

THE IMPACT OF SPIRITUALITY ON PAIN THROUGH A SELF-TRANSCENDENCE
LENS AMONG WOMEN WITH ADVANCED BREAST CANCER

By

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ABSTRACT

THE IMPACT OF SPIRITUALITY ON PAIN THROUGH A SELF-TRANSCENDENCE LENS AMONG WOMEN WITH ADVANCED BREAST CANCER

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With up to 83% of women with advanced breast cancer reporting pain (Puetzler, Feldmann, Brascher, Gerhardt, & Benrath, 2014), management of this symptom continues to be a critical problem. Spirituality (a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning) is one area that has not yet been adequately investigated, as it may positively impact the experience of pain in this population. The purpose of this dissertation was to examine the impact of spirituality on pain in women with advanced breast cancer within the context of a Complementary and Integrative Health (CIH) intervention, using the Theory of Self-Transcendence (ST) as a guide. This dissertation is comprised of three manuscripts: 1) Literature review; 2) Report of a quantitative secondary data analysis; 3) Report of a qualitative study. Each address the central topic; the impact of spirituality on pain.

Manuscript 1 is a scoping literature review characterizing how pain and spirituality have been conceptualized, assessed, and addressed among women with advanced breast cancer. Forty-two publications were included. Most focused on pain ($n = 33$), while others addressed pain and spirituality ($n=5$), and exclusively spirituality ($n=4$). Women cited dimensions of spirituality as important for coping with their disease, suggesting the value of spirituality to cope with pain. A gap in understanding spirituality and its influence on pain in this population was identified.

Manuscript 2 is a secondary analysis based on a National Cancer Institute-funded randomized controlled trial of foot reflexology for women with advanced breast cancer ($n=256$)

(Wyatt, Sikorskii, Holmstrom, & Luo, 2011-2016). This manuscript examined demographic and clinical factors associated with pain and spirituality, the impact of spirituality on pain, and how spirituality and pain impacted engagement with the CIH intervention. Results revealed that various demographic and clinical factors were associated with pain and/or spirituality. The impact of spirituality on pain was not significant over time. Spirituality and pain were not associated with engaging in reflexology sessions.

Manuscript 3 describes a phenomenological qualitative study examining pain and spirituality in women with advanced breast cancer, as well as perceived relationships between these concepts. N=9 semi-structured interviews were conducted. Data were analyzed using an open-coding process. Themes included: 1) Spirituality provides positive cognitive framing to help women face pain; 2) Spirituality brings about positive emotions such as peace and tranquility despite pain; 3) Spiritual practices serve as pain self-management tools; 4) Connection with others and service activities (aspects of spirituality) help women cope with pain.

The findings from these three manuscripts advance nursing science by providing new insight into the nature of pain and spirituality. The Theory of ST was supported, and potentially extended, through findings from each of the three manuscripts. This work impacts nursing by providing novel insights into the nature of pain and spirituality in women with advanced breast cancer, and how spirituality may impact perceptions associated with how pain is experienced. This dissertation is the first step in a program of research to develop CIH-based, nurse-led pain management interventions for patients with cancer, which may include spirituality.

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This dissertation is dedicated to my family, friends and mentors;
Your love and support mean so much.
Also, to my own sense of spirituality, which has brought me to this work.

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KEY TO ABBREVIATIONS

BPI = Brief Pain Inventory

CARES = Cancer Rehabilitation Evaluation System

CIH = Complementary and Integrative Health

CINAHL = Cumulative Index to Nursing and Allied Health Literature

FACT-B = Functional Assessment of Cancer Therapy – Breast Cancer

IPA = Interpretive Phenomenological Analysis

LTQL = Long Term Quality of Life

MBSR = Mindfulness-Based Stress Reduction

MeSH = Medical Subject Headings

MDASI = M.D. Anderson Symptom Inventory

NCCIH = The National Center for Complementary and Integrative Health

NRS = Numeric Rating Scale

PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PRISMA-ScR = Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

PROMIS = Patient Reported Outcomes Measurement Information System

QOL = Quality of Life

RQ = Research Question

ST = Self Transcendence

US = United States

VAS = Visual Analogue Scale

CHAPTER 1: INTRODUCTION

One in 8 women in the United States (US) will be diagnosed with breast cancer during their lifetime (American Cancer Society, 2019) and 37% of these women have cases which are at an advanced stage, defined as stage III (locally advanced) or IV (metastatic) (Susan G. Komen, 2018). Up to 83% of women with advanced breast cancer report experiencing pain (Puetzler et al., 2014), making pain management a top priority for this population. Pain is defined as *a distressing experience which has interacting sensory, cognitive and emotional components, which may be associated with actual or perceived tissue damage* (Bushnell, Ceko, & Low, 2013; International Association for the Study of Pain, 1979; Wang, Jackson, & Cai, 2016; Williams & Craig, 2016).

Women with advanced breast cancer have indicated that spirituality serves as a resource when facing their disease (Gaston-Johansson, Haisfield-Wolfe, Reddick, Goldstein, & Lawal, 2013; Krigel, Myers, Befort, Krebill, & Klemp, 2014; Mosher et al., 2013; Rosenzweig, Wiehagen, Brufsky, & Arnold, 2009). Spirituality is a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning (Steinhauser et al., 2017; Sun, So Young, & Jin Sook, 2017; Weathers, McCarthy, & Coffey, 2016), which may serve as a resource when facing cancer and its associated symptoms (Flanigan, Wyatt, & Lehto, 2019; Krigel et al., 2014; Mosher et al., 2013; Visser, de Jager Meezenbroek, & Garssen, 2018). Spirituality can positively alter the disease experience (Gaston-Johansson et al., 2013; Rosenzweig et al., 2009), therefore, it may also serve as a resource for altering the experience of pain (Flanigan et al., 2019; Visser et al., 2018). There is growing interest in spirituality as an aspect of comprehensive care for those with advanced disease (Piderman et al.,

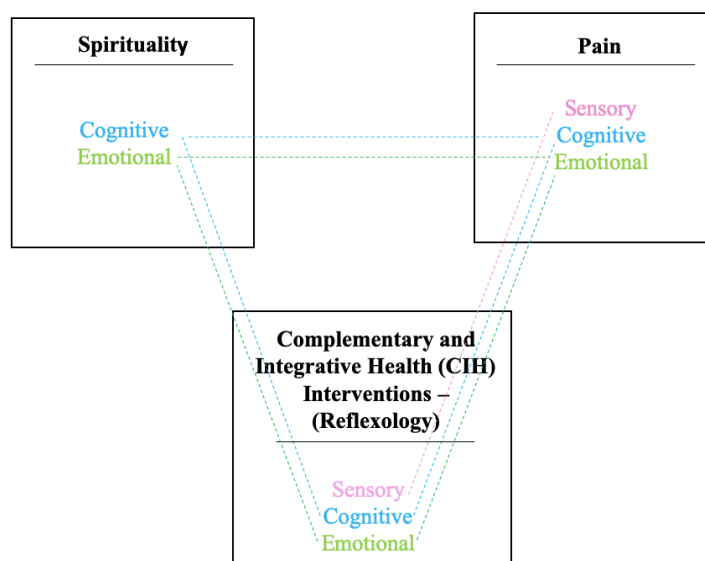
2015). Spirituality is one area that has not yet been adequately investigated, as it may impact the experience of pain among women with advanced breast cancer.

A popular approach to pain management among breast cancer patients is through the use of Complementary and Integrative Health (CIH) interventions (Boon, Olatunde, & Zick, 2007). CIH interventions focus on caring for the mind, body, and spirit and are often used in conjunction with allopathic treatments (National Cancer Institute, 2019), making these interventions especially well-suited to address pain from a comprehensive perspective. Since a CIH approach recognizes that mind, body and spirit are involved in healing (Reynolds, 2006), these interventions are inherently connected to spirituality and may be important tools in the comprehensive care of women with advanced breast cancer.

The main concepts included in this dissertation (spirituality, pain, CIH interventions) are closely aligned in that they each focus on variations of sensation, cognition and emotion. Figure 1.1 illustrates the natural linkages between these concepts. For spirituality, this concept is often viewed as a unique phenomenon connected with the sacred and transcendent (Balducci, 2019), yet when using self-report, spirituality is viewed through the lens of cognitive and emotional experience. This aligns with current evidence showing that spirituality contributes to alterations in various thoughts and emotions (Gregg, 2011; Harvey, 2008; Weathers et al., 2016). For pain, this symptom is comprised of sensory, cognitive and emotional components which work together to create the overall symptom experience (Arnstein, 2018; Bushnell et al., 2013; Peters, 2015). Spirituality may impact pain by positively altering thoughts and emotions, thus changing the painful experience. For CIH interventions (described in more detail below), these interventions are uniquely suited for inclusion in this dissertation because they work by targeting sensory, cognitive and emotional mechanisms (National Cancer Institute, 2019; Reynolds, 2006).

Therefore, these interventions are closely related to spirituality and are they are also well positioned to influence pain via psychological routes. Reflexology is the exemplar case of a CIH intervention which will be included in this work (also described in more detail below).

Figure 1. 1 Connections Between Main Dissertation Concepts: Spirituality, Pain and Complementary and Integrative Health (CIH) Interventions



Preliminary quantitative studies have demonstrated significant relationships between spirituality and pain in varying samples of cancer patients (Bai, Brubaker, Meghani, Bruner, & Yeager, 2018; Delgado-Guay et al., 2016; Hui et al., 2011), indicating that spirituality may alter how this symptom is experienced. Yet the impact of spirituality on pain has not yet been examined among women with advanced breast cancer, or within the context of a CIH intervention. Further, qualitative studies have indicated that women report using spirituality as a key resource for facing the challenges associated with their disease experience (Krigel et al., 2014; Mosher et al., 2013). A gap remains in understanding how spirituality may impact the way women experience symptoms associated with their advanced breast cancer, such as pain.

This dissertation has synthesized literature supporting the impact of spirituality on pain, identified gaps in the current literature which require further investigation, quantitatively

explored the impact of spirituality on pain in a sample of women with advanced breast cancer enrolled in a CIH intervention trial, and qualitatively explored how women with advanced breast cancer describe their spirituality, pain, and the link between these concepts. Since pain and spirituality are highly individual experiences, both can be impacted by unique variations in demographic and clinical factors (e.g., age, race/ethnicity, disease stage) (Hospice and Palliative Nurses Association, 2007; Paice & Ferrell, 2011). Because of this, pain and spirituality were examined within the context of select demographic and clinical factors.

This dissertation is comprised of three manuscripts: 1) Scoping literature review on pain and spirituality; 2) Quantitative secondary data analysis of pain, spirituality and demographic /clinical factors; 3) Qualitative study of pain and spirituality. Each of the three manuscripts included in this dissertation are guided by Pamela Reed's theory of Self Transcendence (ST) (P. Reed, 2015). This theory includes concepts of vulnerability (awareness of mortality), ST (expanding boundaries on multiple personal levels), well-being (a subjective sense of health or wholeness), and personal/contextual factors. Vulnerability is seen as a condition which fosters increased ST, and ST is a tool for enhancing well-being. Personal/contextual factors potentially influence each concept. Applied to this dissertation, advanced breast cancer is a condition which contributes to vulnerability. Spirituality is an expression of ST, pain level is the outcome which indicates one aspect of well-being (where lower pain serves as an indicator of higher well-being), and demographic/clinical factors represent personal/contextual factors which may contribute to both concepts, pain and spirituality. This theoretical approach is described in more detail below.

Overall, spirituality may be an important component of supportive care for women with advanced breast cancer who are experiencing pain. The purpose of this dissertation is to examine

the impact of spirituality on pain in women with advanced breast cancer both with and without a CIH intervention, while considering demographic and clinical factors.

Background & Significance

This section of the dissertation will discuss the significance of pain, spirituality, CIH interventions, demographic factors and clinical factors, all within the context of advanced breast cancer. Current literature will be synthesized, leading to each of the research questions addressed in this dissertation. The parent study that the quantitative secondary analysis (Manuscript 2) is based on will also be described below, along with a brief introduction to the qualitative study (Manuscript 3).

Pain & Spirituality

Pain is defined as *a distressing experience which has interacting sensory, cognitive and emotional components, which may be associated with actual or perceived tissue damage* (Bushnell et al., 2013; International Association for the Study of Pain, 1979; Wang et al., 2016; Williams & Craig, 2016) *and that may be influenced by spirituality*. Sensory components speak to the specific sensation, quality and location of the pain. Cognitive components are comprised of the thoughts and beliefs related to the pain experience. These include appraisals, causal attributions, expectations and level of attention to the experience of pain (Peters, 2015). Emotional components include feelings which are interwoven into, and serve to alter, the painful experience (Peters, 2015). These three components are interconnected and continuously work together to create the overall experience referred to as “pain” (Arnstein, 2018; Bushnell et al., 2013; Peters, 2015). Because pain is constructed of interacting sensory, cognitive and emotional components, altering any of these can result in modulation of the pain experience (Bushnell et al., 2013; Zeidan & Vargo, 2016). This dissertation will examine the influence of spirituality on

pain, as is it hypothesized that spirituality may impact two of the three components of pain (cognitive and emotional), serving to positively alter the overall painful experience.

Spirituality is defined as *a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning* (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016), *which serves as a resource when facing cancer and its associated symptoms* (Flanigan et al., 2019; Krigel et al., 2014; Mosher et al., 2013; Visser et al., 2018). Spirituality is often cited by advanced breast cancer patients as being important for facing their disease (Krigel et al., 2014; Mosher et al., 2013), and it may also be significant when facing the symptoms associated with cancer, such as pain (Flanigan et al., 2019). Spirituality plays an important role throughout the lifespan but can become particularly important when faced with the vulnerability of a life-threatening disease such as advanced cancer (Balducci, 2019; Lazenby, McCorkle, & Sulmasy, 2014; Piderman et al., 2015).

Spirituality may influence pain in various ways; by altering even one of pain's three components (sensory, cognitive, emotional), the experience of pain can be changed. There is no current evidence that the sensory component of pain can be impacted by spirituality, but by changing the cognitive and emotional components, the total severity of the pain experience may be altered (Arnstein, 2018; Bushnell et al., 2013). For the cognitive component, patients have reported that spirituality can offer a broader sense of the self and the universe, making painful experiences seem less significant (Harvey, 2008). Cognitive reframing of painful experiences can significantly alter this component of pain, changing the intensity of a painful experience and the interference it has on one's life (Barkwell, 1991; Ersek & Ferrell, 1994; Petpichetchian & Brenner, 2004). For the emotional component of pain, cancer patients have reported that spiritual beliefs such as connection with a higher power and meaning can offer a sense of emotional

safety and security in the face of difficulty (Gregg, 2011; Yeager et al., 2016). Feelings of safety and security (compared with feelings of fear) can lessen painful experiences (Lumley et al., 2011; Raphael et al., 2010). Positive emotions have been found to decrease the intensity of pain (Bushnell et al., 2013; Peters, 2015), while negative emotional states such as anxiety, depression and anger can intensify pain (Bushnell et al., 2013; Peters, 2015). Pain can also exacerbate psychological distress (Lumley et al., 2011; National Cancer Institute, 2018), although this phenomenon is not the main focus of this dissertation. Overall, spirituality may serve to modify negative thoughts and emotions associated with pain, modulating both the cognitive and emotional components and transforming the painful experience (Keefe, Rumble, Scipio, Giordano, & Perri, 2004; Wiech et al., 2009).

Spirituality may also indirectly impact pain through a behavioral route. Preliminary evidence indicates that those with higher spirituality may use more self-management interventions for symptoms such as pain (Harvey, 2008; Polzer & Miles, 2005; Zarei, Vagharseyyedin, & Gorganie, 2015), thus indirectly improving the severity of this symptom. This phenomenon may be especially prevalent with CIH pain management interventions, since these interventions are based on spiritual underpinnings (Hsiao et al., 2008; McGrady & Moss, 2018; National Cancer Institute, 2019; B. Smith et al., 2008a). This phenomenon will be expanded upon below (see ‘Complementary and Integrative Health Interventions’) and will be examined throughout this dissertation.

Overall, current literature points to multiple avenues whereby spirituality may impact components of pain, therefore altering how this symptom is experienced. Spirituality may directly impact pain through alterations in thoughts and emotions and may also indirectly impact pain by enhancing the uptake of pain management interventions. Yet the relationship between

spirituality and pain has not been examined in women with advanced breast cancer. A gap remains in understanding how spirituality may impact various components of pain, therefore altering overall severity of the painful experience, in women with advanced breast cancer. This dissertation begins addressing this gap, examining the impact of spirituality on pain among women with advanced breast cancer through a scoping literature review (Manuscript 1), a quantitative secondary analysis (Manuscript 2) and a qualitative study (Manuscript 3).

Pain in Advanced Breast Cancer

Pain is a vast and complex concept, carrying various meanings throughout the literature. Research on pain in advanced breast cancer patients is prevalent (Barragan-Campos et al., 2014; Bell et al., 2016; Butler et al., 2009; Carson, Carson, Olsen, Sanders, & Porter, 2017; Di Franco et al., 2014; Perroud et al., 2016; Sheean, Kabir, Rao, Hoskins, & Stolley, 2015). Five unique definitions of pain (Bushnell et al., 2013; International Association for the Study of Pain, 1979; McCaffery, 1968; Saunders, 1964; Williams & Craig, 2016) have been drawn upon to develop the definition used in this work: *a distressing experience which has interacting sensory, cognitive and emotional components, which may be associated with actual or perceived tissue damage* (Bushnell et al., 2013; International Association for the Study of Pain, 1979; Wang et al., 2016; Williams & Craig, 2016) *and that may be influenced by spirituality*. Although pain severity assessments are sometimes considered to only capture the sensory component of this symptom, the three components (sensory, cognitive, emotional) are interconnected (Arnstein, 2018; Bushnell et al., 2013; Peters, 2015). Thus, assessment of pain severity captures all three components, reflecting the overall pain experience.

Pain is classified in various ways such as by duration (acute, chronic), severity (mild, moderate, severe), body part (e.g., bone pain), etiology (nociceptive, somatic, visceral,

neuropathic), or other factors (e.g., breakthrough pain, referred pain, mixed pain, refractory pain, total pain, cancer pain) (Clark, 1999; Deandrea et al., 2014; M. Jensen et al., 2017; Leysen, Adriaenssens, Nijs, Lahousse, & Beckwee, 2018; Paice & Ferrell, 2011). See Table 1.1 for an overview of many common pain classification types.

Table 1. 1 Overview of Common Pain Classifications

Pain Classification	Definition
Acute pain	Experienced short-term. Related to an identifiable cause and resolves when this specific healing process is complete (generally noted as < 3-6 months)
Bone pain	Related to damage/disease in bone
Breakthrough pain	Experienced despite taking regular long-acting pain medication around the clock
Cancer pain	Resulting from cancer treatment or cancer itself
Central sensitization pain	Resulting from an increased responsiveness of nociceptive neurons in the central nervous system
Chronic pain	Experienced long-term (generally noted as > 3-6 months). Often related to complex psychological and physiological processes.
Mild/Moderate/Severe pain	Classifications based on pain intensity/severity, often generated based on pain's interference with daily life
Mixed pain	Resulting from combined nociceptive, neuropathic, and/or central sensitization etiologies
Myofascial pain	A common form of somatic pain arising from muscles; Usually associated with trigger points
Neuropathic pain	Related to damage/disease in nervous system
Nociceptive pain	More general term specifying pain related to damage/disease in the body in response to a specific stimulus
Referred pain	Experienced elsewhere than the believed source of the pain
Refractory pain	Describes a case when conventional therapeutic options are ineffective to manage pain
Somatic pain	Related to damage/disease in skin, muscle or tissue
Total pain	Suffering encompassing a person's physical, psychological, social, spiritual, and practical struggles
Visceral pain	Originating from an organ or organs

Various types of pain are experienced by nearly all individuals across the lifespan, but pain is especially prevalent in patients with advanced cancer due to a variety of physiological

and psychological processes (International Association for the Study of Pain, 2009). In those with advanced cancer, different types of pain can be related to different aspects of the disease (e.g., tumor growth resulting in nerve compression, metastases to bones) and its treatment (e.g., surgery, chemotherapy, hormonal therapy, radiation) (Paice & Ferrell, 2011); while each pain experience is comprised of a unique combination of sensory, cognitive and emotional factors. Although most pain in cancer patients has been attributed to the cancer itself, a proportion may also be attributed to changes in physical activity or to other comorbid conditions such as back pain or osteoarthritis (Posternak et al., 2016). For those with advanced cancer, pain can also carry psychological and existential significance, as it can be perceived as a sign of disease progression and/or impending death (McPherson, Hadjistavropoulos, Lobchuk, & Kilgour, 2013; Otis-Green, Sherman, Perez, & Baird, 2002; Von Moos et al., 2016).

