43.8% (7)
Use of short-acting opioid PRN ('as needed') for cancer-related pain	
Taking	100.0% (16)
Current (within approximately the past 3 months) use of other medication(s) for cancer-related pain	
NSAIDS	
Yes	12.5% (2)
No	87.5% (14)
Acetaminophen	
Yes	43.8% (7)
No	56.3% (9)

Antidepressants	
Yes	31.3% (5)
No	68.8% (11)
Anticonvulsants	
Yes	50.0% (8)
No	50.0% (8)
Steroids	
Yes	18.8% (3)
No	81.3% (13)
Topical anesthetics	
No	100.0% (16)
Sedative/anti-anxiety medication	
Yes	18.8% (3)
No	81.3% (13)

Table 9d. Self-Reported Health Conditions - Patient and Caregiver			
Variable	**Total (N=32)**	**Patient (n=16)**	**Caregiver (n=16)**
Diagnosis of other medical problems			
Depression or anxiety	43.8% (14)	75.0% (12)	12.5% (2)
Other chronic pain (separate from cancer-related pain)	28.1% (9)	31.3% (5)	25.0% (4)
Other medical problems	25.0% (8)	31.3% (5)	18.8% (3)
Osteoarthritis	15.6% (5)	25.0% (4)	6.3% (1)
Lung disease	12.5% (4)	12.5% (2)	12.5% (2)
Heart disease	9.4% (3)	12.5% (2)	6.3% (1)
Ulcer of stomach disease	9.4% (3)	18.8% (3)	6.3% (1)
Diabetes	9.4% (3)	18.8% (3)	6.3% (1)
Kidney disease	6.3% (2)	12.5% (2)	0.0% (0)
Liver disease	6.3% (2)	12.5% (2)	0.0% (0)

Neurological disease (like Multiple Sclerosis)	6.3% (2)	12.5% (2)	0.0% (0)
Rheumatoid arthritis	0.0% (0)	0.0% (0)	0.0% (0)

Table 9e. – Baseline Confidence in Pain Management, Perceived Effectiveness of Current Pain Regimen, Patient Pain Inference in Daily Activities, and Patient ECOG – Reported by Patient and Caregiver

Variable	Total (N=32) (Mean [SD]); range)	Patient (n=16) (Mean [SD]); range)	Caregiver (n=16) (Mean [SD]); range)
Confidence in pain management	4.0 (1.2); 1-5	4.2 (1.1); 1-5	3.8 (1.4); 1-5
Effectiveness of current regimen to control cancer pain	3.5 (1.1); 1-5	3.7 (0.9); 2-5	3.3 (1.2); 1-5
Pain interference in day-to-day activities	3.0 (1.2); 1-5	3.5 (1.0); 2-5	2.5 (1.2); 1-5
Functional status/ECOG	2.9 (1.0); 1-5	2.9 (1.1); 1-5	2.9 (0.9); 2-4

* All responses are in the form of Likert-style scales from 1-5; 1= "not at all" to 5= "very."

Feasibility and Acceptability of Acupuncture/pressure

Feasibility of Acupuncture/pressure

Table 10 displays non-pharmacologic therapies used for cancer-related pain as reported by both patients and caregivers. The percentage of patients and caregivers who reported they had tried acupuncture/pressure was 43.8% (n=14/32). Other more commonly utilized nonpharmacologic therapies included: positioning 96.9% (n=31), being with other people 96.9% (n=31), and rest/sleep 96.9% (n=31).

Table 10. Use of Non-Pharmacologic Therapies to Manage Patient's Cancer Pain and Belief in Effectiveness

Therapy	Patient and Caregiver Report of Therapies Tried in Past to Manage Pain			Belief in Effectiveness		
	Total who indicated 'yes' (n=32)	Patients (n=16)	Caregivers (n=16)	Total who indicated 'yes'	Patients who indicated 'yes'(n=16)	Caregivers who

				(n=32)		indicated 'yes' (n=16)
Comfortable or special position	96.9% (31)	100% (16)	93.8% (15)	87.5% (28)	93.8% (15)	81.3% (13)
Being with other people	96.9% (31)	100% (16)	93.8% (15)	50.0% (16)	50.0% (8)	50.0% (8)
Resting/sleep	96.9% (31)	100% (16)	93.8% (15)	87.5% (28)	87.5% (14)	87.5% (14)
Listening to music/watching TV	93.8% (30)	93.8% (15)	93.8% (15)	62.5% (20)	56.3% (9)	68.8% (11)
Exercise/activity/walking	93.8% (30)	100% (16)	87.5% (14)	40.6% (13)	25.0% (4)	56.3% (9)
Massage	87.5% (28)	93.8% (15)	81.3% (13)	37.5% (12)	50.0% (8)	25.0% (4)
Distracting activity, like sewing or handiwork	84.4% (27)	93.8% (15)	75% (12)	31.3% (10)	37.5% (6)	25.0% (4)
Ice/heat	81.3% (26)	81.3% (13)	81.3% (13)	37.5% (12)	37.5% (6)	37.5% (6)
Over the counter (OTC) creams or ointments	75.0% (24)	68.8% (11)	81.3% (13)	21.9% (7)	25.0% (4)	18.8% (3)
Prayer/meditation	71.9% (23)	75% (12)	68.8% (11)	40.6% (13)	37.5% (6)	43.8% (7)
Progressive muscle relaxation/taking deep breaths	68.8% (22)	75% (12)	62.7% (10)	34.4% (11)	43.8% (7)	25.0% (4)
Guided imagery/hypnosis	43.8% (14)	43.8% (7)	43.8% (7)	6.3% (2)	6.3% (1)	6.3% (1)
Acupuncture/pressure	43.8% (14)	43.8% (7)	43.8% (7)	15.6% (5)	18.8% (3)	12.5% (2)

* *Patients and caregivers could report belief in effectiveness for each therapy or "I haven't tried this." Use of each therapy above was obtained by separating the patients or caregivers who indicated "I haven't tried this" from those who reported belief in effectiveness.*

Acceptability of Acupuncture/pressure

The percentage of patients and caregivers who reported that acupuncture/pressure was effective to relieve the patient's pain was 15.6% (n=5), including 18.8% (n=3) of patients and 12.5% of caregivers (n=2). Positioning was reported to be effective by 87.5% (n=28) of patients and caregivers and 93.8% of patients (n=15), and sleep was reported effective by 87.5% (n= 14) of patients and caregivers. Hypnosis/guided imagery was reported effective by 6.3% of patients (n= 1) and caregivers (n= 1).

Belief in the effectiveness of the patient's pain regimen was evaluated on both patient and caregiver surveys using a Likert-style scale with responses from "not at all" to "very," coded as 1-5 and 9 for "I don't know" (Table 9e). There was not a significant difference in belief in the effectiveness of the current pain regimen to manage pain between patients and caregivers who used acupuncture/pressure (M = 3.54, SD = 1.20) and patients and caregivers who did not use acupuncture/pressure (M = 3.39, SD = 0.98); t(29) = 0.38, p = 0.71.

Self-efficacy in Pain Management

Patients and caregivers who reported trying acupuncture/pressure to alleviate cancer-related pain had significantly lower confidence in pain management (M = 3.43, SD = 1.40) than patient and caregivers who did not use acupuncture/pressure (M = 4.50, SD = 0.82); t (20.34) = 2.52, p = 0.02. Using multiple linear regression, use of acupuncture/pressure continued to significantly predict confidence in pain management among both patients and caregivers when controlling for QoL based on functional status and pain interference in daily activities (Table 11).

Table 11. Confidence in Pain Management Regressed on Use of Acupuncture/pressure, Controlling for Functional Status (Equation 1) and Pain Interference in Daily Activities (Equation 2)

Variable	Equation 1			Equation 2		
	b	β	p	b	β	p
Acupuncture/pressure	-1.18* (0.43)	-0.49	0.01	-1.08* (0.44)	-0.45	0.02
Functional Status	-0.22 (0.22)	-0.18	0.33			
Pain Interference				-0.11 (0.19)	-0.10	0.57

Constant	5.18		4.82
R^2	0.22		0.19

Note: *p < 0.05

Relationship of Demographic and Clinical Variables to Acupuncture Use

The demographic and clinical characteristics of patients who reported use of acupuncture/pressure compared to those who did not use acupuncture/pressure are summarized in Tables 12a-b. The number of total patients at time of the survey download was 16, including 7 identified acupuncture users and 9 non-users. There are currently more patients enrolled in the BESI-C parent study, and these participants would be added to create a total value of greater than 10 for each reported cell prior to consideration of publication. P-values are included to indicate significance, determined using t-tests for the 2 continuous variables (age and level of education) and chi-squared tests for categorical variables. A p-value is not listed for all variables due to values of 0% or 100% in the data which limited the ability to perform these statistical tests. Level of education was close to reaching statistical significance at p = 0.05; higher educational level was associated with acupuncture use.