Current allopathic approaches to pain management are used with considerable success, yet women with advanced breast cancer continue to report significant levels of pain (Cleeland et al., 2013; Perroud et al., 2016). The impact of beliefs and emotions about pain on the way this symptom is experienced is well-documented among women with advanced breast cancer (Shen, Redd, Winkel, & Badr, 2014), yet little intervention work addresses the cognitive and emotional aspects of pain in this population. Spirituality may serve as one avenue for supporting women with advanced breast cancer who are experiencing pain, in combination with allopathic treatments. By addressing the emotional and cognitive dimensions of pain, the overall symptom experience can be changed. A gap remains in understanding how to best manage pain in women with advanced breast cancer, which may include approaches which facilitate spirituality.

Spirituality in Advanced Breast Cancer

Although various definitions of spirituality have been offered, most include the common elements of connection and meaning (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016). Three definitions were reviewed and synthesized to develop the definition of spirituality used within the context of this work which is: *a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning* (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016) *which serves as a resource when facing cancer and its associated symptoms* (Flanigan et al., 2019; Krigel et al., 2014; Mosher et al., 2013; Visser et al., 2018). Connection with the self generally encompasses a sense of insight into one's own beliefs and values, and even acceptance or appreciation for one's self. Connection with others and nature can be described as an appreciative relationship for other beings and/or for the natural world. Connection with a higher power refers to a relationship with a force outside or greater than one's self, often beyond the observable world. And finally, a sense of meaning is described as an awareness of one's unique role or purpose in life (P. Reed, 2015; Vachon, Fillion, & Achille, 2009; Weathers et al., 2016). While spirituality may be viewed as a unique phenomenon associated with the sacred and transcendent (Balducci, 2019), spirituality is assessed using self-report in this work; therefore, it must be viewed through the lens of participants' cognitive and emotional experience.

Some definitions of spirituality rely heavily on religious underpinnings, yet this definition is existentially focused, encompassing spirituality in a broader set of women, regardless of religiosity. Women with advanced breast cancer have cited dimensions of spirituality such as connection with a higher power and finding a sense of meaning as key aspects of their disease experiences (Krigel et al., 2014; Mosher et al., 2013; Pacsi, 2015). The suffering inherent in a

diagnosis of advanced disease often brings up spiritual questions and concerns, yet spirituality is also cited as an important aspect for coping with advanced cancer (Gaston-Johansson et al., 2013; Lazenby et al., 2014). Spirituality can improve ability to cope with adversity, enhance inner strength and provide a sense of well-being and peace (Weathers et al., 2016); important tools when facing pain. Overall, positive thoughts and emotions brought about by spirituality may contribute to alterations in cognitive and emotional aspects of the pain experience.

Spiritual distress refers to impairment(s) in one or more dimensions of spirituality (i.e., connection to self, others, nature, higher power, sense of meaning) (Hospice and Palliative Nurses Association, 2007). Forty-four percent of patients with advanced cancer report spiritual distress (Hui et al., 2011), although this has not yet been examined among women with advanced breast cancer. Cancer patients who report inadequately supported religious/spiritual needs have been found to use significantly more healthcare resources in the last week of life compared with those having adequately supported needs (\$4,947 vs. \$2,833, $p=.03$) (Balboni et al., 2011). Thus, efforts to support spirituality are especially important in patients with advanced cancer. A gap remains in understanding how to more fully support spirituality in women with advanced breast cancer and how spirituality may impact pain experiences. This dissertation work begins to address this gap, examining how women with advanced breast cancer describe their spirituality and its impact on their pain.

Complementary and Integrative Health (CIH) Interventions

Use of CIH interventions is extremely common in women with breast cancer. In 2005, 81.9% of breast cancer survivors reported using either a CIH product or therapist(s), marking a significant increase since the prior survey in 1998 (Boon et al., 2007). A 2007 national survey found that CIH intervention use among adults was greater for women, especially those 30–69

years of age (Barnes, Bloom, & Nahin, 2008). Additionally, women undergoing therapy for breast cancer are more likely to engage in CIH interventions compared to women not undergoing cancer therapy (Albahraini, Alwhaibi, Alburakan, & Asiri, 2018). Another recent survey showed that 85% of patients at one comprehensive cancer center reported CIH use (Luo & Asher, 2017). Taken together, these findings indicate that women with advanced breast cancer may use an especially high proportion of CIH interventions, warranting a need for research which considers CIH interventions in this population.

An integrative health perspective combines conventional allopathic treatments (pharmacologic approaches, radiation and surgery) with complementary therapies which have been shown to be safe and effective (National Cancer Institute, 2019). The National Center for Complementary and Integrative Health (NCCIH) has recently defined three categories of CIH interventions (National Center for Complementary and Integrative Health, 2018). These are 1) “Natural products” category, including herbs/botanicals, vitamins and minerals, and probiotics; 2) “Mind-body” category, including a large and diverse group of procedures or techniques administered or taught by a trained practitioner or teacher; and 3) “Other” category, including any CIH interventions which do not fit into the first two groups (National Center for Complementary and Integrative Health, 2018). Reflexology is one CIH intervention which has strong evidence for aiding in pain management (Wyatt et al., 2017). Although various CIH interventions have demonstrated efficacy in reducing pain, reflexology, currently classified under the category of mind-body therapies, is the CIH intervention which will be included in this dissertation work.

CIH interventions are often used for pain management, although the mechanisms underlying the effects of these interventions are not yet well understood. Preliminary evidence

suggests that some mind-body therapies may be able to alter cognitive and emotional states, therefore modulating experiences of pain (Bushnell et al., 2013). Yet varying mechanisms of action have been offered depending on the specific CIH intervention under study. CIH interventions have inherent spiritual underpinnings, often evolving from spiritual practices and traditions, (McGrady & Moss, 2018; National Cancer Institute, 2019). Therefore, use of these therapies may be influenced by spirituality, yet this has not yet been examined in women with advanced breast cancer. This dissertation begins addressing this gap, examining how spirituality may impact engagement with a specific CIH pain management intervention, reflexology, among women with advanced breast cancer.

Reflexology. Reflexology is a CIH intervention in which different amounts of pressure are applied to specific points on the feet or hands (National Cancer Institute, 2019). These points are postulated to correspond to different parts of the body, resulting in energetic and physiological changes (Reflexology Association of America, 2018). By bringing overall balance to the body and eliciting the body's ability to heal, reflexology is intimately connected with both spirituality and the experience of pain (McGrady & Moss, 2018). Although the specific underlying mechanisms are not yet well understood, it has been hypothesized that stimulation of specific reflexes can influence various biological pathways which have a positive impact on symptoms (Wyatt, Sikorskii, Rahbar, Victorson, & You, 2012; Wyatt et al., 2017) and that CIH interventions such as reflexology may elicit the body's innate healing abilities (McGrady & Moss, 2018). Four prevailing hypothesis of reflexology's mechanisms of action have been cited in the literature: 1) activation of receptors which release oxytocin (Cronfalk, Strang, & Ternstedt, 2009); 2) release of energetic congestion and promotion of energy flow and circulation which supports bodily processes (Wilkinson, Lockhart, Gambles, & Storey, 2008); 3)

activation of the relaxation response (McVicar et al., 2007); and 4) alterations of processing in the neuromatrix of the central nervous system (Stephenson & Dalton, 2003; Stephenson, Swanson, Dalton, Keefe, & Engelke, 2007). Furthermore, since reflexology initiates systematic effects, its benefits are not temporally limited and may be cumulative over time (Wyatt, Sikorskii, Holmstrom, & Luo, 2006-2010).

Reflexology is an ancient practice, with many traditional cultures promoting manipulation of the feet to enhance health and well-being, although the therapy has been given various names (Frambes et al., 2017). Reflexology is currently classified as a mind-body therapy (National Center for Complementary and Integrative Health, 2018), yet it was previously categorized as a ‘manipulative and body-based therapy,’ acknowledging its focus on hands-on body movement and manipulation (National Center for Complementary and Alternative Medicine, 2000). Reflexology has been found to significantly decrease pain reports in people with various cancers (Grealish, Lomasney, & Whiteman, 2000; Stephenson et al., 2007) and specifically in women with advanced breast cancer (Wyatt et al., 2017). Despite the energetic and spiritual underpinnings of this intervention, recent analysis revealed that reflexology use did not significantly impact self-reported level of spirituality in women with advanced breast cancer (Flanigan & Cui, 2019). In the quantitative component of this dissertation, spirituality and pain will be examined within the context of a longitudinal randomized controlled trial (RCT) of reflexology (Wyatt et al., 2011-2016). This dissertation work provides the first look at how spirituality may impact pain in the context of a reflexology intervention, and how spirituality may impact engagement with a reflexology intervention among women with advanced breast cancer.

Intervention Engagement. Although many CIH self-management interventions for pain have been developed and tested, an important component of successful use is ensuring the routine engagement with these interventions on a regular basis. Symptom self-management refers to as the day-to-day management of symptoms by individuals over the course of an illness, including the incorporation of symptom-relieving strategies into daily life (Grady & Lucio-Gough, 2014; Yamanaka, 2018). In the context of this work, intervention engagement is defined as the use of the CIH intervention (reflexology) and is operationalized as number of reflexology sessions completed. Preliminary evidence shows that spirituality can enhance engagement with self-management interventions in various diseases (Harvey, 2008; Polzer & Miles, 2005; Zarei et al., 2015). Due to the inherent spiritual underpinnings in CIH interventions (McGrady & Moss, 2018; National Cancer Institute, 2019), those with higher self-reported spirituality may be more open to engaging in such therapies than those with lower self-reported spirituality (Hsiao et al., 2008; B. Smith et al., 2008a). Therefore, it is hypothesized that spirituality may impact how women with advanced breast cancer engage with their CIH-based self-management interventions.

Although the reflexology intervention in the parent study was provided by a friend or family lay caregiver (described below under ‘Parent Study’), spirituality may still serve as a resource which can encourage patients to use the intervention along with their lay caregivers. If spirituality could enhance the use of the reflexology intervention, it could indirectly aid in the management of pain. Additionally, pain itself can be a motivating factor to engage in behaviors which may help reduce this symptom (Auvray, Myin, & Spence, 2010). The impact of spirituality and pain level on engagement with a CIH pain management intervention is not yet known, leaving a gap in the literature. This dissertation will begin to address this gap, exploring

how spirituality and pain may impact engagement with a reflexology intervention among women with advanced breast cancer.

Demographic and Clinical Factors

Preliminary work examining demographic and clinical factors in relation to pain and spirituality within varying populations and has yielded mixed results. Although the studies discussed below provide an overview of which demographic and clinical factors may be important predictors of more severe pain or issues with spirituality, a gap exists in understanding some potentially important demographic and clinical factors in women with advanced breast cancer. Therefore, this dissertation examines the impact of potentially significant demographic and clinical factors on pain and spirituality within a sample of women with advanced breast cancer. Findings will begin to provide information on which women may be at greatest risk for experiencing pain. Findings may also guide future studies to target interventions towards women who might require the most spiritual support, when considering spirituality as a resource for altering pain experiences.

Demographic/Clinical Factors and Pain. Various studies in different populations have indicated relationships between pain and demographic factors such as race/ethnicity (Castel et al., 2007; Kwok & Bhuvanakrishna, 2014; Stuver et al., 2012), marital status (Aneja & Yu, 2016; Posternak et al., 2016) and employment status (Posternak et al., 2016; Rustøen, Fossa, Skarstein, & Moum, 2003). Yet many studies also show mixed results regarding relationships between pain and other demographic factors such as age (Belfer et al., 2013; Gagliese, Gauthier, & Rodin, 2007; Gauthier et al., 2018; Soltow, Given, & Given, 2010; Stuver et al., 2012) and religious preference (Closs & Briggs, 2013). Various clinical factors have also been associated with pain such as disease stage (C. Given, Given, Azzouz, Kozachik, & Stommel, 2001), metastasis status

(Rustøen et al., 2003; Wyatt, Sikorskii, Tamkus, & You, 2013) and menopausal status (Mazor et al., 2018; Meriggiola, Nanni, Bachiocco, Vodo, & Aloisi, 2012). No studies have been identified which specifically examine the relationship between pain and type of treatment received (e.g., chemotherapy, radiation, hormonal therapy), yet this may still be an important factor to examine due to unique treatment side effects.

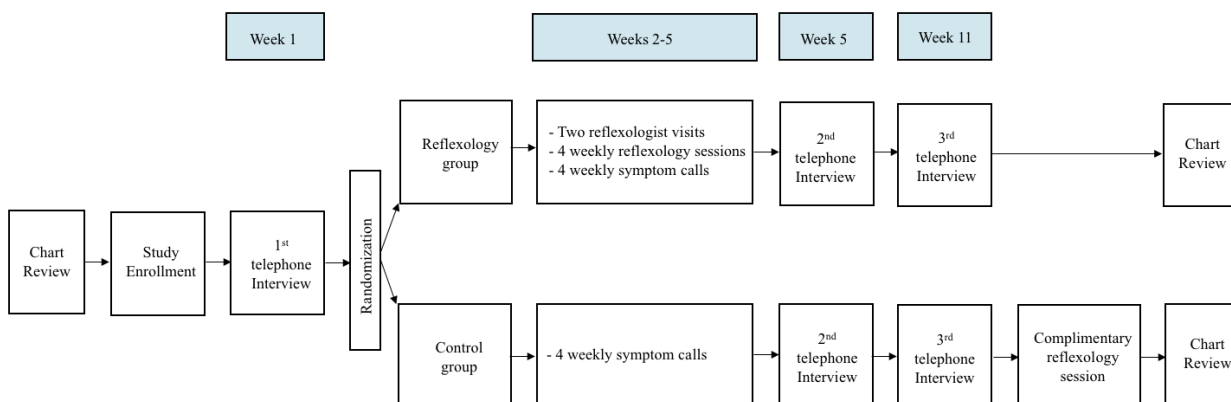
Demographic/Clinical Factors and Spirituality. Demographic and clinical factors have also been examined in relation to spirituality with mixed results. Level of self-reported spirituality has been found to be significantly associated with age (Mystakidou et al., 2008), and spirituality has also been found to be associated with marital status and religious preference (Jugjali, Yodchai, & Thaniwattananon, 2018). One study reported no association between spirituality and employment status (Rodrigues, Nader, de Melo e Silva, dos Santos Tavares, & Fernandes Martins Molina, 2017). No studies have been identified which specifically examine relationships between spirituality and race/ethnicity or level of education, yet these may be important factors to examine. Women from different racial/ethnic backgrounds may experience spirituality differently (Gaston-Johansson et al., 2013; Levine, Yoo, Aviv, Ewing, & Au, 2007), and preliminary research reports associations between level of education and level of engagement with various aspects of religion and spirituality (Schwadel, 2011). Clinical factors have also been examined in relation to spirituality, yielding significant associations with disease stage (Schnoll, Harlow, & Brower, 2000), treatment type (Mystakidou et al., 2008) and menopausal status (Pimenta, Maroco, Ramos, & Leal, 2014). One study reported no significant associations between spirituality and metastasis status (Mystakidou et al., 2008) although this relationship may be important to examine in the context of this work, as metastatic status could be indicative of a poorer prognosis. This dissertation aims to provide clarity on which demographic and

clinical factors are most important to consider in this population when examining pain and spirituality.

Parent Study (Manuscript 2)

The parent study which Manuscript 2 of this work is based on was the National Cancer Institute (NCI)-funded “Home-based symptom management via reflexology for advanced breast cancer patients” (5R01CA157459) (Wyatt et al., 2011-2016). This 5-year study focused on training friend or family lay caregivers to provide reflexology to women with advanced breast cancer, with the hypothesis that this therapy could decrease symptoms and improve quality of life (QOL). Reflexology is commonly delivered by certified reflexologists, yet prior studies of lay reflexology practitioners have also reported successful reduction in symptoms among women with advanced breast cancer (Stephenson et al., 2007; Wyatt et al., 2012); therefore, this is the method that was applied in the parent study. After a baseline interview, women were randomized using minimization procedure at the central study office to one of two groups: 1) Four weeks of home-based, lay caregiver-delivered foot reflexology and symptom assessment calls (reflexology group); or 2) Four weekly symptom assessment calls only (attention control group). Weekly calls were conducted during weeks 2-5 to assess the severity and interference of common cancer symptoms. During these calls, the number of reflexology sessions completed was also assessed using a standardized weekly call form, potentially acting as a reminder to engage in the reflexology sessions. Data were then collected again via telephone at week 5 and at week 11 to assess intervention effects and engagement with the reflexology intervention. See Figure 1.2 for an overview of the parent study design.

Figure 1. 2 Overview of Parent Study Design: “Home-based symptom management via reflexology for advanced breast cancer patients” (5R01CA157459) (Wyatt et al., 2011-2016)



Original Qualitative Study (Manuscript 3)

Manuscript 3 reports on an original qualitative study using a phenomenological approach (Benner, 1994; J. Smith, 1995). Nine women with advanced breast cancer were recruited to complete 45-60-minute semi-structured interviews asking about their spirituality, their pain and the impact of their spirituality on their pain experiences. Interviews were guided by a qualitative interview protocol and were recorded and transcribed verbatim. An open-coding approach following established interpretive phenomenological analysis traditions (Benner, 1994; J. Smith, 1995) was used to identify major and minor themes.

Synthesis

Including spirituality as a part of comprehensive care has the potential to be a valuable tool when women with advanced breast cancer are facing pain. Therefore, this area warrants further investigation. The main concepts in this dissertation (spirituality, pain, and CIH interventions) are connected in that each has a focus on the human experiences of sensation, cognition and emotion. Spirituality may directly decrease pain through cognitive and emotional mechanisms and could also enhance uptake of a CIH pain management intervention, indirectly decreasing pain. These hypotheses have not yet been examined, leaving a gap in the science. Nurses are on the forefront of pain management and are leaders in addressing pain from a CIH perspective. This dissertation work provides novel insights which can contribute to enhancing

and further individualizing nursing care. Advancing nursing science in the areas of spirituality and pain will set the foundation for a program of research leading to the development of nurse-led CIH-based interventions for pain management in advanced cancer patients, and later translation of these interventions into clinical practice.

In summary, this dissertation will examine the impact of spirituality on pain in women with advanced breast cancer while also considering demographic and clinical factors. This work will update the state of the science on pain and spirituality among women with advanced breast cancer. It will also quantitatively examine the impact of spirituality on pain and how spirituality relates to the use of a CIH intervention (reflexology) which has been shown to decrease pain levels (Wyatt et al., 2017). Finally, will explore the impact of spirituality on pain through a qualitative phenomenological lens. Since these areas have not yet been examined among women with advanced breast cancer, this work provides novel insights into the role of spirituality in comprehensively supporting women who are experiencing pain.

Theoretical Framework

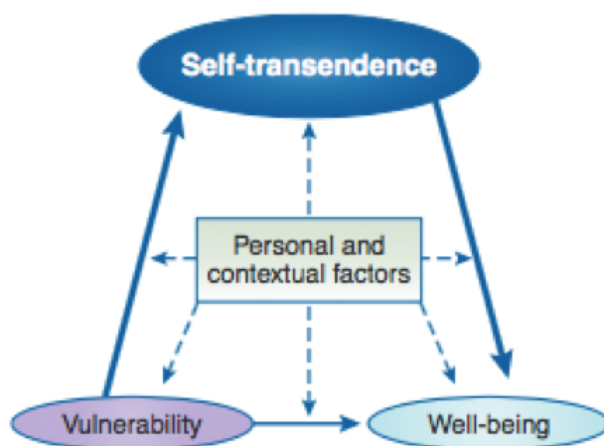
This dissertation work is guided by the Theory of Self-Transcendence (ST) (P. Reed, 2015). The theory of ST and the accompanying model by P. Reed (2015) provide the theoretical foundation when considering spirituality, pain, demographic and clinical factors and a CIH intervention in the context of advanced breast cancer. In the following sections, the original model is presented, followed by the adapted model for this dissertation, and finally the operational model which was applied for this dissertation study.

Theory of Self-Transcendence

The theory of ST and its accompanying conceptual model include of four main concepts: 1) Vulnerability; 2) Self-transcendence (ST); 3) Well-being; and 4) Personal and contextual

factors. These concepts are related in that vulnerability serves as a resource to enhance ST, and ST helps facilitate well-being. Personal and contextual factors may influence every other component of the theory (P. Reed, 2015). This theory is not specific to advanced breast cancer populations and has been applied to a variety of situations (P. Reed, 2015). See Figure 1.3 for the conceptual model accompanying this theory.

Figure 1. 3 Model Accompanying Pamela Reed’s Theory of Self-Transcendence



Reed, P., Pamela Reed's theory of self-transcendence, in *Nursing theories & nursing practice*, M. Smith and M. Parker, Editors. 2015, A. Davis Company: Philadelphia, PA.

Vulnerability. Vulnerability is an increased awareness of personal mortality (P. Reed, 2015). Although vulnerability can be brought about by various circumstances, health-related events that are life threatening or that involve loss are most commonly cited as increasing this awareness (P. Reed, 2015).

Self-Transcendence. ST is defined as the capacity to expand self-boundaries in various ways that enhance well-being (P. Reed, 2015). Boundaries can be expanded in four ways: Intrapersonally (greater awareness of one's beliefs, values and dreams), interpersonally (connecting with others, nature and surrounding environment), transpersonally (relating to dimensions beyond the ordinary, observable world) and/or temporally (integrating one's past and

future in a way that expands and gives meaning to the present) (P. Reed, 2015). Reed's view of transcendence does not imply detachment from self or others, but rather moving from earlier developmental forms of the self (old ways of thinking and being) to enhanced awareness and connectedness (P. Reed, 1996).

Well-being. Well-being is defined broadly as a subjective feeling of health or wholeness as based on the person's own criteria at a given point in time (P. Reed, 2015). Well-being has been operationalized in various ways throughout the literature, including patient self-reports of physical and/or mental health (Coward, 2003; JadidMilani, Ashktorab, AbedSaeedi, & AlaviMajd, 2015; McCarthy, Hall, Crawford, & Connelly, 2018), indicating varied aspects of well-being which may be assessed.

Personal and contextual factors. Reed defines personal and contextual factors as any factors that may influence the relationships among vulnerability, self-transcendence, and well-being (P. Reed, 2015). These factors are essential for understanding relationships between key concepts. Some potential factors may include age, gender, ethnicity, education, illness status, or other factors concerning one's social, cultural and physical environment (P. Reed, 2015).

Theory of ST: Model relationships. Relational statements in ST theory describe vulnerability as a condition which can lead to enhanced ST, and ST as a resource which can help facilitate well-being. Increased awareness of one's mortality (vulnerability) can trigger positive inner strengths which are aligned with ST. ST, in turn, may directly influence well-being, functioning as a resource which can help one transform loss or difficulty into growth and healing (P. Reed, 2015). In the accompanying model, vulnerability is also seen as directly leading to well-being, although this relationship is demonstrated with a narrower arrow and is not thoroughly discussed in Reed's work (P. Reed, 2015). Personal and contextual factors are seen as

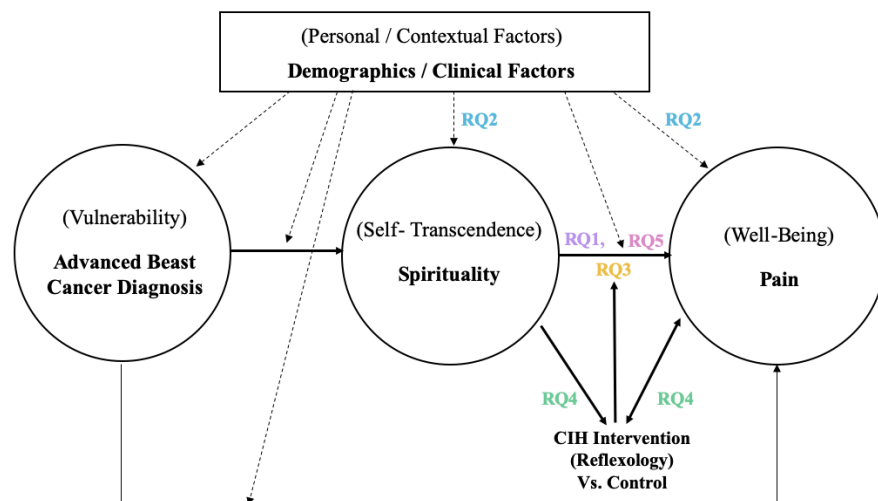
influencing vulnerability, ST, well-being, and the relationships between these three concepts (P. Reed, 2015).

Limitations. Although this theory and accompanying model provide a useful approach for examining key concepts of spirituality and pain in the context of advanced breast cancer, some important limitations must also be noted. First and foremost, the concepts included in ST theory are not the same as the key concepts of this dissertation work. The theory of ST was modified, indicating that spirituality is an expression of ST, pain level is the outcome which indicates one aspect of well-being (where lower pain serves as an indicator of higher well-being), and demographic/clinical factors may be associated with both concepts, pain and spirituality. Although careful consideration was taken to examine the conceptual overlap, important differences between ST and spirituality may have been overlooked, and aspects of well-being and pain may not align as well as intended. This is a main limitation of the application of ST theory in this dissertation, since the central focus of this dissertation is the impact of spirituality on pain (illustrated by modifications to original ST theory and the accompanying model). Next, although ST theory has been applied in various intervention studies (Chen & Walsh, 2009; Coward, 2003; Stinson & Kirk, 2006), the theory does not explicitly describe how a CIH intervention may be integrated, and the accompanying model does not include an intervention component. Finally, the model accompanying ST theory includes a small arrow between vulnerability and well-being which is left out of Reed's text describing the theory; this relationship will not be examined when the theory is applied to the current dissertation work. Despite these limitations, ST theory provides a justifiable framework to guide this dissertation.

Conceptual model: Adapted Theory of Self-Transcendence in advanced breast cancer

Pamela Reed's Theory of ST has been applied in various samples of breast cancer patients (Coward, 2003; Matthews & Cook, 2009; Thomas, Burton, Quinn-Griffin, & Fitzpatrick, 2010), and was adapted to optimally guide this dissertation work. Reed has recommended operationalizing the broad concepts offered in the original theory using more specific, measurable terms to make this theory applicable to various situations (P. Reed, 2015). The adapted model (Figure 1.4) includes four main concepts: 1) Vulnerability expressed as advanced breast cancer; 2) ST expressed as spirituality; 3) Well-being expressed as the pain experience; and 4) Personal and contextual factors expressed as demographic and clinical factors which can impact all components of the model.

Figure 1. 4 Conceptual Model: Theory of Self-Transcendence applied in the context of advanced breast cancer (vulnerability) to assess relationships between demographic/clinical factors (personal/contextual factors), spirituality (ST) and pain (well-being)



Note: RQ = Research question (described below under 'Research Questions')

Although modifications were made, ST theory and the accompanying model were selected to provide a foundation to address the aims of this research for many reasons. First, this framework was selected for its ability to accurately depict the relationship between spirituality

and pain as supported by current literature, demonstrating that spirituality can alter how pain is experienced (Bai et al., 2018). Second, this framework includes the concept of vulnerability which is operationalized as advanced breast cancer, aligning with the finding that women with advanced breast cancer often report increased awareness of their mortality (Krigel et al., 2014; Mosher et al., 2013). And finally, personal/contextual factors are included, which are key elements of the proposed work and are important for understanding the other concepts. All arrows from the original model were carried into this adapted conceptual model, although not all will be operationalized in this work. The full adapted conceptual model is described below.

Vulnerability. For this work, vulnerability is expressed as advanced breast cancer. Multiple studies have found that women with advanced breast cancer report increased awareness of their mortality (Krigel et al., 2014; Mosher et al., 2013), therefore this diagnosis is a condition which facilitates an increase in vulnerability. The population of interest in Manuscript 1 (scoping literature review), Manuscript 2 (quantitative secondary analysis) and Manuscript 3 (qualitative study) are women with advanced breast cancer. Therefore, this population presents an increased level of vulnerability.

Self-Transcendence. In this work, ST is expressed as spirituality. As described above, spirituality is defined as *a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning* (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016). Each of these dimensions closely align with Reed's conceptual definition of ST (enhanced awareness and connectedness in intrapersonal, interpersonal, transpersonal and temporal dimensions).

Well-being. Pain is the aspect of well-being which is focused on in this work (whereby lower pain serves as one indicator of higher well-being). Various indicators of well-being have

been used throughout the literature (including patient self-reports of physical and mental health). Pain aligns well with the definition of well-being in that it is a subjective feeling based on a person's own criteria at a given point in time (P. Reed, 2015).

Personal and contextual factors. Personal/contextual factors are those characteristics which may impact spirituality and/or pain. These are expressed as specific demographic factors (race/ethnicity, marital status, education, religious preference, employment) and clinical factors (disease stage, metastasis, recurrence, treatment type, menopausal status) hypothesized to impact spirituality and/or pain among women with advanced breast cancer.

CIH intervention. 'CIH Intervention vs. Control' was added to the model to reflect the study conditions, since Manuscript 2 of this work employs a reflexology intervention. As described above (see 'Reflexology' section under 'Background & Significance'). Reflexology is a CIH intervention in which different amounts of pressure are applied to specific points on the feet or hands (National Cancer Institute, 2019). Reflexology has strong evidence for reducing pain in women with advanced breast cancer (Wyatt et al., 2017), and is the CIH intervention incorporated in this dissertation.

Adapted conceptual model relationships. The adapted framework asserts that advanced breast cancer is a situation which inherently contributes to increased awareness of mortality. This awareness of mortality can enhance spirituality. Literature supports the idea that awareness of mortality (brought about by breast cancer) can result in expanded boundaries of self-concept, aligned with spirituality (Coward & Kahn, 2004; Thomas et al., 2010). In turn, spirituality can serve as a resource which alters how pain is experienced (with a specific focus on the cognitive and emotional components of pain).

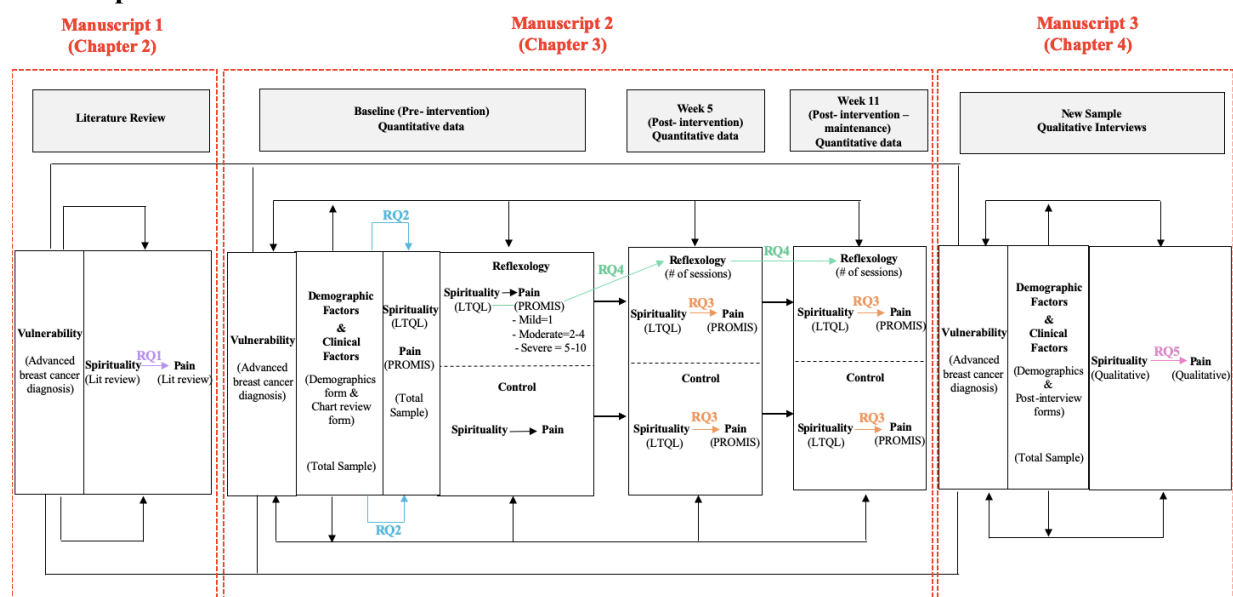
Both the original concepts and the concepts of interest for this work were retained in the modified conceptual model to clearly show the overlap between the original model and adapted version. All arrows from the original model were retained, including the bolded arrows leading from advanced breast cancer diagnosis/vulnerability to spirituality/ST, then to pain/well-being. Dashed arrows leading from personal/contextual and demographic/clinical factors to all concepts and relationships were also included, indicating that these factors may impact all other areas of the model (vulnerability, spirituality, pain, and model relationships). A thin arrow leading from vulnerability to well-being was also retained from the original model, although this relationship will not be examined in the current work. Additionally, ‘CIH intervention vs. control’ was added with appropriate arrows to show how a CIH-based intervention (reflexology) could be included in this context of this work, marking a significant change from the original model. Arrows were added which appropriately reflect the state of the science; spirituality may influence engagement with the intervention, the intervention can impact pain directly, and pain could also influence engagement with the intervention. Finally, the CIH intervention may also modify the impact of spirituality on pain. “RQ” was added in appropriate areas to signify where the research questions for this dissertation fit within the model (see ‘Research Questions’ below). These areas are the main foci of this dissertation work.

Operational model: Adapted Theory of Self-Transcendence in advanced breast cancer

This modified model based on ST theory was then adapted further for application within the specific context of this dissertation work, while retaining the key variables. Since this dissertation work is comprised of three manuscripts completed in phases, 1) Scoping literature review; 2) Quantitative secondary analysis; and 3) Qualitative study, multiple timepoints were added to the model. Boxes were added to show which components of the model correspond with

each manuscript in this three-manuscript dissertation. Additionally, the quantitative phase is based on longitudinal data (baseline, weeks 5 and 11) and includes reflexology and control groups at each time point, marking a significant change from the original model. Although multiple timepoints were added, the relationship between key variables from the original and modified conceptual models remain the same in that vulnerability (advanced breast cancer) is a precursor to spirituality (ST), spirituality (ST) impacts pain (well-being) at each time point, and demographic/clinical factors (personal/contextual factors) may impact all other concepts in the model. See Figure 1.5 for the operational model of this work.

Figure 1.5 Operational Model: Theory of Self-Transcendence applied to assess relationships between demographic/clinical factors (personal/contextual factors), spirituality (ST) and pain (well-being) in the context of women with advanced breast cancer (vulnerability) in a literature review, a reflexology intervention trial and in a separate sample via qualitative interviews within a three-manuscript dissertation



Note: RQ = Research question (described below under ‘Research Questions’)

The instruments used to assess key concepts in this work are described below, see the [Appendix](#) for copies of each. To assess pain and spirituality, well-tested quantitative instruments were used (Manuscript 2), along with a newly developed qualitative interview protocol

(Manuscript 3). Data on demographic and clinical factors, as well as number of reflexology sessions, were collected using various instruments, each described below.

Advanced breast cancer. Women with an advanced breast cancer, defined as stage III (locally advanced) or IV (metastatic) (Susan G. Komen, 2018), are the population of interest for each phase of this dissertation. Since these women have reported increased awareness of mortality (Krigel et al., 2014; Mosher et al., 2013), this diagnosis is aligned with vulnerability. Women in all three manuscripts of this dissertation had an advanced breast cancer diagnosis.

Spirituality (Manuscript 2). The assessment of spirituality for Manuscript 2 was based on self-report data from baseline, week 5 and week-11 of the parent study, using the Long-Term Quality of life (LTQL) Philosophical/Spiritual subscale. The LTQL uses an existential approach to spirituality which can apply to a broad set of women, regardless of religiosity. This instrument was developed based on the four dimensions of QOL offered by Ferrell, Grant, Padilla, Vemuri, and Rhiner (1991) and focus groups by Wyatt, Kurtz, and Liken (1993). It includes four subscales: somatic, philosophical/spiritual, health habits, and social/emotional (Wyatt & Friedman, 1996). The spiritual subscale consists of 11 items reflecting increased insight and appreciation since cancer diagnosis (connection with self/others/higher power/nature, meaning and heightened awareness of mortality) (Wyatt & Friedman, 1996; Wyatt, Kurtz, Friedman, Given, & Given, 1996). Items are measured on a 5-point rating scale, with 0 indicating low spirituality and 4 indicating high. This instrument has been primarily tested with female cancer survivors and the philosophical/spiritual subscale has shown high reliability ($\alpha = .87$) (Wyatt et al., 1996). More recent work has also found high reliability in this subscale among women with advanced breast cancer ($\alpha = .80$) (Kamp et al., 2019). Evidence of validity was established through significant correlation with the Cancer Rehabilitation Evaluation System (CaRES)

measure (Wyatt et al., 1996) and with satisfactory correlation with the Functional Assessment of Cancer Therapy - Breast Cancer (FACT-B) (Kamp et al., 2019).

The LTQL Philosophical/Spiritual Subscale was selected for the operationalization of spirituality because this instrument aligns very closely with the adopted conceptual definition of spirituality. The LTQL includes items focused on connection with self (e.g., “I follow my inner voice when making health decisions”), others (e.g., “Since having had cancer, I have a greater appreciation for the time I spend with friends and family”), nature (e.g., “Since having had cancer I tend to notice things in nature more, such as sunsets, raindrops and spring flowers”), higher power (e.g., “I feel a guiding energy in my life which has my best interest in mind”), and a sense of meaning (e.g., “Since having had cancer, I don’t take life’s little things for granted”). There is close overlap between the conceptual definition of ST, the conceptual definition of spirituality and items included on the LTQL Spiritual/Philosophical subscale.

Pain (Manuscript 2). Extending from the conceptualization of pain provided above, this concept was operationalized using the Patient Reported Outcomes Measurement Information System (PROMIS) – 29 Profile v1.0 pain intensity item for Manuscript 2. Assessment of pain intensity was based on data from baseline, week 5 and week-11 of the parent study, where pain was one of the symptoms measured as part of the overall PROMIS-29 Profile v1.0. Although pain intensity is often believed to only capture the sensory component of pain, the sensory, cognitive and emotional components are interconnected and each contribute to the overall pain experience (Arnstein, 2018; Bushnell et al., 2013; Peters, 2015). Thus, all three dimensions of pain are captured in this assessment, but it is not possible to tell the relative contribution of each. Recent work also supports this notion, finding that pain intensity ratings are often a compilation of multiple factors, including thoughts and emotions (M. Jensen et al., 2017). Developers of the

PROMIS instruments have defined pain in a multidimensional way, and although their definition does not explicitly include sensory, cognitive and emotional components, it does stress that “pain is what the patient says it is” (Riley et al., 2010), reflecting the complex and subjective nature of this symptom. Overall, the pain definition offered by PROMIS developers complements the definition used in this dissertation.

PROMIS-29 Profile v1.0 is a collection of short forms which assess various health related quality of life domains including pain, fatigue, depression and anxiety (HealthMeasures, 2018). The PROMIS instruments were developed with extensive research based on item response theory (Cella et al., 2010; Cella et al., 2007; Reeve et al., 2007). In the PROMIS-29 Profile v1.0, pain is assessed with 1-item asking, “In the past 7 days, how would you rate your pain on average?” This item is rated on a rating scale from 0 “no pain” to 10 “worst imaginable pain.” Extensive testing of reliability and validity has been conducted on the entire PROMIS-29 Profile v1.0, yielding strong evidence of validity and $\alpha = 0.92\text{--}0.96$ in a large study with cancer patients (R. Jensen et al., 2015). The PROMIS pain assessment was recently found to perform as well as a legacy instrument, the M.D. Anderson Symptom Inventory (MDASI), when examining responsiveness to a CIH pain management intervention (Sikorskii et al., 2018). Since all women in this study have advanced breast cancer, a chronic disease, the average pain they report over the previous seven days is assumed to be more chronic in nature. Although an assessment over a longer duration would be optimal, this 7-day assessment is more appropriate than the commonly used 24-hour assessment when attempting to capture the chronicity of pain in cancer patients.