Table 12a. Comparison of Demographic Characteristics of Patients Identified as Acupuncture/pressure Users and Non-Acupuncture/pressure Users				
Demographic Variables (Patient)	**Acupuncture Use (n=7)**	**No Acupuncture Use (n=9)**	**Effect size**	**p – value**
Age (Mean [SD)]; range)	63.1 (10.8); 41-75	64.3 (8.6); 46-74	0.12	p = 0.81
Preferred gender				p = 0.34
Male	42.9% (3)	66.7% (6)		
Female	57.1% (4)	33.3% (3)		
Racial identity				p = 0.44
White	85.7% (6)	100.0% (9)		

African-American/Black	14.3% (1)	0.0% (0)		
Ethnic identity				n/a
Non-Hispanic	100.0% (7)	100.0% (9)		
Current occupational status				p = 0.85
Employed, full or part-time	14.3% (1)	11.1% (1)		
Not employed	85.7% (6)	88.9% (8)		
Education level (Mean [SD]); range)	3.4 (1.7); 1-6	2.1 (0.4); 1-6	1.05	p = 0.05
Less than high school	0.0% (0)	11.1% (1)		
High school graduate	85.7% (6)	22.2% (2)		
Some college	14.3% (1)	22.2% (2)		
2-year degree	0.0% (0)	11.1% (1)		
4-year degree	0.0% (0)	22.2% (2)		
Graduate/doctorate	0.0% (0)	11.1% (1)		

Table 12b. Comparison of Clinical Characteristics of Patients Identified as Acupuncture/pressure Users and Non-Acupuncture/pressure Users

Clinical Variables (Patient)	Acupuncture Use (n=7)	No Acupuncture Use (n=9)	Effect size	p – value
Patient's primary cancer diagnosis				p = 0.09
Advanced, localized	28.6% (2)	0.0% (0)		
Advanced, metastatic	71.4% (5)	100.0% (9)		
Average constant pain level (0-10) (Mean (SD)]; range)	5.33 (2.25); 2-9	4.33 (1.03); 3-6	0.57	p = 0.10
Average acute pain level (0-10) (Mean (SD)]; range)	6.50 (2.35); 3-9	7.29 (2.14); 4-10	0.35	p = 0.33
Current pain level (0-10) (Mean (SD)]; range)	4.83 (2.48); 2-9	4.00 (1.87); 1-7	0.38	p = 0.29
Taking a long-acting/sustained release opioid for cancer-related pain				p = 0.27
Yes	57.1% (4)	55.6% (5)		

No	42.9% (3)	44.4% (4)		
Taking a short-acting opioid PRN for cancer-related pain				n/a
Taking	100% (7)	100.0% (9)		
Other medication(s) for cancer-related pain (within past 3 months)				
NSAIDS				p = 0.09
Yes	28.6% (2)	0.0% (0)		
No	71.4% (5)	100.0% (0)		
Acetaminophen				p = 0.27
Yes	42.9% (3)	44.4% (4)		
No	57.1% (4)	55.6% (5)		
Antidepressants				p = 0.81
Yes	42.9% (3)	22.2% (2)		
No	57.1% (4)	77.8% (7)		
Anticonvulsants				p = 0.27
Yes	42.9% (3)	44.4% (4)		
No	57.1% (4)	55.6% (5)		
Steroids				p = 0.09
Yes	0.0% (0)	33.3% (3)		
No	100.0% (7)	66.7% (6)		
Topical anesthetics				n/a
No	100.0% (7)	100.0% (9)		
Sedative/anti-anxiety medication				p = 0.09
Yes	28.6% (2)	11.1% (1)		
No	71.4% (5)	88.9% (8)		

* For the purposes of this educational dissertation research, we reported on cells with < 10 participants. Please note that prior to publication, < 10 participates would be censured or more participants included due to prospective data collection.

CHAPTER FIVE

Discussion and Conclusion

Discussion

The primary aim of this dissertation research was to explore the feasibility and acceptability of acupuncture/pressure as reported by patients and their family caregivers to manage advanced cancer pain. Secondary aims were to evaluate the relationship between acupuncture/pressure use and self-efficacy in managing cancer pain, and to assess if demographic and clinical variables predicted acupuncture/pressure use. To complete these aims, a secondary data analysis was undertaken using data from the parent study, National Institutes of Health R01 study, *Characterizing the Complexity of Advanced Cancer Pain in the Home Context*.

Findings from this study revealed several key points, including: 1) Feasibility and acceptability of non-pharmacologic therapies for management of advanced cancer pain that can be self-administered compared to practitioner-facilitated therapies is strong, as evaluated through self-reported use; 2) acupuncture/pressure was one of the least utilized non-pharmacologic therapies for management of advanced cancer pain; 3) acupuncture/pressure use was associated with decreased self-efficacy in pain management; and 4) demographic and clinical variables did not predict use of acupuncture/pressure. The following sections will discuss the results in more detail and put them into the context of current literature regarding use of acupuncture and other non-pharmacologic therapies for chronic and cancer-related pain.

Feasibility and Acceptability of Non-Pharmacologic Therapies for Management of Advanced Cancer Pain

Understanding use of non-pharmacologic including CAM therapies for symptom management among patients with cancer is important as the prevalence of use is estimated to be approximately 80%; however, as few as 14% of patients discuss use of non-pharmacologic symptom management therapies with their medical providers (Latte-Noir & Mao, 2019). Prior research found that reasons patients did not report use of CAM therapies to their medical providers included concern for a negative response and belief that physicians would not be supportive (Mao et al., 2011). The discrepancy between use of non-pharmacologic therapies among patients with cancer and what is reported to their providers may also be related to high use of therapies that can be self-managed compared to practitioner-facilitated therapies. For therapies that require a practitioner to facilitate use, such as acupuncture, hypnosis, or forms of exercise therapy, patients may be more likely to discuss these approaches with their medical providers for practical reasons, such as to obtain referrals, than therapies that can be self-managed. The results of this analysis indicate high feasibility and acceptability of self-managed strategies for pain management – the most frequently utilized non-pharmacologic therapies reported by both patients and caregivers included positioning, sleep/rest, and being with other people (all >95%). The non-pharmacologic therapies with the highest reported effectiveness were positioning and sleep/rest by 87.5% (n= 28) of both patients and caregivers.

There is a paucity of current literature which specifically discusses the comparison of self-reported use and effectiveness of non-pharmacologic and CAM therapies among patients with cancer. One article, Mao et al. (2011), was found which compared use of CAM therapies among cancer survivors using data from the 2007 National Health Interview Survey. In this study, the CAM therapies with highest reported use among cancer survivors were chiropractic/osteopathic (34.6%), herbs (32.5%), and massage (19.4%) (Mao et al., 2011).

Reported use of CAM therapies across all modalities in Mao et al. (2011) was less than in our study as acupuncture/pressure and hypnosis were the least frequently used CAM therapies at 43.8% (n= 14) respectively and may be related to the earlier timeframe as Mao et al. (2011) used data from the 2007 National Health Interview Survey. Our findings are consistent with more recent research that compares the use of different types of non-pharmacologic and CAM therapies by patients who are also taking opioid pain medications (Almutairi et al., 2019; Eaton et al., 2018). For example, one available study that compared use of non-pharmacologic therapies among patients with chronic pain requiring opioid medications found that positioning (84.2%) and rest (82.5%) were the most utilized strategies (Almutairi et al., 2019). Although the study sample included patients with chronic pain – and not specifically cancer – the results are relevant to our findings as all patients in the parent study for this analysis were using opioid pain medications.