Clinically-meaningful cut points have been developed for different variations of 0-10 pain assessments, making these assessments more interpretable and relevant (B. Given et al., 2008). Various methods for developing symptom cut points have yielded different results (M.

Jensen, Smith, Ehde, & Robinson, 2001; Li, Harris, Hadi, & Chow, 2007; Paul, Zelman, Smith, & Miaskowski, 2005; Serlin, Mendoza, Nakamura, Edwards, & C.S., 1995). For the purposes of this work, the following cut points were adopted: mild=1; moderate=2-4; severe=5-10 (B. Given et al., 2008). These cut points are optimal because they were developed based on assessments of cancer patients' average pain over the past week (B. Given et al., 2008; Jeon, Given, Sikorskii, & Given, 2009), perfectly aligning with the PROMIS pain assessment question used in this work.

Pain and Spirituality (Manuscript 3). An interview protocol was created in collaboration with content experts and experienced qualitative researchers to guide the qualitative interviews for Manuscript 3. This protocol was designed to serve as an extension of the quantitative instruments used for Manuscript 2, providing a more comprehensive look at pain, spirituality, and the relationship between the two concepts, than could be offered by the quantitative instruments. Content was amended throughout the research process to ensure it was optimally relevant to achieve the study's purpose. The qualitative research protocol included an introduction to the research, a broad question about women's experiences with advanced breast cancer, additional open-ended questions to explore women's perceptions of the impact of spirituality on pain, and more focused questions to elicit elaboration on these phenomena. Questions were included which provided insight into spirituality's influence on both the cognitive and emotional components of pain.

Demographic and clinical factors. For Manuscript 2, demographic and clinical factors were assessed in at baseline using a standardized demographics form and chart review form developed for the parent study (Wyatt et al., 2011-2016). The demographics form included information on level of education (high school graduate/some high school, some college, 4-year college graduate or >4 year college degree), racial/ethnic background (white, black/African

American or other and Hispanic or Latino or not Hispanic or Latino), religious preference (Christian, Jewish, Buddhist, Hindu, Muslim, other or none), marital status (never married, married/living with partner, divorced/separated or widowed), menopausal status (premenopausal, perimenopausal, postmenopausal or unknown) and employment status (full time, part time, retired or other). Each item was assessed via patient self-report using a multiple-choice format. The chart review form included information on participant age (numeric), disease stage (III or IV), metastasis (yes or no), recurrence (yes or no) and treatment type (chemotherapy, hormonal therapy or both). Data were abstracted from participants' medical records by a trained study team member onto this standardized form.

For Manuscript 3, a standardized demographics form was created based on the forms from the quantitative phase. All demographic and clinical factors were captured on this form, using the same operationalization. Participants were asked to provide this information during the meeting in which they completed their qualitative interview. These data were used to characterize the samples and to compare samples of women in the quantitative and qualitative phases of the dissertation.

Reflexology (Manuscript 2). As discussed above, reflexology is the CIH intervention which was included in the parent study in Manuscript 2. The Ingham method of reflexology was used (Byers, 2001) to create a cancer-specific reflexology protocol. Following this protocol, women received 15 minutes of reflexology per foot, totaling a 30-minute foot reflexology session. Participants were encouraged to complete at least one session per week with their lay caregiver. CIH intervention engagement was operationalized via number of reflexology sessions completed, and assessed using a standardized weekly call form and debriefing form developed for the parent study (Wyatt et al., 2011-2016). Number of reflexology sessions was assessed

during weekly calls in weeks 2-5 by asking patients to self-report the number of 30-minute sessions completed. Number of reflexology sessions was also assessed and during debriefing in the week 11 interview (assessing sessions in weeks 6-11) by asking patients to self-report how many sessions they had completed since their prior interview in week 5. Number of sessions was pooled for weeks 2-5 and for weeks 6-11 and analyzed to reflect the varied studied conditions (weeks 2-5 active intervention vs. 6-11 maintenance period).

Operational model relationships. The modified operational model was designed to depict each manuscript of the dissertation: 1) Literature review; 2) Quantitative secondary analysis; 3) Qualitative study. Colored arrows are included to indicate where the research questions (RQs; included below under ‘Research Questions’) align with this modified operational model. Each relationship in the modified operational model will be described below, with a specific focus on the RQs.

This operational model first includes vulnerability (represented by advanced breast cancer diagnosis) preceding every other component of the model. On the far left, a box is included to depict a literature review examining the state of the science on the impact of spirituality on pain in women with advanced breast cancer. This is depicted as a separate box since it is focused on the current literature rather than a set sample of women. It is connected to other boxes through ‘Vulnerability (Advanced breast cancer diagnosis),’ as the focus on this population is carried through each of the three manuscripts.

To the right of the literature review depiction are a series of boxes depicting the quantitative component of the study, which has multiple time points. Demographic factors (race/ethnicity, marital status, education, religious preference, employment) and clinical factors (disease stage, metastasis, recurrence, treatment type, menopausal status) may impact spirituality

and pain, shown at each time point. The arrows in the original ST model leading from demographic and clinical factors to all model relationships were removed, since these will not be examined. As in the original and modified conceptual models, demographic and clinical factors are related to each other concept, and spirituality is shown as impacting pain at each time point (reflecting the current state of the science on this relationship).

On the far right, a box is included depicting the qualitative component of this work (Manuscript 3). Connection with the literature review (Manuscript 1) and quantitative phase (Manuscript 2) is depicted through ‘vulnerability’ indicates that each phase focuses on women with the same vulnerability condition (advanced breast cancer diagnosis). Manuscript 3 qualitatively examined the impact of spirituality on pain, while considering demographic and clinical factors. In the model, vulnerability is seen as preceding demographic and clinical factors, which then leads to the impact of spirituality on pain.

Colored text indicating “RQ”s was added along with colored lines to depict where each research question is positioned within this modified operational model. The RQ1 arrow indicates a research question examining the state of the science relative to the impact of spirituality on pain among women with advanced breast cancer. This question is addressed with a review of current literature detailing the impact of spirituality on pain in a broad population of women with advanced breast cancer (Manuscript 1). The RQ2 arrow indicates a research question examining the impact of demographic/clinical factors on spirituality and pain in women who have not yet received a reflexology intervention. This will be addressed through a quantitative analysis of demographic and clinical factors in relation to pain and spirituality at baseline (Manuscript 2). Next, the RQ3 arrow indicates the impact of spirituality on pain at weeks 5 and 11, in both women receiving reflexology and those in the control group. This question will be addressed by

quantitatively examining the impact of spirituality on pain in both groups over time, while considering demographic and clinical factors (Manuscript 2). The RQ4 arrow connects spirituality to pain, then to number of reflexology sessions. This question explores how spirituality impacts engagement with the reflexology intervention (as indicated by number of sessions) in women with varying levels of pain, while considering demographic and clinical factors (Manuscript 2). And finally, RQ5 arrow indicates a research question examining the impact of spirituality on pain in a new sample of women with advanced breast cancer using qualitative methods. This question will be addressed with an original qualitative study examining pain, spirituality, and the impact of spirituality on pain in a new sample of women not receiving reflexology (Manuscript 3).

Purpose

The purpose of this dissertation is to advance nursing science related to spirituality and pain in women with advanced breast cancer. This will first be done through a literature review which updates the current state of the science on pain, spirituality and the impact of spirituality on pain (RQ1) and identifies potential gaps. Next, the relationship between demographic factors (race/ethnicity, marital status, education, religious preference, employment) and clinical factors (disease stage, metastasis, recurrence, treatment type, menopausal status) and both pain and spirituality will be examined in a sample of women with advanced breast cancer (RQ2). Additionally, the impact of spirituality on pain will be explored within the context of a reflexology intervention (RQ3). The dissertation then examines the relationship between spirituality and reflexology intervention engagement among women with varying levels of pain (RQ4). Finally, the dissertation will provide a broad look at how women with advanced breast

cancer describe their pain, spirituality, and the impact their spirituality may have on the pain experiences (RQ5).

Research Questions

The Theory of ST applied to women with advanced breast cancer has been used to guide the following research questions, which are to be addressed in this dissertation.

Among women with advanced breast cancer...

1. What is the current state of the science on the impact of spirituality on pain?
2. Which demographic factors (age, race/ethnicity, marital status, education, religious preference, employment) or clinical factors (disease stage, metastasis, recurrence, treatment type, menopausal status) are associated with spirituality and/or pain at baseline?
3. What is the impact of spirituality on pain over time (baseline through week 11), in the reflexology group versus the control group, after controlling for demographic and clinical factors?
4. Within the reflexology group, does spirituality impact engagement with the reflexology intervention over time (at baseline, weeks 5 & 11) among women who report various levels of pain, when controlling for demographic and clinical factors?
5. How do these women describe how (or if) their spirituality impacts their pain experiences?

Dissertation Format

This dissertation is formatted with a multiple manuscript approach. Chapters 2, 3 and 4 each serve as individual manuscripts which address the research questions identified above. The chapters include:

Chapter 2 (Manuscript 1)

Chapter 2 is a review of the current literature focusing on pain and/or spirituality in women with advanced breast cancer. This paper establishes the state of the science regarding pain and spirituality in this population by examining how each concept is conceptualized, assessed and addressed, as well as how the concepts may be related. A modified version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (Moher, Liberati, & Altman, 2009) was employed, along with the PRISMA-extension for Scoping Reviews (PRISMA-ScR) checklist to enhance methodological rigor and reporting (Tricco et al., 2018). Searches were conducted in PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsychInfo, Cochrane Library, Open Grey, OAIster, and a large university library database including work published from 2006-2018. Keywords included: breast neoplasms, breast cancer, advanced, stage III, stage IV, stage three, stage four, pain, pain management, spirituality, spiritual quality of life, spiritual well-being and existential. This paper is published in Pain Management Nursing.

Chapter 3 (Manuscript 2)

Chapter 3 examines the demographic and clinical factors associated with pain and with spirituality in women with advanced breast cancer, the impact of spirituality on pain, and how spirituality and pain level impact engagement with a CIH-based pain management intervention (reflexology). This manuscript is a quantitative secondary data analysis from a nationally-funded RCT of foot reflexology for women with advanced breast cancer (Wyatt et al., 2011-2016). This manuscript has been submitted to Oncology Nursing Forum for publication consideration.

Chapter 4 (Manuscript 3)

Chapter 4 describes an original qualitative study examining pain and spirituality in women with advanced breast cancer, as well as how they see these concepts as related. Participants were recruited via a mailing through the tumor registry of a community cancer center. Interviews were conducted with N=9 women. All interviews were recorded and transcribed verbatim, and data were analyzed using an open-coding process following an interpretive phenomenological analysis process (J. Smith, P. Flowers, & M. Larkin, 2009). This paper is formatted for submission to Cancer Nursing.

Chapter 5

Chapter 5 of this dissertation provides a synthesis of findings, recommendations for future research and conclusions. Implications for nursing research, education, practice and health policy are discussed.

Contribution to Science

Overall, this dissertation provides a broader perspective on pain and spirituality in advanced disease. This work contributes to nursing science in five major areas related to women with advanced breast cancer: 1) Updating the state of the science related to pain, spirituality, and spirituality's impact on pain in women with advanced breast cancer, 2) Examining how demographic and/or clinical factors may impact the experience of pain and spirituality when engaged in a CIH intervention, 3) Understanding the impact of spirituality on the pain experience when engaged in a CIH intervention, 4) Exploring how spirituality may impact engagement with a CIH symptom management intervention, and 5) Understanding how women with advanced breast cancer describe their pain, their spirituality, and the connection between the two.

First, previous literature related to women with advanced breast cancer was reviewed to update the state of the science on pain, spirituality, and the impact of spirituality on pain. This work identified a gap in understanding spirituality and its potential influence on pain in this population, guiding the subsequent work in this dissertation.

Second, although some preliminary evidence exists linking specific demographic and clinical factors to both pain and spirituality in various populations, many of these links are inconclusive or not yet examined in the context of advanced breast cancer. This lack of knowledge leaves a gap in understanding which sub-populations of women might be most at risk of experiencing pain. Findings will lay the groundwork to begin understanding which sub-populations of women are most at risk for issues with pain and spirituality, which factors are most important to control for in future studies, and how to more appropriately target interventions to sub-groups of women in this population.

Third, limited previous literature reports significant relationships between spirituality and pain in various samples of cancer patients, but this has not yet been studied in women with advanced breast cancer. Further understanding the impact of spirituality on pain in this population represents the first step in a program of research leading to the development of interventions to facilitate spirituality as part of comprehensive pain management. Additionally, the context of a CIH intervention (reflexology) provides a novel look at how the impact of spirituality on pain may vary based on the use of the intervention.

Next, there is evidence that spirituality can enhance self-management of various symptoms and diseases, therefore, this work builds on these findings to see how self-reported spirituality may relate to the number of reflexology sessions completed in women with varying pain levels. If spirituality is able to enhance engagement with reflexology, it could eventually be

harnessed as a tool to help with self-management of pain via other CIH-based symptom management interventions.

Finally, examining spirituality, pain, and the impact of spirituality on pain through a qualitative, phenomenological lens provides a rich look at these phenomena and builds a context for previous quantitative findings. Although prior studies suggest that spirituality may serve as a resource for facing the symptoms associated with advanced breast cancer, no qualitative work has specifically examined pain and spirituality together in this population (Flanigan et al., 2019). The quantitative instruments used for Manuscript 2 may not fully capture the multidimensional experiences of pain and spirituality for women with advanced breast cancer. This qualitative work provides insights into the mechanisms underlying spirituality's potential impact on pain. This qualitative work will be used to identify next steps in a program of research examining how to best approach pain from a comprehensive perspective.

Overall, this work adds to the growing literature on the utilization of CIH interventions and provides insights into the optimal management of pain for women with advanced breast cancer. Novel findings are offered which indicate the importance of considering pain and spirituality as complex, multidimensional phenomena which are unique to each patient. This dissertation provides the first steps to establish a program of research aimed at improving pain management through spirituality via a ST lens for women with advanced breast cancer.

CHAPTER 2: SPIRITUAL PERSPECTIVES ON PAIN IN ADVANCED BREAST CANCER: A SCOPING REVIEW

Abstract

Objectives: To characterize how pain and spirituality have been conceptualized, assessed, and addressed, and how these concepts may be related among women with advanced breast cancer.

Design: A scoping review was conducted including publications of various methodologies.

Data Sources: Searches were conducted in PubMed, CINAHL, PsychInfo, Cochrane Library, Open Grey, OAIster, and a large university library database (published 2006–2018).

Review/Analysis Methods: Research questions and criteria were formulated at the outset, followed by identification of publications, charting data, and collating results.

Results: Forty-two publications met criteria. Most ($n = 33$) focused exclusively on pain, five pain and spirituality, and four exclusively spirituality. Conceptual definitions were not explicitly provided but were implied. Most assessments used 0–10 Numeric Rating Scales (pain) and qualitative methods (spirituality). Pain management primarily focused on radiotherapy and pharmaceuticals and two publications identified spiritual interventions. No publications directly examined the impact of spirituality on pain. Findings of qualitative studies including both concepts suggest the potential value of spirituality as a mechanism to cope with pain.

Conclusions: This review identified significant unmanaged pain in women with advanced breast cancer. Women identified dimensions of spirituality as important for coping with their disease. A gap in understanding spirituality and its potential influence on pain in this population was identified.

Nursing Practice Implications: Nurses can utilize multidimensional assessments to better capture the complex nature of pain. Additionally, nurses can support women in activities such as

exploring existential concerns and making meaning of their advanced breast cancer experiences, including their pain.

Introduction

Of the one in eight women diagnosed with breast cancer in the United States (American Cancer Society, 2019), 37% are at an advanced stage, defined as stage III (locally advanced) or IV (metastatic) (Susan G. Komen, 2018). The overall five-year relative survival rate for advanced breast cancer is estimated at 15-22% in distant or metastatic disease (American Cancer Society, 2019), making symptom management and the alleviation of existential concerns top priorities. Women with advanced breast cancer often experience pain from both their disease and treatment, with studies reporting up to 83% of women experience this symptom (Puetzler et al., 2014). Pain is a distressing multidimensional experience including physical sensations, emotional, and cognitive components (Wang et al., 2016; Williams & Craig, 2016), yet a unidimensional assessment approach is often used. Pain can carry important psychological and existential significance, as it may be perceived as a sign of disease progression and/or impending death in people with advanced cancer (McPherson et al., 2013; Von Moos et al., 2016). Interpretations of pain are influenced by the context in which it occurs, including culture, beliefs, expectations, and past experiences (Brant, Dudley, Beck, & Miaskowski, 2016), indicating that pain is much more complex than merely physical sensations. Pain can lead to various negative consequences, impact multiple dimensions of quality of life (QOL) (Paice & Ferrell, 2011), and even result in cancer treatment dose delays and interruptions (Wyatt, Sikorskii, Tesnjak, Victorson, & Srkalovic, 2015).

Spirituality has not been adequately investigated in the context of pain. Spirituality is a dynamic process in which humans experience connection with the self, others, nature, and/or a

higher power and a sense of meaning (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016) which may serve as a resource when facing cancer and its associated symptoms. Patients have often reported heightened awareness of existential concerns, such as angst about life's meaning and purpose, as the result of cancer, which, if unaddressed, can compromise spiritual well-being and increase distress (Reynolds, 2006). Spiritual distress is defined as impairment(s) in one or more dimensions of spirituality (Hospice and Palliative Nurses Association, 2007). One study reported spiritual distress among 44% of the sample of patients with a variety of advanced cancers (Caldeira, Timmins, de Carvalho, & Vieira, 2016), indicating a need for additional work in this area. Estimates of the impact of spiritual distress on pain among women with advanced breast cancer have not yet been studied and will be important to examine due to the unique treatments (i.e., hormonal therapies) and symptom experiences (i.e., hormone-related, likelihood of experiencing bone metastasis and bone pain) in this population (National Cancer Institute, 2017; Rosenfield & Stahl, 2006).

The potential role of spirituality in pain experiences is not well understood, but hypotheses have been offered relative to how these concepts may be related. In some cultural paradigms, pain is seen as a test of one's faith or strength, and bearing pain is favorably perceived (Ahlam Al-Natour, Sharaf Al Momani, & Abeer Qandil, 2017), which could impact the way women with breast cancer relate to their pain. Additionally, a strong sense of spirituality carries the capacity to provide meaning in life, which may increase feelings of inner strength, and buffer the negative influence of pain experiences (Ahlam Al-Natour et al., 2017). It is known that poor psychological adjustment to pain can exacerbate the pain experience and decrease functional ability (Alves, Vieira, Mathias, & Gozzani, 2013); enhancing spirituality could potentially serve as an avenue to improve psychological adjustment to pain, therefore, positively

altering how this symptom is experienced (Krigel et al., 2014). Furthermore, modifying expectations, interpretations, and judgments about pain have the capacity to impact how this symptom is experienced (Wiech et al., 2009), and spirituality has the potential to induce such changes, ultimately by targeting the emotional and cognitive dimensions of pain.

In recent years, there has been growing evidence for the effects of spirituality on both mental and physical well-being (Akbari et al., 2016); however, much of the literature does not focus on advanced breast cancer. In a recent study with African American patients reporting different stages and types of cancer pain (N = 102), higher spirituality was significantly associated with lower pain severity and lower pain interference, with the hypothesis that spirituality can serve as a protective factor against pain (Bai et al., 2018). Because African American women often experience and relate to spirituality differently than Caucasian women (Gaston-Johansson et al., 2013), additional investigation is needed to see how spirituality is expressed and how it may relate to symptoms such as pain in other populations.