The most frequently utilized non-pharmacologic therapies reported by this study included: sleep/rest, positioning, and being with other people. This is particularly noteworthy as these therapies can be self-managed at home (i.e., outside of a specific clinic or medical space) without need to access a specialized practitioner to facilitate or deliver the therapy. This finding has significant implications for the delivery of symptom management in advanced cancer because the results demonstrate that patients and their family caregivers are more likely to engage in therapies that can be self-managed in addition to pharmacologic management of pain.

Our results confirm prior work validating the importance of sleep/rest and its relationship to the management of difficult symptoms. Sleep/rest was one of the non-pharmacologic interventions with highest reported effectiveness by 87.5% of both patients (n= 14) and caregivers (n= 14). Earlier research has found that sleep/rest is an important lifestyle

modification for management of symptoms among patients with cancer (Latte-Noir & Mao, 2019) and established that poor sleep quality is related to higher pain levels including increased pain response and inflammation (Whale & Gooberman-Hill, 2022). Our findings related to both high reported frequency (i.e., self-reports of trying the non-pharmacologic intervention) and reported effectiveness of sleep as an intervention for cancer-related pain are not surprising. Although sleep/rest is also a daily activity, the survey asks about effectiveness as a strategy for pain management. The high reported effectiveness of sleep/rest indicates that patients and their family caregivers may intuitively understand through lived experience the importance of sleep for pain management without necessarily understanding the biophysical relationship between sleep and pain.

"Being with other people" as a strategy for pain management may have been high in this sample as most caregivers (81.3%, n=13) indicated that they were either married or a significant other to the patient. Although being with others was one of the top three most frequently utilized non-pharmacological strategies, only 50% of both patients (n= 8) and caregivers (n= 8) reported that being with others was effective to decrease the patient's pain. Being a caregiver for a patient with cancer has the potential for high physical and psychological burden including autonomic nervous dysfunction, immune system changes, and depression (Teixeira et al., 2018), indicating that complex interpersonal dynamics of the caregiver role may be related to the relatively lower report of effectiveness. Another explanation for the relatively lower reported effectiveness of being with other people may be that if the majority of patients and caregivers are married cohabitating partners, they may perceive being with others as close to their baseline living situation and therefore unable to determine if this has affected the patient's pain.

Feasibility and Acceptability of Acupuncture/pressure for Management of Advanced Cancer Pain

Among the participants in this study, acupuncture/pressure was one of the least frequently reported non-pharmacologic therapies for management of cancer-related pain. Less than half (43.8%, n= 14) of the total sample of both patients and caregivers reported that they had ever tried acupuncture/pressure and only 15.6% (n= 5) of patients and caregivers indicated that they believed acupuncture was effective to relieve the patient's cancer-related pain. Important caveats to this finding include that our study did not specify whether the patient had used acupuncture, acupressure, or both modalities. The reported use also does not include the number of times acupuncture/pressure was tried, e.g. once or enough times to produce a significant treatment effect.

The reported use and belief in effectiveness of acupuncture/pressure in our study differs from prior research that surveyed patients with cancer currently in treatment; Widgren, Frannson, & Per (2022) found that only 1% of patients reported that they had received acupuncture during treatment, however 56% of patients believed acupuncture would be effective for their pain. A notable difference between Widgren, Fransson, and Per (2022) and this research is that the reported belief in effectiveness for pain was hypothetical as their survey included mainly participants who had not tried acupuncture. Another survey of patients with cancer including patients currently in treatment, survivors, and their informal caregivers found acceptability of acupuncture to be 34.5% among patients and 48.0% among caregivers (Tack et al., 2021). The difference between reported feasibility and acceptability of acupuncture/pressure in our study and the available literature, in addition to the potential impact of evaluating belief in efficacy based on experience, may be related to the fact that our sample included patients with advanced cancer pain who had completed treatment versus patients currently in treatment. Importantly, these survey findings from the prior literature suggest that interest in trying acupuncture/pressure

for cancer-related pain may be higher than reported use, indicating that barriers exist in the ability to access acupuncture.

Feasibility and acceptability of acupuncture/pressure among patients with cancer and their primary caregivers may be influenced by perceived barriers. An analysis of barriers to use of acupuncture among breast cancer survivors found that lack of knowledge, lack of insurance coverage, cost, and inability to access to a qualified provider were the main reasons patients did not receive acupuncture for their symptoms (Bao et al., 2018). These identified barriers may be shared among all patients with cancer and are perhaps even more likely among patients with advanced cancer represented in our study who may have higher symptom burden and decreased functional status limiting ability to travel outside of the home.

Relationship of Acupuncture/pressure to Self-Efficacy and QoL

Use of acupuncture/pressure was associated with decreased self-efficacy in pain management when controlling for QoL measured by functional status and pain interference in activities. An integrative review of self-efficacy and symptom management among patients with cancer found that while higher self-efficacy was associated with improved physical and emotional well-being, patients with lower self-efficacy had both greater symptom burden and higher functional status (White et. al, 2019). As in this study self-efficacy was evaluated through confidence in pain management, the patients with highest symptom burden and their caregivers who feel limited in their own ability to manage pain may be more likely to seek a practitioner-facilitated therapy for additional support.

Decreased self-efficacy in symptom self-management among patients with cancer is associated with depression in addition to higher pain levels (Foster et al., 2015). Reported depression and anxiety was high among patients in our sample (75%, n= 12). Considering that

there is a known bi-directional relationship between pain and negative emotions including depression and anxiety (Michaelides & Zis, 2019), the high reported presence of these negative emotions may also be both contributors to and indicators of both higher total symptom burden and decreased self-efficacy. Acupuncture has been shown to be as effective as pharmacologic treatment for cancer-related depression (Wang et al., 2022). In addition to the need for additional support with symptom management, the relationship between use of acupuncture/pressure and decreased self-efficacy may also be explained by the potential benefits of acupuncture/pressure for both pain and negative emotions that are associated with decreased self-efficacy and higher pain levels.

Relationship of Demographic Variables to Use of Acupuncture/pressure for Cancer Pain

A unique feature and strength of this sample is that it represents a more varied age and educational population than the typical user of complementary and alternative medicine (CAM) in the United States - e.g., white women of higher education and economic status (Bao, 2018; Cui et al., 2017; Ludwick et al. 2020; Vapiwala et al., 2006). Among patients with cancer, patients who reported male gender and aged 65 or older have decreased interest in acupuncture treatment (Widren, Fransson, & Efverman, 2022). Furthermore, patients who identify as underrepresented minorities (e.g. non-white) and patients with less than a college education are more likely to report difficulty accessing acupuncture (Bao et al., 2018).

More patients in our sample self-identified as male sex (56.3%, n= 9) than female sex (43.8%, n= 7), the mean age of patients was 63.8 years, and 62.5% (n=20) of the sample reported a high-school education or less. Although there were no statistically significant differences in demographic variables at a p-value of less than 0.05 between patients who reported use of acupuncture/pressure and those who did not, level of education was close at p= 0.05 and an

effect size of 1.05. The percentage of male patients, mean age close to 65 years, and education level in our sample may also explain the lower reported use of acupuncture/pressure compared to other non-pharmacologic therapies.

Relationship of Clinical Variables to Use of Acupuncture/pressure for Cancer Pain

Surprisingly, we found no significant differences between patients who used acupuncture/pressure and patients who did not use acupuncture/pressure when clinical variables including cancer stage, pain characteristics, use of long and short-acting opioid medications, and non-opioid medications for pain were considered. Although there no statistically significant difference in reported use of acupuncture/pressure between patients with advanced, metastatic disease and advanced, localized disease, among the patients who reported use of acupuncture/pressure there were more patients with metastatic (71.4%, n =5) than localized (28.6%, n= 2) disease. Mean reported pain levels for constant, acute, and current pain by patients in our sample were in the moderate to moderate-severe range at 5.33, 6.50 and 4.83 respectively. The available research suggests that among patients with cancer, patients with advanced disease and higher baseline pain levels may have the greatest benefit from acupuncture treatment (Miller et al. 2019). Considering that all patient participants on our sample had advanced disease and reported significant pain with concurrent use of opioid pain medications, these clinical characteristics indicate high potential for benefit from acupuncture/pressure for management of their pain.

There were not any significant differences in use of non-opioid medications for pain such as antidepressants and anticonvulsants which could have indicated treatment for various types of pain, for example, neuropathic pain. Among 16 patient participants, there was a wide range of 11 primary cancer diagnoses as obtained from the EHR and 7 self-reported primary pain

locations, limiting results that could have indicated a specific type of pain. Future research with a larger sample size may be able to determine differences in clinical variables that could provide information regarding indications for acupuncture/pressure use for different types of cancer-related pain; for example, nociceptive and neuropathic pain, or constant and acute pain episodes among patients with advanced cancer.