Multiple studies looking at samples of patients with various types and stages of cancers have found significant relationships between pain and spirituality as well (Delgado-Guay et al., 2016; Hui et al., 2011; Wang & Lin, 2016), gathering support for the value of addressing spiritual needs as part of comprehensive symptom management. Because individuals with different types of cancer often undergo unique treatments and face unique symptom experiences, assessment and management of symptoms must be as individually tailored as possible (Deshields, Potter, Olsen, & Liu, 2014). This review is built on the promising findings of the studies mentioned and aims to begin investigating the impact of spirituality on pain in a specific population, women with advanced breast cancer. Understanding pain and spirituality in women with advanced breast cancer may provide insights on how to optimally address the complex

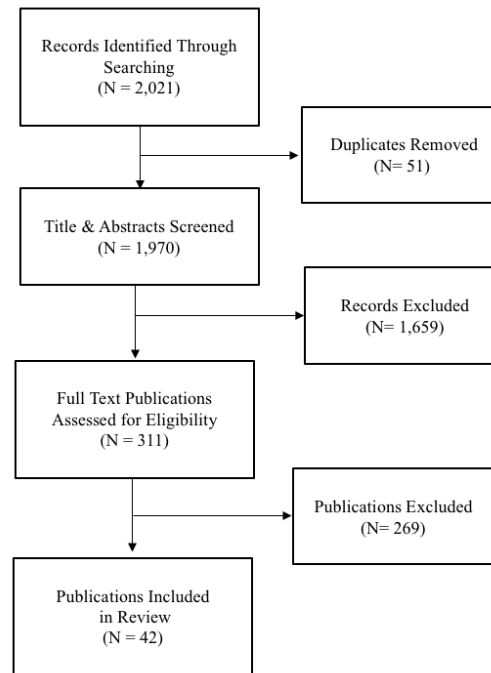
symptom of pain and provide comprehensive care for these women. Therefore, the purpose of this scoping review was to examine how pain and spirituality have been conceptualized, assessed, and addressed in women with advanced breast cancer, and evaluate what is known about the impact of spirituality on pain in this population.

Review Methods

A scoping review is an iterative process, requiring multiple searches and creative variations to examine, summarize, synthesize, and identify gaps in the existing literature (Arksey & O'Malley, 2005). This methodology is especially useful when areas under investigation are vast and complex and/or when research questions are broad because scoping reviews allow for inclusion of publications of various methodologies, including theoretical and narrative reviews, qualitative and quantitative research (Peterson, Pearce, Ferguson, & Langford, 2017; Tricco et al., 2018). Such an approach is well suited to evaluating the state of the science relative to pain and spirituality, which are both broad and complex concepts on their own, and even more so when examining them together.

This scoping review was guided by the methodological framework proposed by Arksey and O'Malley (2005) and includes five main stages: 1. Identification of the research question and eligibility criteria; 2. Identification of relevant publications; 3. Selection of publications; 4. Charting the data; and 5. Collating, summarizing and reporting the results. A modified version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was used to depict this work (Moher et al., 2009) (see Figure 2.1). The PRISMA-extension for Scoping Reviews (PRISMA-ScR) checklist was also used to enhance methodological rigor and reporting of this review (Tricco et al., 2018).

Figure 2. 1 Modified PRISMA Diagram to Depict Flow of Search Process



Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement*. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Stage 1. Define Research Questions & Criteria

Research questions. Among women with advanced breast cancer...

1. How is pain conceptualized, assessed, and addressed?
2. How is spirituality conceptualized, assessed, and addressed?
3. Does spirituality impact the pain experience?

Eligibility criteria. Publication inclusion criteria were: (a) adults ≥ 18 years-old, (b) women with an advanced breast cancer diagnosis (Stage III or IV), (c) results reported on patient pain and/or spirituality, (d) published in English, (e) published 2006–2018 (see Table 2.1).

Table 2. 1 Scoping Review Inclusion Criteria

Inclusion Criteria
Age: ≥ 18 years old
Participants with advanced breast cancer diagnosis (Stage III or IV)
Finding related to patient pain and/or spirituality
Published in English
Published 2006–2018

Publications with mixed samples (i.e., early stage and advanced breast cancer or different types of advanced cancers) were included only if advanced breast cancer findings were reported independently in order to specifically capture the experiences of women with advanced breast cancer. Publications were restricted to the last 11.6 years (2006–2018) since a comprehensive review on bone pain in advanced breast cancer was published in 2006 (Rosenfield & Stahl, 2006). This review serves to update past reviews and approach pain more comprehensively in order to capture a broad view of the current state of the science.

Stage 2. Identifying Relevant Publications

A review was conducted in PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsychInfo, Cochrane Library, Open Grey, OAIster, and a large university library database to curate published work and other relevant (grey) literature. Criteria were set at the outset of the study and consistent terms were applied to each search engine, along with subject headings from the US National Library of Medicine's Medical Subject Headings (MeSH), and database-specific key words (see Table 2.2). An iterative process was used, adding new terms and combinations as they emerged from the literature. A manual search through key journals followed the database search. Reference lists of relevant reviews and original studies were also screened for additional citations.

Table 2. 2 Scoping Review Example Search Strategy

Area	Search Terms (MeSH terms when available)
Population:	<i>Breast Neoplasms, breast cancer, advanced, stage III, stage IV, stage three, stage four, metasta*</i>
Pain:	<i>Pain, pain management, pain control, pain reduction</i>
Spirituality:	<i>Spirituality, spiritual quality of life, spiritual QOL, spiritual well-being, spiritual well being, spiritual wellbeing, spirit*, existential</i>

Stage 3. Selecting Publications

Initial searching yielded 2,021 results. When imported into Endnote reference management software 51 duplicates were removed. After screening each record for relevance, 311 potential records were identified. The full text articles (n = 311) were accessed for further evaluation against inclusion criteria, with 42 publications included in the final review (2.08% of identified citations). Screening and identifying publications were completed by the first author. Primary reasons for exclusion were early stage breast cancer population, missing stage information lack of pain or spirituality outcome, and/or a focus on women who had completed treatment and no longer had signs of active disease.

Stage 4. Charting Data

A descriptive-analytical method was used for data extraction, where standard information was obtained from each publication (Arksey & O'Malley, 2005). Information including (a) author, (b) type of publication, (c) sample, (d) purpose, (e) study design/methods, (f) pain and/or spirituality definition, (g) pain and/or spirituality assessment, (h) pain and/or spirituality intervention, and (i) key findings were included in an initial table, which was then reduced to include only key elements (see Table 2.3).

Table 2. 3 Characteristics of Included Publications within Scoping Review (N=42)

Author(s)	Sample	Design	Pain and/or Spirituality Assessment	Pain and/or Spirituality Intervention	Key Findings
Abernethy et al. (2010)	N = 50, mean age 51 (31–79 years)	Prospective, single-arm, phase 2 pilot study	Pain: MD Anderson Symptom Inventory (MDASI) Spirituality: FACIT—Spiritual Well- Being Scale (FACIT-Sp)	Pain & Spirituality: ‘Pathfinder’ intervention	Significant changes not found in spirituality- FACIT-S: meaning/peace subscale slightly improved (non-significant), faith subscale did not improve. Pain assessed but outcomes not reported.
Ahmad et al. (2011)	N = 3, Malay Muslim Women, mean age 41.7 (39–47 years)	Qualitative	Spirituality: in-depth interviews	Spirituality: N/A	Two main themes were revealed: “illness as an awakening” and “hope and freedom comes from surrendering to God.” Highlighted importance of understanding cancer experience within the appropriate cultural context (especially so for spirituality).
Arathuzik (2009)	N = 19, 20–80 years	Qualitative, grounded theory	Pain: 1–3 hour semi-structured interviews	Pain: N/A	Living with suffering: a fluid non-linear process, patients endure suffering and use coping strategies to deal with pain based on disease state. Three main coping strategies: struggling, surrendering and adjusting to pain. Use depends upon age, pain duration, pain intensity, and past experience with pain.
Atahan et al. (2010)	N = 100, median age 50 (27–84 years)	RCT [†]	Pain: VAS [‡]	Pain: Radiotherapy and zoledronic acid	No significant differences in pain between radiotherapy doses.

Table 2.3 (cont'd)

Badr and Milbury (2011)	N = 191, mean age 52.2 (23–78 years)	Longitudinal, observational, prospective	Pain: Multidimensional Pain Inventory	Pain: N/A	Patients scored significantly lower on pain severity than other published values for this population. Partner responses to pain associated with patient pain behaviors.
Barragan-Campos et al. (2014)	N = 31, mean age 55.1 (38.0–75.8 years)	Longitudinal, retrospective	Pain: VAS [‡]	Pain: Percutaneous Vertebroplasty	90.3% pain relief was achieved. Reduction pre-intervention to post-intervention ($p < 0.001$).
Bell et al. (2016)	N = 165, median age 63 years	Open-label, randomized, phase II study	Pain: BPI [§]	Pain: Oral letrozole vs. letrozole plus oral palbociclib	No significant differences in pain severity or interference between groups.
Butler et al. (2009)	N = 125, mean age 53	RCT [†]	Pain: Pain Rating Scale	Pain: Supportive-expressive group therapy with hypnosis plus education vs. education-only	At baseline, 48% reported current pain (mean = 2.2). “Pain in this moment” and “suffering in this moment” were highly correlated. Intervention group reported significantly less increase in pain intensity and suffering over time. No significant effect on frequency of pain episodes or amount of constant pain.
Carson et al. (2017)	N = 0 (study protocol, not yet completed)	Study protocol for a single-blinded, randomized, attention-controlled, trial	Pain: BPI [§] -Short Form	Pain: Yoga, 8 weekly 120-minute sessions and home practice.	Challenges include recruitment (adequate inclusion of minorities, limiting and controlling for selection bias), tailoring yoga intervention for special needs, maximizing adherence and retention. Planned to be completed in 2017.

Table 2.3 (cont'd)

Carson et al. (2007)	N = 13, mean age 59	Pilot study	Pain: 100-mm VAS [‡]	Pain: Yoga of Awareness Program, 8 weekly 120-minute sessions and home practice.	Non-significant trends toward reduced pain. Increased yoga practice significantly associated with lower levels of next-day pain.
Cleeland et al. (2013)	N = 2046, median age 56.5 years	Randomized, double-blind, phase 3 study	Pain: BPI [§] -Short Form	Pain: Denosumab versus zoledronic acid	Denosumab improved pain prevention and had comparable pain palliation compared with zoledronic acid. Fewer denosumab-treated patients used strong opioid analgesics.
Cooper (2011)	N = 1, age 64	Case study	Spirituality: qualitative recall of 16 patient encounters	Spirituality: Spiritual care by chaplain	Patient “found a greater peace about the purpose and meaning of her life in the face of dying”. Claimed “her own spiritual authority to meet the challenge of living and dying”, relinquished fear of God and replaced with “faith she was acceptable to the Holy One”.
Di Franco et al. (2014)	N = 193, age not reported	Longitudinal, retrospective, non-randomized	Pain: 11-point NRS [¶] and Pain Intensity Difference	Pain: Radiotherapy, individualized	Mean baseline pain was 7.32, after 180 days reduced to 4.36 ($p < 0.001$).
Furlan, Trovo, Drigo, Capra, and Trovo (2014)	N = 13, mean age 56.4 years	Single-arm, prospective, Phase I clinical trial	Pain: NRS [¶] and analgesic consumption	Pain: Radiotherapy	Average pain decreased from 4.9 to 1.0 ($P < 0.001$). 11 patients had pain relief in the radiated field. 6 stopped analgesic drug consumption.
Iakovou et al. (2014)	N = 63, mean age 57.7 years	Prospective, non-randomized	Pain: Modified Wisconsin Test	Pain: Radiopharmaceuticals	Pain palliation was complete (score decreased more than 2) in 52% of patients, partial (decreased 1 or 2) in 31%, and absent in 16%. All radiopharmaceuticals had same therapeutic effect.

Table 2.3 (cont'd)

Ismail-Hamash, Umberger, Aktas, Walsh, and Cheruvu (2018)	N = 86, mean age 61.5 (30–92 years)	Cross-sectional	Pain: Empirical symptom checklist (“present” or “absent”)	Pain: N/A	Pain symptom cluster did not have a significant mediation effect on performance. Women reporting pain were more likely to be bedridden and have psychoneurological symptoms
Kokkonen et al. (2017),	N = 128 mean age 60 (34–84 years)	Non-randomized, prospective, cross-sectional, observational	Pain: NRS [¶] , RAND SF-36 and European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30	Pain: N/A	Mean pain in movement (0–10) was 3.2. Mean disability caused by pain (0–10) was 4.4.
Krigel et al. (2014)	N = 15, mean age 56.8 (32–75 years)	Qualitative, focus groups, Interpretive phenomenological	Spirituality: 90-minute semi-structured group interviews	Spirituality: N/A	Women spoke of existential concerns such as increased awareness of their mortality, preparing for death, handling uncertainty and the search for meaning.
Kumar et al. (2013)	N = 147, mean age 47	RCT [†]	Pain: Verbal pain scale (0–10)	Pain: Sudarshan Kriya and Pranayam, one 18hr workshop over 3 days, 20 min daily at-home practice.	Pain perception reduced by 3 points in intervention group, compared with control.
Kundel et al. (2013)	N = 29, median age	Longitudinal, non-randomized	Pain: 0–10 scale and analgesic consumption	Pain: Radiotherapy/ pharmaceutical	Response rate (complete=0 and no increase in analgesic consumption, and partial=reduction

Table 2.3 (cont'd)

	59 (35–84 years)				≥ 2 no increase in analgesic consumption) - 86%.
Lee et al. (2017)	N = 18, median age 53.5 (35–67 years)	Non-equivalent control group pre-/posttest study	Pain: Wisconsin BPI [§]	Pain: 8-week mindfulness-based stress reduction program	Mean pain decreased from 3.44 to 3.11 in intervention group and increased from 1.78 to 3.11 in control group. No significant difference between groups in average pain ($z = -1.749$, $P \leq .080$).
Mohammed et al. (2012)	N = 1, 63 years old	Case study	Pain: VAS [‡]	Pain: Intrathecal ziconotide	VAS began at 9/10, decreased to 7/10 on day 3 and 6/10 on day 6 of treatment. Dosage increased on days 7 & 9. VAS decreased to 3–4/10 on day 10.
Mosher et al. (2013)	N = 44, mean age 57.9	Qualitative, expressive writing	Pain & spirituality: Open ended expressive writing essays, 20 minutes each	Pain & spirituality: N/A	176 essays analyzed. 3 main themes: 1) QOL concerns (physical symptom burden, emotional distress, body image disturbance, and disrupted daily activities); 2) Social constraints on disclosure of cancer-related concerns may exacerbate distress 3) Awareness of life's brevity and search for meaning. 61% of women reported pain. Existential issues: heightened awareness of eventual death/impact on family(43%), search for meaning in suffering(25%).
Niklasson, Paty, and Ryden (2017)	N = 16, mean age 56 (38–74 years)	Qualitative, semi-structured interviews	Pain: focused interview and NRS [¶] ,	Pain: N/A	All participants spontaneously reported pain (most commonly reported symptom). Mean severity was 8/10.
Pacsi (2015)	N = 6, 30–45 years	Qualitative, semi-structured interviews	Pain & spirituality: 90-min interviews, (beginning with	Pain & spirituality: N/A	Four key themes: uncertainty, coping, loving, and believing. Under coping, women mentioned enduring pain and adverse effects. Spirituality encompassed throughout all

Table 2.3 (cont'd)

			“What is your personal experience living with advanced breast cancer?”)		themes, such as believing, and relying on faith and hope to help fight their breast cancer.
Perroud et al. (2016)	N = 20, mean age 57 (38–78 years)	Secondary analysis of a longitudinal, nonrandomized, Phase II clinical trial	Pain: BPI [§] , Spanish version	Pain: Metronomic cyclophosphamide and celecoxib	30% reported pain at baseline. There was significant decrease in proportion of patients reporting pain from baseline to end of treatment ($p \leq 0.046$).
Puetzler et al. (2014)	N = 52, mean age 65.7 (30–86 years)	Cross-sectional and prospective cohort designs	Pain: NRS [¶] ,	Pain: Comprehensive pharmacologic cancer pain therapy (CPT)	83% of the patients experienced pain at baseline, of whom 35% were not prescribed any pain medication. Significant and clinically relevant improvements in pain were found after CPT.
Reed et al. (2012)	N = 235, mean age 55 (25–84 years)	Cross-sectional	Pain: Functional Assessment of Cancer Therapy-Breast QoL	Pain: N/A	34% reported significant pain. Among women with bone metastases, nearly half reported significant pain.
Sheean et al. (2015)	N = 25, mean age 58.8 years	Cross-sectional	Pain: Patient Generated Subjective Global Assessment (PG-SGA)	Pain: N/A	72% of women reported pain.

Table 2.3 (cont'd)

Shen, Redd, Winkel, and Badr (2014)	N = 201, mean age 52.2 years	Secondary analysis of a longitudinal, retrospective, study	Pain: BPI [§] , brief Survey of Pain Attitudes (SOPA) and 17-item Pain Behaviors Checklist	Pain: N/A	Belief that medical cure for pain exists buffered the positive association between pain severity and pain behaviors.
Smith et al. (2011)	N = 44, mean age 51.5 (31–79 years)	Longitudinal, prospective, single-arm, pilot study	Spirituality: FACIT-Sp	Spirituality: 'Pathfinder' intervention (including cognitive restructuring, mind/ body technique instruction, self-care and end-of-life planning)	After adjusting for patient characteristics, spirituality was found to have significant associations with despair ($P < 0.01$) and emotional well-being ($P < 0.05$).
Smyth et al. (2016)	N = 529, median age 54.5 years	Post-hoc analysis of a phase III clinical trial	Pain: BPI [§] -Short Form	Pain: Gemcitabine plus paclitaxel or paclitaxel alone	Worst pain and pain interference had significant prognostic effect for survival (both hazard ratios 1.07 for 1-point increase; $p \leq 0.0061$). Median survival for patients by BPI-SF worst pain score = 0 was 23.8, = 1–4 was 17.9, = 5–10 was 14.6 (log-rank $p = 0.0065$).
Stuver et al. (2012)	N = 611, subset of the entire sample of various cancers (mean age 61.2 years)	Retrospective, cross-sectional	Pain: Intensity on 0–10 NRS [¶] , and/or VAS [‡] , Obtained from medical record	Pain: N/A	69.6% of breast cancer patients reported no pain; 12.6% reported 'low' (1–3), 10.5% reported moderate (4–6) and 7.4% reported severe (7–10). Younger age, minority race, and recent onset of advanced disease were associated with severe pain.

Table 2.3 (cont'd)

Thornton, Andersen, and Blakely (2010)	N = 104, mean age 53 years	Cross-sectional	Pain: 7-item Pain Interference scale from BPI [§]	Pain: N/A	Mean pain was 14.25. Evidence for stress hormones as a common mechanism for the co-occurrence of pain, depression, and fatigue.
Twelves et al. (2017)	N = 733, mean age 55 (28-84 years)	Post-hoc analysis of an open-label, longitudinal, randomized, trial	Pain: EORTC QLQ-C30	Pain: Etipirinecan pegol (NKTR-102) or single agent treatment of physician's choice (from commonly used cytotoxics)	On a 0–100 transformed scale, mean in Etipirinecan pegol group was 32.3; Mean in treatment of physician's choice group was 35.3.
Westhoff et al. (2015)	N = 434, age not reported	Longitudinal, prospective	Pain: 11-point NRS [¶]	Pain: Radiation therapy	Of breast cancer patients: 355 (82%) responded to radiation therapy (decrease in pain score by ≥ 2 points without analgesic increase, or analgesic decrease without increase in pain), 79 (18%) did not.
Willis et al. (2015)	Review, N = 33 publications reviewed (1984–2013)	Review of the literature, qualitative and quantitative	Pain & spirituality: varied, review article	Pain & spirituality: N/A	Pain: Studies indicated the significant problem of pain. Experiencing pain was a trigger for fear for some women who perceived that this symptom as a sign of disease progression. Spirituality: Living with metastatic disease found to provide an opportunity for personal and spiritual growth. Women described spirituality as a source of strength, peace, and healing which helped them cope with feelings of uncertainty, loss, and fear, and to accept their diagnosis.