Expanding Access to Acupuncture/pressure through APA

Prior research has indicated both the feasibility and acceptability of APA for pain in patients with cancer (Yang et al., 2020; Yeh et al, 2015). A recent systematic review and meta-analysis of auricular acupuncture techniques including APA for cancer-related pain found that APA was associated with reduced pain and analgesic medication use and improved quality of life (Yang et al., 2020). Teaching acupressure as a self-care technique may eliminate logistical barriers to accessing acupuncture/pressure among patients with cancer and be especially relevant for patients with advanced illness whose goals of care are focused on staying at home and reducing visits to the clinic or hospital. Furthermore, there are minimal known adverse effects associated with either acupuncture or acupressure (He et al., 2020). The main known adverse effect of APA is itching at the site due to adhesive which typically resolves following press ball removal. (Tan et al., 2014).   The low-burden nature of acupressure and APA has the potential to be especially meaningful among patients and caregivers who may already be managing multiple symptoms related to cancer and treatments for cancer.

A primary difference between the intended population for the initially proposed dissertation research and the SDA other than the confirmed prevalence of CIPN is that the initial proposal involved post-treatment cancer survivors and the SDA involves patients with a prognosis of less than 1 year. However, a common feature between the two populations is

potentially decreased frequency of appointments at cancer centers and by extension reduced access to acupuncturists for practitioner-facilitated therapy. Although acupuncture is offered at major cancer centers, patients with advanced malignancy who are no longer in treatment may not have the same access to this benefit as patients who are in treatment and, by extension, have more reasons to travel to the cancer centers. For patients with advanced malignancy and high symptom burden, APA could be a low-burden, self-care technique to provide the benefits of acupuncture/pressure for symptom management to patients who are mainly at home. While acupuncture is provided by a licensed acupuncturist or physician, acupressure can be self-managed, and facilitated by other professions including nurses (Yeh et al. 2017) and caregivers. After initial instruction in APA, this technique can then be used for self-management of symptoms at home.

APA and CIPN

The initial dissertation proposal was to evaluate feasibility and acceptability of APA for CIPN among breast cancer survivors. The exact prevalence of CIPN is not known for this secondary data analysis, as this was not specifically asked in the baseline parent study survey. However, there are several features of our study sample that suggest CIPN is a common problem in the sample, including primary cancer sites commonly treated with neurotoxic chemotherapy including breast (6.3%, n= 1), gynecological (12.5%, n= 2) or liquid (lymphoma/leukemia) (18.8%, n= 3), 2) and reported location of cancer-related pain in the extremities or "all over" (43.8%, n= 7). Antidepressants and anticonvulsants are medications commonly used to treat CIPN (Song et al., 2017; Tofthagen et al., 2020), and were used by 81.3% (n= 13) of patients; however, whether this reflects use of these medications to treat CIPN or to treat anxiety and depression (reported by 75%, n= 12 of patients) is unclear from the available survey data. As

reported by our integrative review, prior research has shown that acupuncture including auricular techniques decreases pain and increases QoL among patients with CIPN (Kutcher & LeBaron, 2022). Additional research is indicated on best practices and protocols using APA for CIPN to support self-management of symptoms among both patients with advanced malignancy and cancer survivors.

Limitations

The primary limitation of this study was the small sample size of 32 participants, including 16 patients and 16 informal caregivers. The small sample size precluded some analytic techniques, such as mediation and moderation analyses which typically require a minimum number of 40-50 participants (Sim, Kim & Suh, 2022), and therefore were not feasible due to a sample size of 32 participants. The analysis to compare the demographic and clinical variables between patients who used acupuncture and those who did not use acupuncture did not provide statistically significant differences between the two groups, whereas a larger sample may have produced a more meaningful result. Although a strength of the sample is the diverse gender and educational backgrounds, the sample was also majority Caucasian, non-Hispanic, which may limit generalizability of results to other populations. There was a limitation of central VA as a site. A more urban or diverse sample such as California may have better access and low-cost options for acupuncture.

Additional limitations are related to the survey, which was not developed specifically to evaluate non-pharmacologic therapies. The variables created to determine use of acupuncture/pressure and the other non-pharmacologic therapies in the patient and caregiver survey data allowed for responses of "yes," "no" or "I haven't tried this" for each therapy. Therefore, there was not a means to determine the number of times each non-pharmacologic

therapy was tried using the survey data. Furthermore, there is lack of clarity regarding caregiver report of effectiveness and use of the non-pharmacologic therapies based upon the available survey data - specifically, whether the caregivers were reporting on what they believed is true for the patient or what they facilitated for the patient.

Finally, the survey data from the parent study included acupuncture/pressure as one variable. The distinction between acupuncture and acupressure is an important one due to the need for a practitioner to facilitate acupuncture whereas patients and caregivers may be able to self-manage acupressure as a therapy for pain management. Reported use and relationship to self-efficacy may have been different for acupuncture and acupressure as separate variables, which was not possible from the available survey data.

Conclusion

This study suggests that non-pharmacologic therapies are feasible and acceptable for self-management of pain among patients with advanced malignancy. Importantly, the techniques with highest reported use were therapies that could be self-administered by the patients or their caregivers and did not require access to a practitioner to facilitate. Acupuncture/pressure was one of the least used non-pharmacologic therapies and was associated with decreased self-efficacy, which may be related to barriers to access acupuncture treatment. Self-efficacy may have been higher in relationship to acupressure or lower for acupuncture if there were an ability to evaluate each modality separately.

Research is needed to evaluate feasibility and acceptability of both acupuncture and acupressure among patients with advanced malignancy and their caregivers. In future studies of feasibility and acceptability, acupuncture and acupressure may need to be evaluated separately in

this patient population. Acupuncture requires a practitioner to facilitate, whereas acupressure can be performed at home. Among acupuncture/pressure techniques, APA can be easily self-managed. There may be barriers to acupressure as well, for example, challenges related to pressing the acupoints due to neuropathy including CIPN. If accessibility to practitioner-facilitated therapies is a potential barrier, feasibility and acceptability of acupuncture and acupressure may need to be assessed separately in future studies to demonstrate this difference among patients with cancer.

There are two main areas of future research supported by this dissertation study: 1) feasibility and acceptability of acupuncture and acupressure separately for pain and symptom management among patients with advanced malignancy, and 2) potential benefits and uses of APA among patients with cancer and survivors. This data analysis suggests that additional research on non-pharmacologic and CAM therapies is indicated for patients with advanced malignancy due to high symptom burden and need for symptom self-management techniques that can be performed in the home setting. Non-pharmacologic methods of symptom management were used by close to 100% of patients and their primary caregivers, indicating that nearly all patients with advanced malignancy who use opioid medications for pain management also utilize non-pharmacologic methods as adjunctive techniques. Although this study suggests a potential role for use of acupuncture/pressure among patients with advanced malignancy and their caregivers, there is limited available evidence to support its use. As indicated by the integrative review acupuncture for CIPN, there is a need to develop protocols for use of acupuncture/pressure including APA and consistent measures to evaluate their effects among patients with cancer. Additional research is also indicated to evaluate barriers to using acupuncture/pressure to direct strategies to minimize these barriers.

Expanding access to acupuncture/pressure among patients with cancer and their primary caregivers could provide a significant opportunity to improve pain and QoL. Current evidence suggests that patients with cancer and their primary caregivers are interested in utilizing non-pharmacologic therapies including acupuncture/pressure for management cancer pain, however despite this interest, acupuncture/pressure is not widely used. Although acupuncture use is increasing in the US and has become one of the most frequently offered CAM therapies at major cancer centers, there remain significant barriers to accessing acupuncture/pressure among patients with cancer including cost and insurance coverage. APA could be utilized as a low-burden intervention that reduces barriers to access and provides benefits of acupuncture/pressure for symptom management among patients with advanced cancer pain.

References

Allison, Paul. (1999). *Multiple regression: A primer.* Pine Forge Press: Thousand Oaks, CA.