Table 2.3 (cont'd)

Wyatt et al. (2012)	N = 385, mean age 56 years	Longitudinal RCT [†]	Pain: BPI [§] -Short Form	Pain: Reflexology vs. lay foot manipulation vs. conventional care	Baseline pain for reflexology group = 3.76, lay foot manipulation = 3.87, conventional care = 3.95. In contrast to other reflexology studies, significant effects not found for pain.
Wyatt et al. (2013)	N = 385, mean age 56 years	Secondary analysis of a longitudinal RCT [†]	Pain: BPI [§] -Short Form Spirituality: Long-Term Quality of Life Instrument (LTQL) spirituality subscale	Pain & spirituality: Secondary analysis of Reflexology vs. lay foot manipulation vs. conventional care study	Women with distant metastasis had lower functioning and more pain; no differences in spirituality.
Wyatt et al. (2015)	N = 385, mean age 56 years	Secondary analysis of a longitudinal RCT [†]	Pain: BPI [§] -Short Form	Pain: Secondary analysis of Reflexology vs. lay foot manipulation vs. conventional care study	Summed pain severity significantly associated with dose delays or dose reductions. Direction of associations dependent on women having metastatic disease.
Yeh et al. (2014)	N = 366, mean age 53.7 years	Single-arm, non-comparative, open label, longitudinal,	Pain: European Organization for Research and Treatment of Cancer bone	Pain: Zoledronic acid	Painful site subscale significantly reduced during first 12 months, with the exception of 6-month follow-up. Pain characteristics significantly lower from 2-months onwards.

Table 2.3 (cont'd)

		observational phase IV study	metastases module (EORTC QLQ-BM22) and VAS [‡]		VAS [‡] scores indicated significant reduction in pain.
Zhang et al. (2013)	N = 43, mean age 57.3 (32- 74 years)	Longitudinal, non- randomized	Pain: VAS [‡]	Pain: Percutaneous vertebroplasty combined with zoledronic acid	Pain decreased significantly from 7.6 at 24 hours before intervention to: 3.6 at 24 hours after, 2.0 at 1 month, 2.8 at 3 months, 3.1 at 6 months, and 2.5 at 12 months after intervention (P < .05).

The quality of evidence was not appraised, as this generally is not the focus of scoping reviews (Arksey & O'Malley, 2005) and the aim of this review was to broadly explore pain and spirituality. Additionally, a scoping overview table was created (Table 2.4) along with a diagram (Figure 2.2), which provide data of the focus (pain and/or spirituality) for each of the included publications.

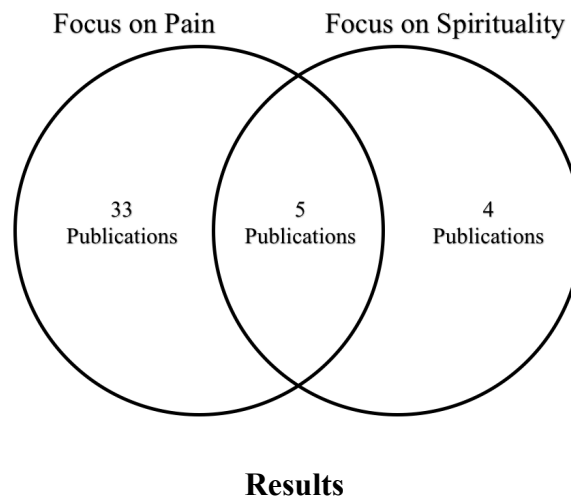
Table 2. 4 Overview of Included Publications within Scoping Review

Publication	Pain	Spirituality
Abernethy et al., 2010	✓	✓
Ahmad et al., 2011		✓
Arathuzik, 2009	✓	
Atahan et al., 2010	✓	
Badr & Milbury (2011)	✓	
Barragan-Campos et al., 2014	✓	
Bell et al., 2016	✓	
Butler et al., 2009	✓	
Carson et al., 2017	✓	
Carson et al., 2007	✓	
Cleeland et al., 2013	✓	
Cooper, 2011		✓
Di Franco et al., 2014	✓	
Furlan, 2014	✓	
Iakovou, 2014	✓	
Ismail- Hamash et al., 2018	✓	
Kokkonen, 2017	✓	
Krigel et al., 2013		✓
Kumar et al., 2013	✓	
Kundel et al., 2013	✓	
Lee et al., 2017	✓	
Mohammed et al., 2012	✓	
Mosher et al., 2013	✓	✓
Niklasson et al., 2017	✓	
Pacsi, 2015	✓	✓
Perroud et al., 2016	✓	
Puetzler et al., 2014	✓	
Reed et al., 2012	✓	

Table 2.4 (cont'd)

Sheean et al., 2015	✓	
Shen et al., 2014	✓	
Smith et al., 2011		✓
Smyth et al., 2016	✓	
Stuver et al., 2012	✓	
Thornton et al., 2010	✓	
Twelves et al., 2017	✓	
Westhoff et al., 2015	✓	
Willis et al., 2015	✓	✓
Wyatt et al., 2012	✓	
Wyatt et al., 2013	✓	✓
Wyatt et al., 2015	✓	
Yeh et al., 2014	✓	
Zhang et al., 2013	✓	

Figure 2. 2 Venn Diagram Depicting Overview of Results within Scoping Review



Stage 5. Collating, Summarizing and Reporting Results

Research Question 1: How is pain conceptualized, assessed, and addressed?

Pain conceptualized and assessed. Of the 42 included publications, 38 focused on pain: 31 reports of quantitative studies, four reports of qualitative studies, one case study, one literature review, and one study protocol. Definitions of pain were not offered in any of the

publications, but pain was generally conceptualized from a physiological perspective and assessed with unidimensional measures (see Table 2.5 for pain assessments used).

Table 2. 5 Pain Assessments Utilized within Results of Scoping Review

Pain Assessment	Publications Using Assessment	Total
Analgesic consumption	Furlan, 2014 Kundel et al., 2013	2
Brief Pain Inventory (BPI) or BPI-Short Form	Bell et al., 2016 Carson et al., 2017 Cleeland et al., 2013 Lee et al., 2017 Perroud et al., 2016 Shen et al., 2014 Smyth et al., 2016 Wyatt et al., 2012 Wyatt et al., 2015	9
BPI -Interference Scale	Thornton et al., 2010	1
Brief Survey of Pain Attitudes (SOPA)	Shen et al., 2014	1
European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30	Kokkonen, 2017 Twelves et al., 2017	2
Empirical symptom checklist (“present” or “absent”)	Ismail- Hamash et al., 2018	1
EORTC Bone Metastases (EORTC QLQ-BM22)	Yeh et al., 2014	1
Functional Assessment of Cancer Therapy-Breast (FACT-B)	Reed et al., 2012	1
MD Anderson Symptom Inventory (MDASI)	Abernethy et al., 2010	1
Modified Wisconsin Test	Iakovou, 2014	1
Multidimensional Pain Inventory (MPI) – Severity Subscale	Badr & Milbury (2011)	1
Numeric Rating Scale (NRS) and/or Visual Analogue Scale (VAS)	Atahan et al., 2010 Barragan-Campos et al., 2014 Carson et al., 2007 Di Franco et al., 2014 Furlan, 2014 Kokkonen, 2017 Kumar et al., 2013 Kundel et al., 2013	14

Table 2.5 (cont'd)

	Puetzler et al., 2014	
	Stuver et al., 2012 Westhoff et al., 2015 Yeh et al., 2014 Zhang et al., 2013 Niklasson et al., 2017	
Pain Behaviors Checklist	Shen et al., 2014	1
Pain Rating Scale	Butler et al., 2009	1
Patient Generated Subjective Global Assessment (PG-SGA)	Sheean et al., 2015	1
Qualitative – interviews, expressive writing	Arathuzik, 2009 Mosher et al., 2013 Pacsi, 2015 Niklasson et al., 2017	4
RAND SF-36	Kokkonen, 2017	1
Varied, case study	Mohammed et al., 2012	1
Varied, review	Willis et al., 2015	1

Overall, pain assessments were most often carried out with Visual Analogue Scales (VAS) and/or Numeric Rating Scales (NRS) (n = 14) or versions of the Brief Pain Inventory (BPI) (n = 9), followed by qualitative assessments (n = 3). Of publications reporting the prevalence of pain in samples of women with advanced breast cancer, estimates ranged from 30% to 83% (Perroud et al., 2016; Puetzler et al., 2014). Variations in pain prevalence reports may be due to varied sample characteristics and assessment methods. For example, the sample with one of the highest pain prevalence reports (72%) also had one of the smallest and most ethnically diverse samples (Sheean et al., 2015). Most studies used patient self-report (Butler et al., 2009; Perroud et al., 2016; E. Reed et al., 2012; Sheean et al., 2015), while one used electronic medical record audits (Stuver et al., 2012), which are entered by providers, a factor that could have influenced findings (Sikorskii et al., 2012). It is likely that assessment periods also varied (i.e., “pain now,” last 24 hours, last seven days), which were not consistently reported and could yield different prevalence estimates.

Pain is often reported in both severity and interference, which can be taken together to gain a more complete understanding of the pain experience as each of these components were found to have significant prognostic effects on survival (Smyth et al., 2016). Severity was most often assessed in this sample of publications; interference was not consistently assessed. For those publications reporting severity, baseline estimates ranged from 1.78 out of 10 (Lee, Kim, Kim, Joo, & Lee, 2017) to 9 out of 10 (Mohammed, Brookes, & Eldabe, 2012), with variations likely due to differing sample characteristics. Although interference was not consistently reported, one publication did report “mean disability caused by pain” as a 4.4 out of 10 (Kokkonen et al., 2017).

Interventions: Pain. A total of 25 interventions for pain in this population were identified. Of these, pain management was primarily implemented with the use of varied pharmaceuticals ($n = 11$) and radiotherapy ($n = 5$). Reports of other interventions included percutaneous vertebroplasty (Barragan-Campos et al., 2014), a combination of percutaneous vertebroplasty and pharmaceutical management (Atahan et al., 2010; Zhang et al., 2013), a ‘Pathfinder’ intervention (including cognitive restructuring, mind/body techniques, self-care and end-of-life planning) (A. P. Abernethy et al., 2010), supportive-expressive group therapy (Butler et al., 2009), yoga (Carson et al., 2017; Carson et al., 2007), Sudarshan Kriya and Pranayam (Kumar et al., 2013), mindfulness-based stress reduction (MBSR) (Lee et al., 2017), and reflexology (Wyatt et al., 2012). Each intervention was tested in varying samples with differing levels of success. Various complementary and integrative therapy interventions were identified for pain management in this population ($n = 7$), yet the majority of intervention studies focused on radiotherapy or pharmaceutical management.

Research Question 2: How is spirituality conceptualized, assessed, and addressed?

Spirituality conceptualized and assessed. Nine publications were identified which focused on spirituality in women with advanced breast cancer. Findings included reports of four qualitative studies, three quantitative studies, one case study, and one literature review. Definitions of spirituality were not offered in any of the publications, but spirituality was generally conceptualized as encompassing faith, meaning, and existential concerns. In multiple qualitative studies, women cited these dimensions of spirituality (primarily a search for meaning in life) as key aspects of their illness experiences. In a literature review of quantitative and qualitative work focused on women’s experiences of metastatic breast cancer, researchers found spirituality was described as “a source of strength, peace, and healing” able to help women cope with feelings of uncertainty, loss, and fear to become more accepting of their diagnosis and to shift the focus of their lives (Willis, Lewis, Ng, & Wilson, 2015).

Spirituality assessments were primarily qualitative (Ahmad, Muhammad, & Abdullah, 2011; Krigel et al., 2014; Mosher et al., 2013; Pacsi, 2015) along with two quantitative studies using the Functional Assessment of Chronic Illness—Spiritual Well-Being Scale (A. P. Abernethy et al., 2010; S. Smith et al., 2011) and one using the Long Term Quality of Life Philosophical/Spiritual subscale (Wyatt et al., 2013). See Table 2.6 for an overview of spirituality assessments used.

Table 2. 6 Spirituality Assessments Utilized within Results of Scoping Review

Publication	Pain	Spirituality
Abernethy et al., 2010	✓	✓
Ahmad et al., 2011		✓
Arathuzik, 2009	✓	
Atahan et al., 2010	✓	
Badr & Milbury (2011)	✓	
Barragan-Campos et al., 2014	✓	
Bell et al., 2016	✓	
Butler et al., 2009	✓	

Table 2.6 (cont'd)

Carson et al., 2017	✓	
Carson et al., 2007	✓	
Cleeland et al., 2013	✓	
Cooper, 2011		✓
Di Franco et al., 2014	✓	
Furlan, 2014	✓	
Iakovou, 2014	✓	
Ismail- Hamash et al., 2018	✓	
Kokkonen, 2017	✓	
Krigel et al., 2013		✓
Kumar et al., 2013	✓	
Kundel et al., 2013	✓	
Lee et al., 2017	✓	
Mohammed et al., 2012	✓	
Mosher et al., 2013	✓	✓
Niklasson et al., 2017	✓	
Pacsi, 2015	✓	✓
Perroud et al., 2016	✓	
Puetzler et al., 2014	✓	
Reed et al., 2012	✓	
Sheean et al., 2015	✓	
Shen et al., 2014	✓	
Smith et al., 2011		✓
Smyth et al., 2016	✓	
Stuver et al., 2012	✓	
Thornton et al., 2010	✓	
Twelves et al., 2017	✓	
Westhoff et al., 2015	✓	
Willis et al., 2015	✓	✓
Wyatt et al., 2012	✓	
Wyatt et al., 2013	✓	✓
Wyatt et al., 2015	✓	
Yeh et al., 2014	✓	
Zhang et al., 2013	✓	

Interventions: Spirituality. Only two studies that provided a spiritual intervention for women with advanced breast cancer were identified. One was the “Pathfinders” intervention,

which consisted of cognitive restructuring, mind/body technique instruction, self-care, and end-of-life planning. Although the intervention was successful in other areas, no significant changes were found in spiritual well-being (A. P. Abernethy et al., 2010). The second intervention was reported in a case study of pastoral care, consisting of 16 unstructured encounters, and positive outcomes, such as an increased sense of peace, acceptance, and purpose, were qualitatively reported by the involved patient (Cooper, 2011).

Research Question 3: Does spirituality impact the pain experience?

Interconnectedness of pain and spirituality. Five publications reported findings related to both pain and spirituality. These include reports of two quantitative studies, two qualitative studies, and one literature review. Of these publications, none specifically looked at the impact of spirituality on pain. One quantitative study assessed pain and spirituality as separate outcomes and examined how each of these variables were impacted by an intervention (A. Abernethy et al., 2010). The second quantitative study examined differences in pain and spirituality in women with and without distant metastases, and found that women with distant metastasis had lower functioning and more pain than those without, but no differences in spirituality were identified (Wyatt et al., 2013).

Findings from the qualitative studies revealed that women with advanced breast cancer cited both pain and spirituality as key aspects of their illness experiences (Mosher et al., 2013; Pacsi, 2015). Women reported experiencing fears of a worsening prognosis and/or impending death, as well as existential questions such as “why me?” when they experienced pain and suffering (Mosher et al., 2013). Additionally, data from qualitative studies showed that women with advanced breast cancer cited connection with a higher power and finding meaning in their experience as key mechanisms for facing their advanced breast cancer (Krigel et al., 2014;

Mosher et al., 2013; Pacsi, 2015). Although these qualitative findings suggest the potential impact of spirituality on pain, no work was identified that explicitly examined this relationship among women with advanced breast cancer.

Discussion

It was clear from this review that women with advanced breast cancer experience significant pain and various interventions are being tested and implemented to manage pain, primarily radiotherapy and pharmaceutical management. Prevalence of the BPI as the second most commonly used pain assessment indicates that some current research is trending towards a multidimensional conceptualization of pain, which is useful for the scientific advancement of pain research. The BPI assesses both pain intensity and interference, an important feature as preliminary evidence suggests spirituality may impact pain interference most (McCabe, Murray, Austin, & Siddall, 2018).

Although a solely physiologic approach to pain was often used, the literature included in this review suggests a need for a comprehensive approach that may incorporate spirituality. Including assessments of spirituality along with queries on perceived impact on pain could provide important information about how women are coping with the existential aspects of pain derived from their advanced breast cancer experience. While both pain and spirituality were assessed within multiple studies, investigators did not report findings specifically related to the impact of spirituality on pain. Additionally, qualitative studies included in this review revealed women with advanced breast cancer cited dimensions of spirituality, such as connection with a higher power and finding meaning in their experience, as key coping mechanisms (Krigel et al., 2014; Mosher et al., 2013; Pacsi, 2015) that could also be applied to how they cope with and experience their pain.

There was a surprising lack of research on spirituality in this population considering the median survival for these women is approximately 24 months (Twelves et al., 2017), bringing existential concerns to the forefront. Overall, findings related to spirituality were sparse, but preliminary evidence from the included qualitative studies, along with quantitative studies in other advanced cancers, support further exploration into how spirituality impacts the way women relate to their disease experience, specifically to their pain. Future work may be able to explore the use of spirituality-enhancing interventions, such as meditative practices (Mackenzie, Carlson, Munoz, & Specia, 2007), Meaning-Centered Psychotherapy (Breitbart et al., 2012) or music therapy (Cook & Silverman, 2013) as components of comprehensive pain management. Based on previous studies, which have demonstrated a relationship between pain and spirituality in mixed cancer populations, future work would be well-served to carry these findings into specific types and stages of cancer to provide more individualized assessment and management.

Limitations

Although the flexible and comprehensive approach of a scoping review is able to capture a broad range of literature, this review still has limitations. First, publications that reported outcomes for different stages of breast cancer together (i.e., stage I–III or I–IV) or various types of cancer were excluded. Due to this reporting approach in various publications, relevant data may have been embedded in reports and missed. Information on the differences in pain and spirituality in various sub-populations (age, race/ethnicity, marital status, etc.) was generally not available. Due to this and the nature of the scoping review, findings may not be applicable to other populations. Additionally, although grey literature was screened through multiple databases, due to the vast and varied nature of this content, some may have been missed.

Implications for Nursing

Despite pain being assessed as the fifth vital sign, advancements in pain management are not fully reaching women with advanced breast cancer, which can have many negative consequences (A. Al-Natour, S. Al Momani, & A. Qandil, 2017; Paice & Ferrell, 2011). In clinical practice, achieving optimal QOL, which is a primary goal for women with advanced breast cancer, requires comprehensive assessment and management of pain, which may include addressing spirituality. Spirituality has been found to be a source of strength and coping in patients with advanced breast cancer, so clinicians can support women in activities, such as exploring existential concerns and making meaning of their experiences, as well as supporting spiritual practices, such as prayer or meditation. Spiritual needs can differ based on prognosis, phase of care, cultural, and personal preferences, so the context of care must always be considered.

With the advent of new targeted therapies and new supportive medications, there is likely to be a growing population of women living with advanced breast cancer (Krigel et al., 2014). Additional research is needed to explore the complex dimensions of pain and if spiritual support can play a role in pain management for these women. Further research could also benefit from examining differences in pain and spirituality in sub-populations of women with advanced breast cancer, such as in different age groups, races/ethnicities, or religious preferences. This work would provide important information about how women with variant demographic characteristics may experience pain and spirituality differently and provide direction towards individualizing care.

Conclusions

This review aimed to provide a broad overview of pain, spirituality, and the potential impact of spirituality on pain in women with advanced breast cancer. Findings on how each of these complex concepts are being conceptualized and assessed was provided, along with a review of interventions aimed at reducing pain and enhancing spirituality. It is widely recognized that women with advanced breast cancer experience pain, which can have many negative impacts, and this review underscores the prevalence in this population. There is strong evidence, despite current approaches to pain management, a proportion of women with advanced breast cancer still have poorly controlled pain. Although radiotherapy and pharmaceuticals are indispensable tools for pain management, the complexity of pain, especially in advanced disease, calls for the integration of broader approaches. Women with advanced breast cancer cited dimensions of spirituality as key aspects of their disease experience; therefore, invoking spirituality may serve as an avenue for enhancing individualized coping with pain and aiding in pain management. Future research aimed at understanding the complex dimensions of the pain experience, including spirituality, in this population is warranted.

This scoping review has examined the literature for two critical concepts for women with advanced breast cancer: pain and spirituality. Although pain has been well studied, it is most commonly approached with a unidimensional conceptualization. Very few studies were found to focus on spirituality, and none were found which explored the impact of spirituality on pain in women with advanced breast cancer. While existing work suggests a link between pain and spirituality for various cancer populations and those who are near end of life, advanced breast cancer is an area ripe for in-depth investigation.

CHAPTER 3: PAIN AND SPIRITUALITY OUTCOMES IN WOMEN WITH ADVANCED BREAST CANCER

Abstract

Objectives: To examine pain and spirituality, demographic/clinical factors associated with pain and spirituality, the impact of spirituality on pain over time in the intervention versus control groups, and how pain and spirituality impact engagement with a reflexology intervention in a randomized controlled trial.

Sample & Setting: Advanced breast cancer patients (n=256) enrolled in home-based caregiver-delivered foot reflexology intervention.

Methods & Variables: Secondary analyses were conducted with baseline and post-intervention data, using stepwise model building, linear mixed effects modeling and negative binomial regression. Measures: Patient Reported Outcomes Measurement Information System-pain intensity; Long-Term Quality of Life-Spiritual/Philosophical subscale; and demographic/clinical variables.

Results: Mean scores were 3.6/10 for pain and 3.2/4.0 for spirituality at baseline. Participants who were younger, not married/living with a partner, not employed, or were receiving hormonal therapy had increased odds of having more baseline pain. Participants who were older, non-Caucasian or were Christian had increased odds of higher baseline spirituality scores. The impact of spirituality on pain was not significant over time in either group. In the reflexology group, spirituality and pain were not associated with engaging in intervention sessions.

Implications for Nursing: These women experienced moderate pain, on average. Patients with specific demographic/clinical characteristics may require additional support with pain management and spiritual care.

Introduction

Up to 83% of women with advanced breast cancer report pain (Puetzler et al., 2014), indicating novel approaches to managing pain in this population are needed. Pain is a distressing experience with interacting sensory, cognitive and emotional components, which may be associated with actual or perceived tissue damage (Bushnell et al., 2013; International Association for the Study of Pain, 1979; Wang et al., 2016; Williams & Craig, 2016). Pain can be the result of cancer, treatment or comorbidities (Posternak et al., 2016), and it can adversely affect all areas of quality of life (QOL) (Paice & Ferrell, 2011; Rodriguez, Ji, Wang, Padhya, & McMillan, 2019). Spirituality may positively impact the experience of pain in women with advanced breast cancer, yet this is one area that has not yet been adequately investigated (Flanigan et al., 2019; Visser et al., 2018). The overarching purpose of this study was to examine the impact of spirituality on pain over time in these women.

Conceptually, this study is grounded in an adaptation of Reed's Theory of Self-Transcendence (ST) (P. Reed, 2015), a theory that has been applied in various samples of breast cancer patients (Coward, 2003; Matthews & Cook, 2009; Thomas et al., 2010). In ST theory, vulnerability (awareness of mortality) serves as a resource to enhance ST (expand self-boundaries in various ways), and ST helps facilitate well-being (subjective feeling of health or wholeness). Personal/contextual factors may influence other components of the model (P. Reed, 2015). Modified and applied to this work, spirituality is an expression of ST, pain level is the outcome indicating one aspect of well-being (where lower pain serves as an indicator of higher well-being), and demographic/clinical factors may contribute to both concepts, pain and spirituality.

Managing pain associated with cancer can be costly (Ferrell, 2000) and pain can result in significant suffering (Arathuzik, 2009), so spirituality's impact on the experience of pain may open avenues to innovative interventions. Spirituality is a dynamic process whereby humans experience connection with self, others, nature and/or higher power and a sense of meaning (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016), which may serve as a resource when facing cancer and its associated symptoms (Flanigan et al., 2019; Krigel et al., 2014; Mosher et al., 2013; Visser et al., 2018). Women with advanced breast cancer have indicated that spirituality serves as a resource when facing their disease (Gaston-Johansson et al., 2013; Krigel et al., 2014; Mosher et al., 2013). Spirituality can positively alter the disease experience (Gaston-Johansson et al., 2013; Rosenzweig et al., 2009); therefore, it may also serve as a resource for altering pain experiences (Flanigan et al., 2019; Visser et al., 2018). Spirituality can be significant throughout the lifespan, but often becomes especially important when faced with a life-threatening disease such as advanced cancer (Balducci, 2019; Lazenby et al., 2014; Piderman et al., 2015).

Enhancing spirituality is hypothesized to alter negative thoughts and emotions associated with pain, modulating both the cognitive and emotional components and transforming the painful experience. Since pain is constructed of interacting sensory, cognitive and emotional components, altering any of these carries potential to modulate the pain experience (Zeidan & Vargo, 2016). Previous studies have built support for this hypothesis, indicating that thoughts and emotions play a profound role in how pain is experienced (Keefe et al., 2004; Wiech et al., 2009). Evidence suggests that spirituality offers a route to positive thoughts and emotions, such as a sense of safety and security, when facing difficult circumstances (Gregg, 2011; Yeager et al., 2016). Multiple studies have reported significant relationships between pain and spirituality

in varying samples of cancer patients (Bai et al., 2018; Delgado-Guay et al., 2016; Hui et al., 2011; Wang & Lin, 2016). This work builds on these findings and extends the inquiry into a new population, women with advanced breast cancer enrolled in a Complementary and Integrative Health (CIH) intervention trial.

Spirituality may also impact pain through a lesser-studied behavioral route, potentially enhancing the uptake of pain management interventions, thus indirectly influencing pain. The current study examines this hypothesis within the context of a CIH intervention. CIH interventions focus on caring for the mind, body, and spirit holistically, recognizing that these are interrelated (National Cancer Institute, 2019). Research suggests that those with higher self-reported spirituality report using more self-management interventions (Harvey, 2008; Polzer & Miles, 2005; Zarei et al., 2015). Further, higher self-reported spirituality may be associated with greater openness toward CIH interventions (Hsiao et al., 2008; B. Smith et al., 2008a). Since CIH interventions have inherent spiritual underpinnings (McGrady & Moss, 2018; National Cancer Institute, 2019), women with higher self-reported spirituality may be more likely to engage than those with lower self-reported spirituality. Therefore, it is hypothesized that spirituality may directly impact pain through alterations in thoughts and emotions, and indirectly impact pain by enhancing the uptake of a CIH-based pain management intervention.

Reflexology is the CIH intervention included in this study. Reflexology entails applying firm pressure to specific points on the feet or hands, corresponding to different parts of the body (National Cancer Institute, 2019; Reflexology Association of America, 2018). The underlying mechanisms are not yet well understood; It is postulated that stimulating these reflexes alters various biological and energetic pathways, causing physiological changes which positively impact symptoms (Stephenson et al., 2007; Wyatt et al., 2012; Wyatt et al., 2017). CIH

interventions, such as reflexology, may also elicit the body's innate healing abilities (McGrady & Moss, 2018).

Since pain and spirituality are highly individual experiences, they may be influenced by demographic/clinical factors. Preliminary work examining demographic/clinical factors in relation to pain and spirituality within varying populations has yielded mixed results (Gagliese et al., 2007; Mystakidou et al., 2008; Posternak et al., 2016; Stuver et al., 2012). Although various demographic/clinical factors may be important predictors of unmanaged pain or issues with spirituality, a gap exists in understanding some potentially important demographic/clinical factors in women with advanced breast cancer. Therefore, this work examines pain and spirituality in a sample of women with advanced breast cancer who are enrolled in a CIH intervention trial, while considering potentially significant demographic/clinical factors.

Objectives

The study objectives were to:

1. Determine the level of pain and the level of spirituality at baseline, prior to engaging in reflexology;
2. Examine which demographic/clinical factors were associated with pain and with spirituality at baseline;
3. Explore the impact of spirituality on pain over time (baseline through week 11), in the reflexology group versus the control group, when controlling for demographic/clinical factors;
4. Distinguish how pain level and spirituality may impact engagement in the CIH-based reflexology intervention over time (baseline, week 5 and week 11), when controlling for demographic/clinical factors.

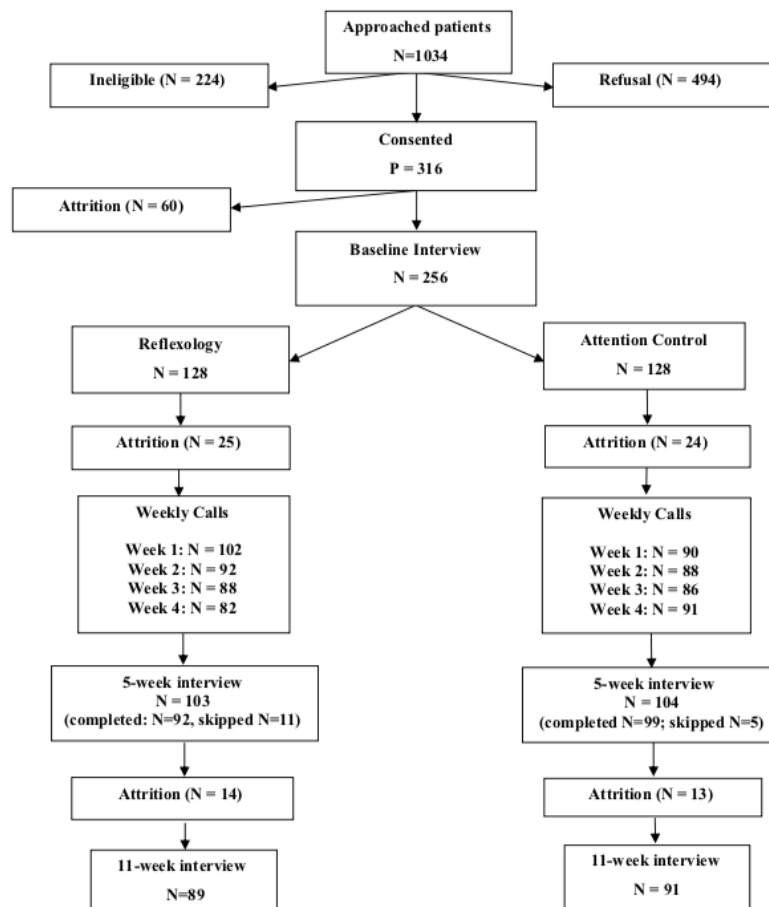
Sample and Setting

A secondary analysis was conducted from “Home-based symptom management via reflexology for advanced breast cancer patients” (5R01CA157459) (Wyatt et al., 2011-2016). This longitudinal randomized controlled trial examined effects of caregiver-delivered foot reflexology on symptoms and QOL (Wyatt et al., 2017). Participants were recruited from nine community-based oncology clinics and two comprehensive cancer centers in the Midwest. Inclusion criteria were: 1) Age ≥ 21 ; 2) diagnosis of advanced breast cancer; 3) able to perform basic activities of daily living; 4) first chemotherapy infusion received; 5) speaks and understands English; 6) access to a telephone; 7) able to hear normal conversation; 8) cognitively oriented; and 9) friend/family member willing to participate. Exclusion criteria were: 1) diagnosis of major mental illness; 2) residing in a nursing home; 3) bedridden; 4) receiving regular reflexology; or 5) diagnoses or symptoms of deep vein thrombosis or painful foot neuropathy. This secondary analysis included data from 256 women (N=128 reflexology, N=128 control at baseline). See Figure 3.1 for an overview of study enrollment.

Methods and Variables

Approval from Institutional Review Boards was obtained before beginning research. In the parent study, nurse recruiters provided information to eligible women, inviting them to participate with a friend/family caregiver. After baseline interviews, women were randomized using a minimization procedure to one of two groups: 1) Reflexology, receiving four weeks of home-based, lay caregiver-delivered foot reflexology (following a 30-minute foot reflexology protocol) and symptom assessment calls; or 2) Attention control, receiving four weekly symptom assessment calls only.

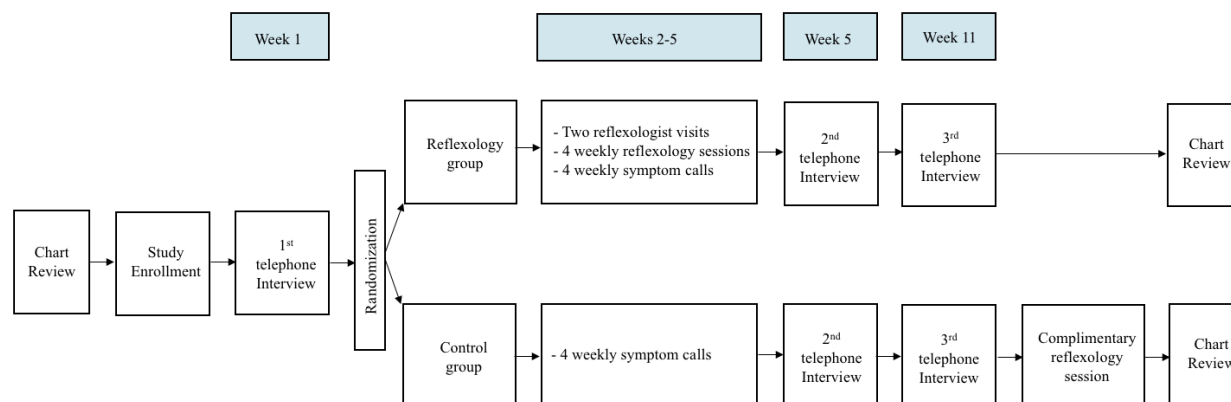
Figure 3. 1 CONSORT chart for “Home-based symptom management via reflexology for advanced breast cancer patients” (5R01CA157459) (Wyatt et al., 2011-2016)



Each woman participated in the study with a friend/family caregiver for 11 weeks. Data were collected via telephone by trained interviewers at baseline, week 5 and week 11, and during weekly symptom assessment calls (weeks 2-5). See Figure 3.2 for an overview of parent study data collection. Weekly calls assessed the severity and interference of common cancer symptoms (including pain), as well as the number of reflexology sessions completed since the last call. Weeks 2-5 were considered the active intervention period, where weekly calls reminded women to engage in reflexology. Weeks 6-11 were considered the maintenance period, to examine intervention sustainability without weekly calls. A review of the medical record was also

completed. The parent study collected additional data, but only data relevant to this secondary analysis are reported here.

Figure 3. 2 Overview of parent study design “Home-based symptom management via reflexology for advanced breast cancer patients” (5R01CA157459) (Wyatt et al., 2011-2016)



Measures

Pain. Pain was assessed using Patient Reported Outcomes Measurement Information System (PROMIS)-29 Profile v1.0 pain intensity item (“In the past 7 days, how would you rate your pain on average?”) at baseline, weeks 5 and 11 (HealthMeasures, 2018). Pain was rated from 0– “no pain” to 10– “worst imaginable pain.” Extensive testing of reliability and validity has been conducted on the PROMIS-29 Profile v1.0, yielding strong evidence of validity and $\alpha=0.92$ – 0.96 in a large study with cancer patients (R. Jensen et al., 2015). In this work, the following cut points were adopted: mild=1; moderate=2-4; severe=5-10. These were developed to indicate clinically meaningful changes in pain among a large sample of cancer patients (B. Given et al., 2008).

Spirituality. Spirituality was assessed using the Long-Term QOL (LTQL)–Spiritual/Philosophical subscale. The LTQL was developed based on four dimensions of QOL (Ferrell et al., 1991) and focus groups (Wyatt et al., 1996). The LTQL is comprised of four subscales: somatic, philosophical/spiritual, health habits, and social/emotional (Wyatt &

Friedman, 1996). The philosophical/spiritual subscale contains 11 items reflecting increased insight and appreciation (connection with self/others/higher power/nature and meaning) (Wyatt & Friedman, 1996; Wyatt et al., 1996). Items are measured on a 5-point scale, with 0 indicating low self-reported spirituality and 4 indicating high. Significant correlation with Cancer Rehabilitation Evaluation System (CaRES), a cancer-specific QOL measure (Ganz, Schag, & Sim, 1992), established evidence of validity of the LTQL (Wyatt et al., 1996). A separate study with this same sample of women showed high reliability on the LTQL philosophical/spiritual subscale ($\alpha=.80$) (Kamp et al., 2019).

Demographic/Clinical Factors. Demographic/clinical factors were assessed at baseline using a standardized demographics form and a chart review form, both developed for the parent study. The demographics form elicited information on education, racial/ethnic background, religious preference, marital status, menopausal status and employment status. Items were assessed via patient self-report using multiple-choice format. The chart review collected information on participant age, disease stage, metastasis, recurrence and type of cancer treatment received.

Number of Reflexology Sessions. Number of 30-minute foot reflexology sessions was assessed during patient weekly calls in weeks 2-5 and during the week 11 interview (assessing sessions completed in weeks 6-11). Patients self-reported the number of sessions completed with their lay caregiver, which was transcribed onto a standardized form. Number of sessions was pooled for weeks 2-5 and 6-11, reflecting the active intervention versus maintenance period.

Analyses

SPSS Version 25.0 and R version 3.6.1 were used for analysis. Available case analyses were conducted. Descriptive statistics were initially examined to describe the sample.

Aim 1: Determine the level of pain and the level of spirituality at baseline, prior to engaging in reflexology. To examine baseline levels of pain and spirituality in this sample of women, means (with standard deviation and variance) were calculated using the entire sample at baseline.

Aim 2: Examine which demographic/clinical factors were associated with pain and with spirituality at baseline. Two separate models were constructed (ordinal regression for pain, truncated regression for spirituality), using stepwise model building procedures. These tests were based on the hypothesis that multiple different demographic factors (age, education, racial/ethnic background, religious preference, marital status, employment status) and/or clinical factors (disease stage, metastasis, recurrence, treatment type, menopausal status) may be associated with spirituality and/or pain.

Aim 3: Explore the impact of spirituality on pain between groups over time. A linear mixed effects model was used, accounting for within-person correlation between time points. Spirituality served as the independent variable and pain as a dependent, with selected demographic/clinical factors as covariates. Intervention group (reflexology vs. control) was included as a moderator, testing the interaction between reflexology and time on pain. A three-way interaction among group, time and spirituality was also tested. It was hypothesized that higher spirituality would contribute to a lower pain level, and that the effect would be stronger in the reflexology group.

Aim 4: Distinguish how pain level and spirituality may impact engagement with a CIT-based reflexology intervention at baseline, weeks 5 and 11. Negative binomial regression was conducted, with pain group (mild/moderate/severe) as an additional variable. Selected demographic/clinical factors were added as covariates. A two-way interaction between pain and

spirituality was tested. Two regressions were conducted, one examining baseline pain and spirituality in relation to number of sessions completed in weeks 2-5, and one examining week 5 pain and spirituality in relation to number of sessions completed in weeks 6-11. These tests were based on the hypothesis that higher spirituality would be a significant predictor of greater number of reflexology sessions performed at each point, regardless of pain level.

Results

Descriptive statistics for this sample are displayed in Table 3.1. Participants had a mean age of 55.7 years, were predominantly Caucasian, married, with metastatic breast cancer, and were most often receiving chemotherapy or targeted therapy.

Table 3. 1 Participant Characteristics by Study Group

	Reflexology Group (N= 128), n (%)	Control Group (N= 128), n (%)
Metastatic cancer		
Yes	80 (62)	81 (63)
No	48 (38)	47 (37)
Recurrent cancer		
Yes	41 (32)	35 (27)
No	87 (68)	93 (73)
Treatment type		
Chemo or targeted therapy (with or without hormonal)	105 (82)	105 (82)
Hormonal therapy only	23 (18)	23 (18)
Race		
Caucasian	105 (83)	107 (84)
Black/African American	13 (10)	13 (10)
Other	9 (7)	7 (6)
Ethnicity		
Hispanic/Latino	5 (4)	6 (5)
Not Hispanic/Latino	123 (96)	122 (95)
Employment		
Full time	28 (22)	38 (30)
Part time	10 (8)	12 (9)
Other	50 (39)	48 (38)
Retired	40 (31)	29 (23)

Table 3.1 (cont'd)

Education		
High school graduate (or GED) or some high school	29 (23)	29 (22)
Some college or 2-year degree	35 (27)	38 (30)
4-year college graduate	20 (24)	33 (26)
More than 4-year college degree	33 (26)	28 (22)
Marital Status		
Never married	14 (11)	13 (10)
Married or living with partner	89 (70)	87 (68)
Divorced/separated	19 (15)	19 (15)
Widowed	6 (4)	9 (7)

Aim 1: Determine the level of pain and the level of spirituality at baseline prior to engaging in reflexology. Mean scores for primary outcomes are displayed in Table 3.2. Mean pain for the entire sample of women was 3.6 out of 10 and mean spirituality was 3.2 out of 4.