Almutairi, B. A., Al Odaibi, F. A., Alnahdi, A. H., Omar, M., Algashami, A., & Alonazi, M. (2023). Cross-cultural adaptation and validation of the Arabic version of the Pain Self-Efficacy Questionnaire in Arab people with chronic low back pain. *Physiotherapy Theory and Practice*, *39*(1), 182–192. https://doi.org/10.1080/09593985.2021.2005196

Almutairi, A. R., Mollon, L., Lee, J., & Slack, M. (2019). A comparison of the pharmacologic and nonpharmacologic strategies used to manage chronic pain: Opioid users versus nonusers. *Journal of the American Pharmacists Association*, *59*(5), 691–697. https://doi.org/10.1016/j.japh.2019.06.009

Ang, L. & Kaptchuk, T. (2011). The care of acupuncture for low back pain: When efficacy and comparative effectiveness conflict. *Spine, 36*(3), 181-182. https://dx.doi.org/10.1097%2FBRS.0b013e3181e15ef8

Bandura, A. (1994). Self-efficacy. In V. S. Ramachaudran (Ed.), *Encyclopedia of human behavior* (Vol 4, pp. 71-81). Academic Press.

Bao, T., Basal, C., Seluzicki, C., Li, S. Q., Seidman, A. D., & Mao, J. J. (2016). Long-term chemotherapy-induced peripheral neuropathy among breast cancer survivors: Prevalence, risk factors, and fall risk. *Breast Cancer Research and Treatment*, *159*(2), 327–333. https://doi.org/10.1007/s10549-016-3939-0

Bao, T., Goloubeva, O., Pelser, C., Porter, N., Primrose, J., Hester, L., Sadowska, M., Lapidus, R., Medeiros, M., Lao, L., Dorsey, S. G., & Badros, A. Z. (2014). A pilot study of acupuncture in treating bortezomib-induced peripheral neuropathy in patients with multiple myeloma. *Integrative Cancer Therapies*, *13*(5), 396–404. https://doi.org/10.1177/1534735414534729

Bao, T., Li, Q., DeRito, J. L., Seluzicki, C., Im, E. O., & Mao, J. (2018). Barriers to acupuncture use among breast cancer survivors: A cross-sectional analysis. *Integrative Cancer Therapies*, *17*(3), 854–859. https://doi.org/10.1177/1534735418754309

Bao, T., Seidman, A. D., Piulson, L., Vertosick, E., Chen, X., Vickers, A. J., Blinder, V. S., Zhi, W. I., Li, Q., Vahdat, L. T., Dickler, M. N., Robson, M. E., & Mao, J. J. (2018). A phase IIa trial of acupuncture to reduce chemotherapy-induced peripheral neuropathy severity during neoadjuvant or adjuvant weekly paclitaxel chemotherapy in breast cancer patients. *European Journal of Cancer*, *101*, 12–19. https://doi.org/10.1016/j.ejca.2018.06.008

Baydoun, M., Barton, D. L., & Arslanian-Engoren, C. (2018). A cancer specific middle-range theory of symptom self-care management: A theory synthesis. *Journal of Advanced Nursing, 74*, 2935-2946. https://doi.org/10.1111/jan.13829

Ben-Arye, E., River, Y., Keshet, Y., Lavie, O., Israeli, P., & Samuels, N. (2018). Effect of a complementary/integrative medicine treatment program on taxane-induced peripheral neuropathy: A brief report. *International Journal of Gynecological Cancer*, *28*(5), 1045–1049. https://doi.org/10.1097/IGC.0000000000001246

Cheng, H. L., Yeung, W. F., Wong, H. F., Lo, H. T., & Molassiotis, A. (2023). Self-acupressure for symptom management in cancer patients: A systematic review. *Journal of Pain and Symptom Management*, *66*(1), e109–e128.https://doi.org/10.1016/j.jpainsymman.2023.03.002

Chien, T. J., Liu, C. Y., Fang, C. J., & Kuo, C. Y. (2019). The efficacy of acupuncture in chemotherapy-induced peripheral neuropathy: Systematic review and meta-analysis. *Integrative Cancer Therapies*, *18*, 1-10. https://doi.org/10.1177/1534735419886662

Cossette, S., Belaid, H., Heppell, S., Mailhot, T., & Guertin, M. C. (2016). Feasibility and acceptability of a nursing intervention with family caregiver on self-care among heart failure patients: a randomized pilot trial. *Pilot and Feasibility Studies*, *2*, 34. https://doi.org/10.1186/s40814-016-0077-8

Cui J, Wang S, Ren J, Zhang J, Jing J. Use of acupuncture in the USA: Changes over a decade (2002–2012). *Acupuncture in Medicine.* 2017;35(3):200-207. doi:10.1136/acupmed-2016-011106

Donald, G. K., Tobin, I., & Stringer, J. (2011). Evaluation of acupuncture in the management of chemotherapy-induced peripheral neuropathy. *Acupuncture in Medicine*, *29*(3), 230–233. https://doi.org/10.1136/acupmed.2011.010025

Eaton, L. H., Jang, M. K., Jensen, M. P., Pike, K. C., Heitkemper, M. M., & Doorenbos, A. Z. (2022). Hypnosis and relaxation interventions for chronic pain management in cancer survivors: a randomized controlled trial. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *31*(1), 50. https://doi.org/10.1007/s00520-022-07498-1

Eaton, L. H., Langford, D. J., Meins, A. R., Rue, T., Tauben, D. J., & Doorenbos, A. Z. (2018). Use of self-management interventions for chronic pain management: A comparison between rural and nonrural residents. *Pain Management Nursing: Official Journal of the American Society of Pain Management Nurses*, *19*(1), 8–13. https://doi.org/10.1016/j.pmn.2017.09.004

ECOG-ACRIN (2022). *ECOG Performance Status Scale.* https://ecog-acrin.org/resources/ecog-performance-status/

Eller, L. S., Lev, E. L., Yuan, C., & Watkins, A. V. (2018). Describing self-care self-efficacy: Definition, measurement, outcomes, and implications. *International Journal of Nursing Knowledge*, *29*(1), 38–48.   https://doi.org/10.1111/2047-3095.12143

Epstein, A. S., Liou, K. T., Romero, S. A. D., Baser, R. E., Wong, G., Xiao, H., Mo, Z., Walker, D., MacLeod, J., Li, Q., Barton-Burke, M., Deng, G. E., Panageas, K. S., Farrar, J. T., & Mao, J. J. (2023). Acupuncture vs massage for pain in patients living with advanced cancer: The IMPACT randomized clinical trial. *JAMA Network Open*, *6*(11), e2342482. https://doi.org/10.1001/jamanetworkopen.2023.42482

Fisher, H. M., Stalls, J., Winger, J. G., Miller, S. N., Plumb Vilardaga, J. C., Majestic, C., Kelleher, S. A., & Somers, T. J. (2023). Role of self-efficacy for pain management and pain catastrophizing in the   relationship between pain severity and depressive symptoms in women with breast cancer and pain. *Journal of Psychosocial Oncology*, *41*(1), 87–103. https://doi.org/10.1080/07347332.2022.2046676

Foster, C., Breckons, M., Cottrell, P., Barbosa, D., Calman, L., Corner, J., Fenlon, D., Foster, R., Grimmett, C., Richardson, A., & Smith, P. W. (2015). Cancer survivors' self-efficacy to self-manage in the year following primary treatment. *Journal of Cancer Survivorship, 9,* 11-19. https://doi.org/10.1007/s11764-014-0384-0

Franconi, G., Manni, L., Schroeder, S., Marchetti, P., & Robinson, N. (2013). A systematic review of experimental and clinical acupuncture in chemotherapy-induced peripheral neuropathy. *Evidence-Based Complementary and Alternative Medicine*, *2013*, 1-7. https://doi.org/10.1155/2013/516916

Gallaway, M. S., Townsend, J. S., Shelby, D., & Puckett, M. C. (2020). Pain among cancer survivors. *Preventing Chronic Disease*, *17*, E54. https://doi.org/10.5888/pcd17.190367

Garcia, M. K., Cohen, L., Guo, Y., Zhou, Y., You, B., Chiang, J., Orlowski, R. Z., Weber, D., Shah, J., Alexanian, R., Thomas, S., Romaguera, J., Zhang, L., Badillo, M., Chen, Y., Wei, Q., Lee, R., Delasalle, K., Green, V., & Wang, M. (2014). Electroacupuncture for thalidomide/bortezomib-induced peripheral neuropathy in multiple myeloma: A feasibility study. *Journal of Hematology & Oncology*, *7*, 41. https://doi.org/10.1186/1756-8722-7-41

Greenlee, H., Crew, K., Capodice, J., Awad, D., Buono, D., Shi, Z., Jeffres, A., Wyse, S., Whitman, W., Trivedi, M. S., Kalinsky, K., & Hershman, D. L. (2016). Randomized sham-controlled pilot trial of weekly electro-acupuncture for the prevention of taxane-induced peripheral neuropathy in women with early stage breast cancer. *Breast Cancer Research and Treatment*, *156*(3), 453-464. https://doi.org/10.1007/s10549-016-3759-2

Hammer, M. J., Ercolano, E. A., Wright, F., Dickson, V. V., Chyun, D., & Melkus, G. D. (2015). Self-management for adult patients with cancer: An integrative review. *Cancer Nursing*, *38*(2), E10–E26. https://doi.org/10.1097/NCC.0000000000000122

Hammond, E., Pitz, M., & Shay, B. (2019). Neuropathic pain in taxane-induced peripheral neuropathy: Evidence for exercise in treatment. *Neurorehabilitation and Neural Repair*, *33*(10), 792–799. https://doi.org/10.1177/1545968319860486

Han, X., Wang, L., Shi, H., Zheng, G., He, J., Wu, W., Shi, J., Wei, G., Zheng, W., Sun, J., Huang, H., & Cai, Z. (2017). Acupuncture combined with methylcobalamin for the treatment of chemotherapy-induced peripheral neuropathy in patients with multiple myeloma. *BMC Cancer*, *17*(1), 1-7. https://doi.org/10.1186/s12885-016-3037-z

Hayes, C. & Hodson, F. J. (2011) A whole-person model of care for persistent pain: From conceptual framework to practical application. *Pain Medicine, 12*, 1738-1749. https://doi.org./10.1111/j.1526-4637.2011.01267.x

He, Y., Guo, X., May, B. H., Zhang, A. L., Liu, Y., Lu, C., Mao, J. J., Xue, C. C., & Zhang, H. (2020). Clinical evidence for association of acupuncture and acupressure with improved cancer pain: A systematic review and meta-analysis. *JAMA Oncology*, *6*(2), 271–278. https://doi.org/10.1001/jamaoncol.2019.5233

HealthMeasures (2024). *Pain Interference – Short Form 6a.* https://www.healthmeasures.net/search-view-measures?task=Search.search

Hershman, D. L., Lacchetti, C., Dworkin, R. H., Lavoie Smith, E. M., Bleeker, J., Cavaletti, G., Chauhan, C., Gavin, P., Lavino, A., Lustberg, M. B., Paice, J., Schneider, B., Smith, M. L., Smith, T., Terstriep, S., Wagner-Johnston, N., Bak, K., & Loprinzi, C. L. (2014). Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *32*(18), 1941–1967. https://doi.org/10.1200/JCO.2013.54.0914

Heymans, M. W., & Twisk, J. W. R. (2022). Handling missing data in clinical research. *Journal of clinical epidemiology*, *151*, 185–188. https://doi.org/10.1016/j.jclinepi.2022.08.016

Hopia, H., Latvala, E., & Liimatainen, L. (2016). Reviewing the methodology of an integrative review. *Scandinavian Journal of Caring Sciences*, *30*(4), 662–669. https://doi.org/10.1111/scs.12327

Jeong, Y. J., Kwak, M. A., Seo, J. C., Park, S. H., Bong, J. G., Shin, I. H., & Parkwo, S. H. (2018). Acupuncture for the treatment of taxane-induced peripheral neuropathy in breast cancer patients: A pilot trial. *Evidence-Based Complementary and Alternative Medicine*, *2018*, 1-11. https://doi.org/10.1155/2018/5367014

Kaptchuk, T. J. (2002). Acupuncture: Theory, efficacy, and practice. *Annals of Internal Medicine*, *136*(5), 374–383. https://doi.org/10.7326/0003-4819-136-5-200203050-00010

Kaptchuk, T. J., Chen, K., & Song, J. (2010). Recent clinical trials of acupuncture in the West: Responses from the practitioners. *Chinese Journal of Integrative Medicine*, *16*(3), 197–203. https://doi.org/10.1007/s11655-010-0197-x

Kolb, N. A., Smith, A. G., Singleton, J. R., Beck, S. L., Stoddard, G. J., Brown, S., & Mooney, K. (2016). The association of chemotherapy-induced peripheral neuropathy symptoms and the risk of falling. *JAMA Neurology*, *73*(7), 860–866. https://doi.org/10.1001/jamaneurol.2016.0383

Katta MR, Valisekka SS, Agarwal P, et al. Non-pharmacological integrative therapies for chronic cancer pain. *Journal of Oncology Pharmacy Practice, 28*(8):1859-1868. doi:10.1177/10781552221098437

Kim, H. J., & Jung, S. O. (2020). Comparative evaluations of single-item pain-intensity measures in cancer patients: Numeric rating scale vs. verbal rating scale. *Journal of Clinical Nursing*, *29*(15-16), 2945–2952. https://doi.org/10.1111/jocn.15341

Kutcher, A. M., & LeBaron, V. T. (2022). Evaluating acupuncture for the treatment of chemotherapy-induced peripheral neuropathy: An integrative review. *Western Journal of Nursing Research*, *44*(2), 169–179. https://doi.org/10.1177/0193945921992538

Latte-Naor, S., & Mao, J. J. (2019). Putting integrative oncology into practice: Concepts and approaches. *Journal of Oncology Practice*, *15*(1), 7–14. https://doi.org/10.1200/JOP.18.00554

Lau, C. H. Y., Wu, X., Chung, V. C. H., Liu, X., Hui, E. P., Cramer, H., Lauche, R., Wong, S. Y. S., Lau, A. Y. L., Sit, R. W. S., Ziea, E. T. C., Ng, B. F. L., & Wu, J. C. Y. (2016). Acupuncture and related therapies for symptom management in palliative cancer care: Systematic review and meta-analysis. *Medicine*, *95*(9), e2901. https://doi.org/10.1097/MD.0000000000002901

LeBaron, V., Alam, R., Bennett, R., Blackhall, L., Gordon, K., Hayes, J., Homdee, N., Jones, R., Lichti, K., Martinez, Y., Mohammadi, S., Ogunjirin, E., Patel, N., & Lach, J. (2022). Deploying the behavioral and environmental sensing and intervention for cancer smart health system to support patients and family caregivers in managing pain: Feasibility and acceptability study. *Journal of Internet Medical Research Cancer (JMIR) Cancer, 8*(3), 1-19. https://doi.org/10.2196/36879

LeBaron, V., Bennett, R., Blackhall, L., Alam, R., Gordon, K., Hayes, J., Homdee, N., Martinez, Y, Ogunjirin, E., Jones, R., Thomas, T. & Lach, J. (2020). Understanding the experience of cancer pain management at home from the perspective of patients and family caregivers to inform design of an in-home smart health sensing system. *Journal of Medical Internet Research Formative Research, 4*(8), e-20836. https://doi.org/10.2196/20836

LeBaron, V., Homdee, N. Ogunjirin, E., Patel, N., Blackhall, L. & Lach, J. (2023). Describing and visualizing the patient and caregiver experience of cancer pain in the home context using ecological momentary assessments. *Digital Health, 2023*(0), 9. https://doi.org/10.1177/20552076231194936

Li, K., Giustini, D., & Seely, D. (2019). A systematic review of acupuncture for chemotherapy-induced peripheral neuropathy. *Current Oncology*, *26*(2), E147–E154. https://doi.org/10.3747/co.26.4261

Liehr, P. & Smith, M. (2017). Middle range theory. *Advances in Nursing Science, 40*(1), 51-63. doi: 10.1097/ANS.0000000000000162.

Lu, Z., Moody, J., Marx, B. L., & Hammerstrom, T. (2017). Treatment of chemotherapy-induced peripheral neuropathy in integrative oncology: A survey of acupuncture and oriental medicine practitioners. *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, *23*(12), 964–970. https://doi.org/10.1089/acm.2017.0052

Lu, W., Giobbie-Hurder, A., Freedman, R. A., Shin, I. H., Lin, N. U., Partridge, A. H., Rosenthal, D. S., & Ligibel, J. A. (2019). Acupuncture for chemotherapy-induced peripheral neuropathy in breast cancer survivors: A randomized controlled pilot trial. *The Oncologist*, *25*(4), 310–318. https://doi.org/10.1634/theoncologist.2019-0489

Ludwick, A., Corey, K., & Meghani, S. (2020). Racial and socioeconomic factors associated with the use of complementary and alternative modalities for pain in cancer outpatients: An integrative review. *Pain Management Nursing: Official Journal of the American Society of Pain Management Nurses*, *21*(2), 142–150. https://doi.org/10.1016/j.pmn.2019.08.005

Maeda, Y., Kim, H., Kettner, N., Kim, J., Cina, S., Malatesta, C., Gerber, J., McManus, C., Ong-Sutherland, R., Mezzacappa, P., Libby, A., Mawla, I., Morse, L. R., Kaptchuk, T. J., Audette, J., & Napadow, V. (2017). Rewiring the primary somatosensory cortex in carpal tunnel syndrome with acupuncture. *Brain: A Journal of Neurology*, *140*(4), 914–927. https://doi.org/10.1093/brain/awx015

Magnowska, M., Iżycka, N., Kapoła-Czyż, J., Romała, A., Lorek, J., Spaczyński, M., & Nowak-Markwitz, E. (2018). Effectiveness of gabapentin pharmacotherapy in chemotherapy-induced peripheral neuropathy. *Ginekologia Polska*, *89*(4), 200–204. https://doi.org/10.5603/GP.a2018.0034

Mandıroğlu, S., Cevik, C., & Aylı, M. (2014). Acupuncture for neuropathic pain due to bortezomib in a patient with multiple myeloma. *Acupuncture in Medicine: Journal of the British Medical Acupuncture Society*, *32*(2), 194–196. https://doi.org/10.1136/acupmed-2013-010491

Mao, J. J., Palmer, C. S., Healy, K. E., Desai, K., & Amsterdam, J. (2011). Complementary and alternative medicine use among cancer survivors: a population-based study. *Journal of Cancer Survivorship: Research and Practice*, *5*(1), 8–17. https://doi.org/10.1007/s11764-010-0153-7

Merluzzi, T. V., Pustejovsky, J. E., Philip, E. J., Sohl, S. J., Berendsen, M., & Salsman, J. M. (2019). Interventions to enhance self-efficacy in cancer patients: A meta-analysis of

randomized controlled trials. *Psychooncology, 28*(9), 1781-1790.
https://doi.org/10.1002/pon.5148.

Michaelides, A., & Zis, P. (2019). Depression, anxiety and acute pain: Links and management challenges. *Postgraduate Medicine*, *131*(7), 438–444.
https://doi.org/10.1080/00325481.2019.1663705

Miller, K. R., Patel, J. N., Symanowski, J. T., Edelen, C. A., & Walsh, D. (2019). Acupuncture for cancer pain and symptom management in a palliative medicine clinic. *The American Journal of Hospice & Palliative Care*, *36*(4), 326–332.
https://doi.org/10.1177/1049909118804464

Molassiotis, A, Suen, L. K. P., Cheng, H., Mok, T. S. K., Lee, S. C. Y., Wang, C. H., Lee, P., Leung, H., Chan, V., Lau, T. K. H., & Yeo, W. (2019). A randomized assessor-blinded waitlist-controlled trial to assess the effectiveness of acupuncture in the management of hemotherapy-induced peripheral neuropathy. *Integrative Cancer Therapies*, *18,* 1-12.
https://doi.org/10.1177/1534735419836501

Molassiotis, A., Cheng, H., Lopez, V., Au, J., Chan, A., Bandla, A., Leung, K., Li, Y., Wong, K., Suen, L., Chan, C., Yorke, J., Farrell, C., & Sundar, R. (2019). Are we mis-estimating chemotherapy-induced peripheral neuropathy? Analysis of assessment methodologies from a prospective, multinational, longitudinal cohort study of patients receiving neurotoxic chemotherapy. *BMC Cancer*, *19*(1), 1-19. https://doi.org/10.1186/s12885-019-5302-4

National Cancer Institute. (2023, November 8). *Acupuncture (PDQ) – Health professional version.* https://www.cancer.gov/about-cancer/treatment/cam/hp/acupuncture-pdq

National Cancer Institute. (2023, September 7). *Cancer Pain (PDQ) – Health Professional Version.* https://www.cancer.gov/about-cancer/treatment/side-effects/pain/pain-hp-pdq#_186_toc

National Center for Complementary and Integrative Health. (2023, December 25). *Statistics from the national health interview survey.* https://www-nccih-nih.gov/health/statistics-from-the-national-health-interview-survey

National Center for Complementary and Integrative Health. (2022, October). *Acupuncture: What you need to know.* https://www.nccih.nih.gov/health/acupuncture-what-you-need-to-know

Nephew, B. C., Incollingo Rodriguez, A. C., Melican, V., Polcari, J. J., Nippert, K. E., Rashkovskii, M., Linnell, L. B., Hu, R., Ruiz, C., King, J. A., & Gardiner, P. (2022). Depression predicts chronic pain interference in racially diverse, income-disadvantaged patients. *Pain Medicine (Malden, Mass.)*, *23*(7), 1239–1248.
https://doi.org/10.1093/pm/pnab342

Nightingale, C., Sterba, K. R., Levine, B., Tooze, J. A., Greven, K., Frizzell, B., Hughes, R. T., Snavely, A., Lesser, G. J., Norona, S., Pleasant, K., & Weaver, K. E. (2022). Feasibility and acceptability of a multi-modality self-management intervention for head and neck cancer caregivers: A pilot randomized trial. *Integrative Cancer Therapies, 21*, 15347354221098984. https://doi.org/10.1177/15347354221098984

Philip, A., Mayahara, M., Fogg, L. F., & Hart, P. D. (2022). The Impact of an education intervention to improve blood pressure control among black non-Hispanic patients and Hispanic patients with chronic kidney disease. *Nephrology Nursing Journal : Journal of the American Nephrology Nurses' Association*, *49*(4), 351–358.

Rostock, M., Jaroslawski, K., Guethlin, C., Ludtke, R., Schroder, S., & Bartsch, H. (2013). Chemotherapy-induced peripheral neuropathy in cancer patients: A four-arm randomized trial on the effectiveness of electroacupuncture. *Evidence-Based Complementary and Alternative Medicine*, *2013*. https://doi.org/10.1155/2013/349653

Schroeder, S., Meyer-Hamme, G., & Epple, S. (2012). Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN): A pilot study using neurography. *Acupuncture in Medicine*, *30*(1), 4–7. https://doi.org/10.1136/acupmed-2011-010034

Sim, M., Kim, S. Y., & Suh, Y. (2022). Sample size requirements for simple and complex mediation models. *Educational and Psychological Measurement*, *82*(1), 76–106. https://doi.org/10.1177/00131644211003261

Snijders, R. A. H., Brom, L., Theunissen, M., & van den Beuken-van Everdingen, M. H. J. (2023). Update on prevalence of pain in patients with cancer 2022: A systematic literature review and meta-analysis. *Cancers*, *15*(3), 591. https://doi.org/10.3390/cancers15030591

Song, S. J., Min, J., Suh, S. Y., Jung, S. H., Hahn, H. J., Im, S. A., & Lee, J. Y. (2017). Incidence of taxane-induced peripheral neuropathy receiving treatment and prescription patterns in patients with breast cancer. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *25*(7), 2241–2248. https://doi.org/10.1007/s00520-017-3631-x

Staff, N. P., Grisold, A., Grisold, W., & Windebank, A. J. (2017). Chemotherapy-induced peripheral neuropathy: A current review. *Annals of Neurology*, *81*(6), 772–781. https://doi.org/10.1002/ana.24951

Starobova, H., & Vetter, I. (2017). Pathophysiology of chemotherapy-induced peripheral neuropathy. *Frontiers in Molecular Neuroscience*, *10*, 1-21. https://doi.org/10.3389/fnmol.2017.00174

Tack, L., Lefebvre, T., Blieck, V., Cool, L., Pottel, H., Eygen, K. V., Derijcke, S., Vergauwe, P., Schofield, P., Chandler, R., Lane, P., Boterberg, T., & Debruyne, P. R. (2021).

Acuuncture as a complementary therapy for cancer care: Acceptability and preferences of patients and informal caregivers. *Journal of Acupuncture and Meridian Studies*, *14*(2), 67–74. https://doi.org/10.51507/j.jams.2021.14.2.67

Tan, J. Y., Molassiotis, A., Wang, T., & Suen, L. K. (2014). Adverse events of auricular therapy: a systematic review. *Evidence-Based Complementary and Alternative Medicine: eCAM*, *2014*, 506758. https://doi.org/10.1155/2014/506758

Teixeira, R. J., Applebaum, A. J., Bhatia, S., & Brandão, T. (2018). The impact of coping strategies of cancer caregivers on psychophysiological outcomes: an integrative review. *Psychology Research and Behavior Management, 11*, 207–215. https://doi.org/10.2147/PRBM.S164946

Teresi, J. A., Yu, X., Stewart, A. L., & Hays, R. D. (2022). Guidelines for designing and evaluating feasibility pilot studies. *Medical Care, 60*(1), 95–103. https://doi.org/10.1097/MLR.0000000000001664

Tofthagen, C. S., Cheville, A. L., & Loprinzi, C. L. (2020). The physical consequences of chemotherapy-induced peripheral neuropathy. *Current Oncology Reports*, *22*(5), 50. https://doi.org/10.1007/s11912-020-00903-0

Usability.gov. (2024, January 21). *System Usability Scale (SUS).* https://www.usability.gov/how-to-and-tools/methods/system-usability-scale.html

Valentine-Davis, B., & Altshuler, L. H. (2015). Acupuncture for oxaliplatin chemotherapy-induced peripheral neuropathy in colon cancer: A retrospective case series. *Medical Acupuncture*, *27*(3), 216–223. https://doi.org/10.1089/acu.2015.1103

Vapiwala, N., Mick, R., Hampshire, M. K., Metz, J. M., & DeNittis, A. S. (2006). Patient initiation of complementary and alternative medical therapies (CAM) following cancer diagnosis. *Cancer journal (Sudbury, Mass.)*, *12*(6), 467–474. https://doi.org/10.1097/00130404-200611000-00006

Wang, F., Zhao, J., Li, Y., Yang, X., Wu, D., Yang, B., Zhang, C., He, Z., Du, L., Zhu, X., Ming, D., Liu, Y., & Tang, D. (2022). Acupuncture and acupressure with improved cancer-related depression of retrospective studies. *Frontiers in Oncology*, *12*, 1036634. https://doi.org/10.3389/fonc.2022.1036634

Whale, K., & Gooberman-Hill, R. (2022). The importance of sleep for people with chronic pain: Current insights and evidence. *JBMR Plus*, *6*(7), e10658. https://doi.org/10.1002/jbm4.10658

White, L. L., Cohen, M. Z., Berger, A. M., Kupzyk, K. A., & Bierman, P. J. (2019). Self-efficacy for management of symptoms and symptom distress in adults with cancer: An integrative review. *Oncology Nursing Forum, 48*(1), 113-128. https/doi.org/10.1188/19.ONF.113-128

Widgren, Y., Fransson, P., & Efverman, A. (2022). Acupuncture in patients undergoing cancer therapy: Their interest and belief in acupuncture is high, but few are using it. *Integrative Cancer Therapies*, *21*. https://doi.org/10.1177/15347354221077277

Yang, J., Wahner-Roedler, D. L., Zhou, X., Johnson, L. A., Do, A., Pachman, D. R., Chon, T. Y., Salinas, M., Millstine, D., & Bauer, B. A. (2021). Acupuncture for palliative cancer pain management: systematic review. *BMJ Supportive & Palliative Care*, *11*(3), 264–270. https://doi.org/10.1136/bmjspcare-2020-002638

Yang, Y., Wen, J., & Hong, J. (2020). The effects of auricular therapy for cancer pain: A systematic review and meta-analysis. *Evidence-Based Complimentary and Alternative Medicine*, 1-10. https://doi.org/10.1155/2020/1618767

Yeh, C. H., Chien, L.-C., Chiang, Y. C., Ren, D., & Suen, L. K.-P. (2015). Auricular point acupressure as an adjunct analgesic treatment for cancer patients: A feasibility study. *Pain Management Nursing*, *16*(3), 285–293. https://doi.org/10.1016/j.pmn.2014.08.005

Yeh, C. H., Lin, W. C., Kwai-Ping Suen, L., Park, N. J., Wood, L. J., van Londen, G. J., & Howard Bovbjerg, D. (2017). Auricular point acupressure to manage aromatase inhibitor-induced arthralgia in postmenopausal breast cancer survivors: A pilot study. *Oncology Nursing Forum*, *44*(4), 476–487. https://doi.org/10.1188/17.ONF.476-487

Wittenberg, E., Buller, H., Ferrell, B., Koczywas, M., & Borneman, T. (2017). Understanding family caregiver communication to provide family-centered cancer care. *Seminars in Oncology Nursing*, *33*(5), 507–516. https://doi.org/10.1016/j.soncn.2017.09.001

Whittemore, R., & Knafl, K. (2005). The integrative review: Updated methodology. *Journal of Advanced Nursing*, *52*(5), 546–553. https://doi.org/10.1111/j.1365-2648.2005.03621.x

Witt, C. M., Balneaves, L. G., Cardoso, M. J., Cohen, L., Greenlee, H., Johnstone, P., Kücük, Ö., Mailman, J., & Mao, J. J. (2017). A comprehensive definition for integrative oncology. *Journal of the National Cancer Institute Monographs*, *2017*(52), 3-8. https://doi.org/10.1093/jncimonographs/lgx012

Wu, M. S., Chen, K. H., Chen, I. F., Huang, S. K., Tzeng, P. C., Yeh, M. L., Lee, F. P., Lin, J. G., & Chen, C. (2016). The efficacy of acupuncture in post-operative pain management: A systematic review and meta-analysis. *PLOS ONE*, *11*(3), e0150367. https://doi.org/10.1371/journal.pone.0150367

Xiong, Z., Wang, T., Gan, L., Ran, J., Min, J., & Lu, G. (2016). Clinical efficacy of acupoint injection for chemotherapy-induced peripheral neuropathy of patients with breast cancer. *World Journal of Acupuncture - Moxibustion*, *26*(2), 20-24. https://doi.org/10.1016/S1003-5257%2817%2930005-3

Yun Hyeongjun, Sun Lingyun, Mao Jun J., Growth of integrative medicine at leading cancer centers between 2009 and 2016: A systematic analysis of NCI-designated comprehensive cancer center websites, *JNCI Monographs*, Volume 2017, Issue 52, November 2017, lgx004, https://doi.org/10.1093/jncimonographs/lgx004

Zajączkowska, R., Kocot-Kępska, M., Leppert, W., Wrzosek, A., Mika, J., & Wordliczek, J. (2019). Mechanisms of chemotherapy-induced peripheral neuropathy. *International Journal of Molecular Sciences*, *20*(6). https://doi.org/10.3390/ijms20061451

Zhang, S., Wu, T., Zhang, H., Yang, Y., Jiang, H., Cao, S., Xie, F., Xia, X., Lü, J., & Zhong, Y. (2017). Effect of electroacupuncture on chemotherapy-induced peripheral neuropathy in patients with malignant tumor: A single-blinded, randomized controlled trial. *Journal of Traditional Chinese Medicine*, *37*(2), 179–184. https://doi.org/10.1016/S0254-6272(17)30042-0

Zhi, W., Ingram, E., Li, S., Chen, P., Piulson, L., & Bao, T. (2018). Acupuncture for bortezomib-induced peripheral neuropathy: Not just for pain. *Integrative Cancer Therapies*, *17*(4), 1079-1086. https://doi.org/10.1177/1534735418788667

Zhou, W., & Benharash, P. (2014). Effects and mechanisms of acupuncture based on the principle of meridians. *Journal of Acupuncture and Meridian Studies*, *7*(4), 190–193. https://doi.org/10.1016/j.jams.2014.02.007

Zhuang, Y., Xing, J., Li, J., Zeng, B. Y., & Liang, F. (2013). Chapter one—History of acupuncture research. In B. Y. Zeng, K. Zhao, & F. R. Liang (Eds.), *International Review of Neurobiology: Volume 11* (pp. 1–23). Academic Press.

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