Table 3. 2 Aim 1 Results: Baseline Values of Outcomes by Study Group

Variable	Mean (SD) Reflexology group	Mean (SD) Control group
PROMIS Pain Severity (0-10 range)	3.57 (2.59)	3.63 (2.83)
LTQL Philosophical/Spiritual Subscale (0-4 range)	3.18 (0.70)	3.22 (0.56)

Aim 2: Examine which demographic/clinical factors were associated with pain and with spirituality at baseline. Ordinal and truncated regressions revealed that some demographic/clinical factors were associated with pain and spirituality (see Table 3.3).

Table 3. 3 Aim 2 Results: The impact of demographic/clinical factors on pain and spirituality

Demographic/Clinical Factor	Pain Estimate (p value)	Spirituality Estimate (p value)
Age	-0.026 (0.027)*	0.034 (0.003)*
Race		
Caucasian	.	-0.636 (0.051)*
Black or African American/Other	.	.
Ethnicity		
Hispanic or Latina	.	.
Not Hispanic or Latina	-0.913 (0.170)	-0.091 (0.876)
Marital status		
Not married or living with partner	.	.
Married or living with partner	-0.668 (0.013)*	-0.206 (0.343)

Table 3.3 (cont'd)

Education		
Less than 4-year college degree	.	.
4-year college degree or more	-0.392 (0.110)	0.087 (0.657)
Religious preference		
Not identified as Christian	.	-0.717 (0.003)*
Christian	.	.
Employment		
Not employed full- or part-time	.	.
Employed full- or part-time	-0.769 (0.004)*	-0.259 (0.223)
Cancer stage		
Documented stage III or IV	.	0.312 (0.257)
Documented stage I or II	.	.
Metastasis		
Yes	.	0.127 (0.533)
No	.	.
Recurrence		
Yes	.	0.070 (0.770)
No	.	.
Treatment type		
Chemotherapy/targeted therapy	.	.
Hormonal therapy only	0.721 (0.023)*	-0.167 (0.489)
Menopausal status		
Postmenopausal	.	-0.356 (0.141)
Premenopausal, perimenopausal or unknown	.	.

* = significant at $p < .05$

For pain, the demographic/clinical factors significantly associated with pain level were age, marital status, employment status and treatment type. Results revealed that participants who were 1) younger, 2) not married or living with a partner, 3) not employed or responded “other” to their employment status, and/or 4) were receiving hormonal therapy, had a slight increase in ordered log odds of having a higher level of pain. For spirituality, the demographic/clinical factors significantly associated with spirituality level were age, race and religious preference. Results revealed that participants who were 1) older, 2) not Caucasian, and/or 3) were Christian, had increased odds of having a higher level of spirituality.

Aim 3: Explore the impact of spirituality on pain between groups over time. Self-reported spirituality was not significantly associated with level of pain in this sample of women (see Table 3.4).

Table 3. 4 Aim 3 results: The impact of spirituality on pain over time (when controlling for demographic/clinical factors)

Parameter	Estimate (β)	Std. Error	df	t	Sig.	95% Conf. Int.	
						Lower Bound	Upper Bound
Spirituality	-0.163	0.188	585.696	-0.871	0.384	-0.532	0.205
Study group * time							
<i>Control wave 1</i>	6.0606	0.995	302.060	6.089	0.000*	4.1020	8.019
<i>Control wave 2</i>	6.100	0.999	308.949	6.103	0.000*	4.133	8.066
<i>Control wave 3</i>	5.459	1.007	313.455	5.423	0.000*	3.4783	7.439
<i>Reflexology wave 1</i>	6.053	1.021	296.770	5.926	0.000*	4.0430	8.064
<i>Reflexology wave 2</i>	5.504	1.033	307.504	5.330	0.000*	3.472	7.536
<i>Reflexology wave 3</i>	5.705	1.042	314.482	5.474	0.000*	3.654	7.755
Age	-0.039	0.015	248.517	-2.650	0.009*	-0.068	-0.010
Race	0.535	0.413	250.300	1.294	0.197	-0.279	1.348
Marital status	0.849	0.325	241.848	2.614	0.009*	0.209	1.489
Employment status	0.704	0.330	244.361	2.138	0.034*	0.055	1.354
Religious preference	0.332	0.376	240.016	0.881	0.379	-0.409	1.073
Treatment type	-1.008	0.377	226.888	-2.672	0.008*	-1.752	-0.265

* = significant at $p < .05$

The three-way interaction between study group, time and spirituality was not found to be significant, and thus, was not included in the results table. The two-way interaction between study group and time was significant ($p < .000$), reflecting that the effect of the reflexology intervention on pain significantly changed over time in this model, as expected.

Aim 4: Distinguish how pain level and spirituality may impact engagement with a CIT-based reflexology intervention at baseline, weeks 5 and 11. Neither spirituality nor pain levels were associated with number of reflexology sessions completed during each time interval

(weeks 2-5 and weeks 6-11) when considering demographic/clinical factors. The interactions between pain and spirituality were also not significant at either time point, and therefore, were not reported. In weeks 6-11, participants identifying as Christian (versus non-Christian) and/or those receiving chemotherapy/targeted therapy (versus hormonal therapy) had slightly higher odds of completing more reflexology sessions. See Table 3.5 and Table 3.6.

Table 3. 5 Aim 4 results: The impact of spirituality and pain level on number of reflexology sessions completed in weeks 2-5 (when controlling for demographic/clinical factors)

Parameter	Estimate (β)	P value
Intercept	0.545	0.349
Spirituality	0.072	0.492
Pain level	0.090	0.121
Age	0.004	0.502
Race <i>Caucasian</i> (vs. <i>Non-Caucasian</i>)	0.267	0.146
Marital status <i>Married or partnered</i> (vs. <i>Not married or partnered</i>)	0.128	0.375
Employment status <i>Employed full- or part-time</i> (vs. <i>Not employed full- or part-time</i>)	-0.097	0.512
Religious preference <i>Christian</i> (vs. <i>Not Christian/refused</i>)	-0.081	0.609
Treatment type <i>Chemotherapy/Targeted therapy</i> (vs. <i>Hormonal therapy</i>)	0.159	0.329

* = significant at $p < .05$

Table 3. 6 Aim 4 results: The impact of spirituality and pain level of number of reflexology sessions completed in weeks 6-11 (when controlling for demographic/clinical factors)

Parameter	Estimate (β)	P value
Intercept	2.500	0.118
Spirituality	0.146	0.586
Pain level	-0.047	0.739
Age	-0.027	0.115
Race <i>Caucasian</i> (vs. <i>Non-Caucasian</i>)	0.725	0.136
Marital status <i>Married or partnered</i> (vs. <i>Not married or partnered</i>)	-0.189	0.608
Employment status <i>Employed full- or part-time</i> (vs. <i>Not employed full- or part-time</i>)	-0.217	0.576
Religious preference <i>Christian</i> (vs. <i>Not Christian/refused</i>)	0.762	0.049*
Treatment type <i>Chemotherapy/Targeted therapy</i> (vs. <i>Hormonal therapy</i>)	1.445	0.000*

* = significant at $p < .05$

Discussion

Women with advanced breast cancer experience a significant level of pain (Cleeland et al., 2013; Perroud et al., 2016; Puetzler et al., 2014), which was confirmed by this study. Using previously validated cut-points (B. Given et al., 2008), these women experienced moderate pain, which can significantly impact QOL (Paice & Ferrell, 2011) and can result in cancer treatment dose delays and interruptions (Wyatt et al., 2015). These findings underscore the need for additional support for comprehensive pain management in this population.

Findings revealed that various demographic/clinical factors, including age, marital status, employment status and treatment type, were associated with pain in this sample. Previous studies

have shown mixed results on the association between age and pain (Belfer et al., 2013; Gagliese et al., 2007; Gauthier et al., 2018; Soltow et al., 2010). Two previous studies reported significant associations between marital status and pain (Aneja & Yu, 2016; Posternak et al., 2016). Prior research also supported the association between employment status and pain (Posternak et al., 2016; Rustøen et al., 2003). Although no research was identified which examined relationships between treatment type and pain in advanced cancer patients, this study found that those women receiving hormonal therapy had slightly higher odds of pain. This may be due to the high incidence of joint and bone pain associated with the use of aromatase inhibitors among advanced breast cancer patients (Laroche et al., 2014; Shi et al., 2013).

Multiple demographic/clinical factors were also found to be associated with spirituality, including age, race and religious preference. The association between age and self-reported spirituality is supported by one previous study which yielded similar findings, suggesting that spiritual aspects of life become more salient with increased age (Mystakidou et al., 2008). The finding that women identifying as non-Caucasian had increased odds of a higher spirituality level was also aligned with previous findings. Studies have indicated that African American patients place particularly high value on spirituality in advanced illness (Bai et al., 2018; Gaston-Johansson et al., 2013; Gregg, 2011; Rosenzweig et al., 2009). Other studies have found that the highest percentage of women with breast cancer identifying as “spiritual” were Asian/Pacific Islanders (Levine et al., 2007), and that Asian American breast cancer survivors were more likely to engage in spiritual practices when compared to Caucasian survivors (Levine, Aviv, Yoo, Ewing, & Au, 2009). The finding that women identifying as religious had increased odds of having a higher level of spirituality is partially supported by prior studies (Ahmad et al., 2011; Gaston-Johansson et al., 2013; Nelson & Breitbart, 2002). Studies support the idea that religion

and spirituality are distinct but related concepts (Lazenby, 2018), and that involvement with religion can strengthen aspects of spirituality such as connection to others and connection with a higher power (Sherman et al., 2015).

Self-reported spirituality was not found to impact pain in this sample of women with advanced breast cancer. This finding contrasts with previous studies which yielded significant relationships between pain and spirituality in various samples of cancer patients (Bai et al., 2018; Delgado-Guay et al., 2016; Hui et al., 2011; Wang & Lin, 2016). This null finding could have been a result of the especially high level of self-reported spirituality within this sample (mean=3.2 out of 4), and thus, little variation in spirituality levels. Previous studies found that higher self-reported spirituality may be associated with greater openness toward CIH therapies (Hsiao et al., 2008; B. Smith et al., 2008a). Due to the nature of the parent study (a CIH intervention, reflexology), women with higher spirituality may have been more likely to enroll than those with lower spirituality. Therefore, the women enrolled in this study may have important differences compared to the entire population of women with advanced breast cancer. Since enrollment in the CIH trial may have influenced results, future research examining spirituality level and impact of spirituality on pain in a sample representative of the overall population of women with advanced breast cancer may provide additional insights.

Spirituality did not impact the uptake of the CIH self-management intervention. This finding is in contrast to previous studies which suggest that higher self-reported spirituality may be related to higher use of self-management interventions (Harvey, 2008; Polzer & Miles, 2005; Zarei et al., 2015). Since the intervention was caregiver-delivered, women were reliant on caregivers to complete their sessions. Thus, various caregiver characteristics or relationship dynamics could have impacted intervention engagement. Understanding the factors associated

with intervention engagement could help predict which patients are most likely to be successful with various interventions. For example, previous work has identified that expectations related to the success of CIH interventions may influence intervention engagement (Rottman, Wyatt, Crane, & Sikorskii, 2020). Research exploring additional patient and caregiver characteristics in relation to intervention engagement is warranted.

Limitations

This study has some limitations to note. First, the sample had low diversity and all women were enrolled in a CIH intervention trial, so findings may not be generalizable to other populations. Additionally, a one-item pain measure is not optimal when examining this complex concept, so specific intricacies of women's pain experiences may have been missed. Since this was a secondary analysis, available measurements were limited. Future research can account for this limitation by using more comprehensive instruments that can examine the complexities of pain. Specific types of pain (acute, chronic, somatic, visceral, neuropathic, etc.) were not assessed, and should be considered in future work. Finally, the use of a lay caregiver-delivered intervention to examine spirituality's effect on intervention engagement is less ideal for a study of this nature. In the parent study, the women with advanced breast cancer likely had a high degree of control over practicing reflexology, but the effect of the caregiver's willingness to engage in the intervention could not be accounted for. Despite these limitations, this work contributes novel insights that may be used to enhance nursing care for women with advanced breast cancer.

Implications for Nursing

These findings provide one of the first examinations of the impact of spirituality on pain among women with advanced breast cancer. Information on which sub-populations of women

are most at risk for issues with pain and spirituality were revealed, which can impact nursing practice and research. Oncology nurses can identify women who may be in need of additional support with pain management. Nurse researchers can use this information to control for important demographic and clinical factors in future studies and to develop targeted interventions for sub-groups of women. Although no significant relationship between level of self-reported spirituality and pain was found, this study does underscore the need for enhanced pain management for women with advanced breast cancer. This sample of women had moderate pain on average, indicating a need for additional research in this area. Further understanding cognitive and emotional aspects of pain among women with advanced breast cancer could be a promising avenue. Future research could focus on developing nurse-led pain management interventions, with mechanisms targeting cognitive and emotional routes, possibly including spirituality. Since pain and spirituality are significant aspects of the advanced breast cancer experience, oncology nurses are urged to holistically manage pain and support spirituality with these women.

Conclusion

Despite significant advancements in care, this sample of women with advanced breast cancer reported experiencing moderate pain. Multiple demographic/clinical factors were found to be associated with pain level (age, marital status, employment status and treatment type) and spirituality (age, race and religious preference). Level of self-reported spirituality was not associated with level of pain in this sample of women; although further investigation is needed. Level of self-reported spirituality and pain were not associated with uptake of the reflexology intervention. Overall, pain and spirituality are important aspects of the disease experience for women with advanced breast cancer.

Knowledge Translation

- Women with advanced breast cancer experience moderate pain, on average.
- Women with certain demographic/clinical characteristics may be at higher risk for experiencing issues with pain and spirituality. Nurses need to employ regular assessments of pain and spirituality in this population.
- Since enhanced pain management is needed in this population, future nursing interventions may consider targeting cognitive and emotional aspects of this symptom.

CHAPTER 4: PAIN AND SPIRITUALITY IN WOMEN WITH ADVANCED BREAST CANCER: INSIGHTS FROM A PHENOMENOLOGICAL QUALITATIVE STUDY

Abstract

Background. Women with advanced breast cancer continue to experience significant pain. Previous studies indicate that spirituality may serve as a resource to alter how pain is perceived; although the impact of spirituality on pain has not yet been examined as a lived experience among women with advanced breast cancer.

Objective. This study qualitatively explored how women with advanced breast cancer describe their experiences with spirituality, their pain, and how they perceived their spirituality as impacting their pain.

Interventions/Methods. A phenomenological approach was taken to examine this objective. Self-Transcendence Theory guided the study design. Women were recruited via tumor registry mailings through a community cancer center. Face-to-face semi-structured interviews (N=9) were conducted. An inductive, interpretive approach to data analysis was employed, using open-coding thematic analysis.

Results. Participants were primarily Caucasian, Christian, with mean age=61. Findings revealed the complex, multidimensional nature of pain and the broad encompassing experiences of spirituality among these women. Themes included: 1) Spirituality provides positive cognitive framing to help women face pain; 2) Spirituality brings about positive emotions such as peace and tranquility despite pain; 3) Spiritual practices serve as pain self-management tools; and 4) Connection with others and service activities (aspects of spirituality) help women cope with pain.

Conclusions. While various routes were mentioned, most women found spirituality to positively alter their experiences with pain. Greater attention to spirituality may open new avenues of research and ultimately expand nurse-designed pain management interventions.

Implications for Practice. Nurses can assess spirituality in their patients, understanding that spirituality is a unique phenomenon that may impact symptom management.

Introduction

Despite significant advancements in symptom management, a high proportion of women with advanced breast cancer report pain (Puetzler et al., 2014). The overall five-year relative survival rate for women with metastatic breast cancer is low (15-22%) (American Cancer Society, 2019), making symptom management a critical concern for these women. Inadequate management of pain inhibits comfort, impedes quality of life (QOL), and may even be associated with reduced survival times for cancer patients (National Comprehensive Cancer Network, 2018). Pain is also one of the most feared and burdensome symptoms of cancer (Van den Beuken-van Everdingen et al., 2007), calling for additional research which can guide comprehensive management.

Pain has been defined as a distressing experience which has interacting sensory, cognitive and emotional components, which may be associated with actual or perceived tissue damage (Bushnell et al., 2013; International Association for the Study of Pain, 1979; Wang et al., 2016; Williams & Craig, 2016). Being a complex, multi-dimensional phenomenon, the experience of pain is known to be modulated by alterations in thoughts and feelings (Bushnell et al., 2013; Peters, 2015; Zeidan & Vargo, 2016). Pain in advanced cancer can be exacerbated by negative thoughts and feelings associated with uncertainty about the future, lack of control, and fear of death (Arnstein, 2018; National Cancer Institute, 2018). Novel approaches are needed which can

alter these negative thoughts and feelings, therefore improving the overall experience of pain; Spirituality is one area which warrants further investigation (Flanigan et al., 2019).

Women with advanced breast cancer have cited spirituality as an important resource for facing their disease experience, including their symptoms (Krigel et al., 2014; Mosher et al., 2013). Spirituality is difficult to define, but is often conceptualized as a human process of experiencing connection and meaning (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016). Spirituality is most commonly defined as a dynamic process by which humans experience connection with self, others, nature and/or higher power and a sense of meaning (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016), which may serve as a resource when facing cancer and its associated symptoms (Flanigan et al., 2019; Krigel et al., 2014; Mosher et al., 2013; Visser et al., 2018). Spirituality can contribute to a broader cognitive understanding of the self and of the universe (Harvey, 2008), making a painful experience seem less significant overall. Additionally, spirituality may offer feelings of emotional safety and security in the face of difficulty (Gregg, 2011; Yeager et al., 2016). Due to these positive effects on thoughts and emotions, spirituality may be one avenue for altering the psychological aspects of pain, serving to modulate painful experiences (Keefe et al., 2004; Wiech et al., 2009). Additionally, there is evidence that spirituality may increase the use of self-management interventions focused on relieving pain (such as exercise, relaxation, medication adherence and activity cycling), thus indirectly improving this symptom (Harvey, 2008; Zarei et al., 2015).

Previous quantitative studies have reported significant relationships between pain and spirituality in varying samples of cancer patients (Bai et al., 2018; Delgado-Guay et al., 2016; Hui et al., 2011; Wang & Lin, 2016), yet there have also been conflicting results (Miller et al., 2020, under review). The impact of spirituality on pain has not yet been examined from a

phenomenological perspective among women with advanced breast cancer. Additionally, explanations of the potential mechanisms underlying the relationship between spirituality and pain have not been explored. Understanding how spirituality may contribute to the overall experience of pain could be the first step in developing comprehensive pain management interventions, which include spirituality. Qualitatively exploring how women with advanced breast cancer describe their lived experience with pain and spirituality, this study intends to provide insight into how these concepts relate.

Pamela Reed's theory of Self Transcendence (ST) was adopted as a conceptual framework for this research (P. Reed, 2015). The theory of ST includes the concepts of vulnerability (awareness of mortality), ST (expanding boundaries on multiple personal levels), well-being (subjective sense of health or wholeness), and personal/contextual factors (P. Reed, 2015). Modified for this study, advanced breast cancer is the condition which contributes to vulnerability, spirituality is aligned with ST, and the lived experience of pain is the outcome which indicates one aspect of well-being. With modifications, ST theory indicates that spirituality may impact the way pain is experienced in women with advanced breast cancer.

Purpose

This study explored the meaning of both pain and spirituality for women with advanced breast cancer and examined the lived connection between women's spirituality and their pain experiences using a phenomenological approach. Understanding how women live out their spirituality, and its possible impact on their pain, provides new insights which can potentially improve comprehensive symptom management.

Methods

This study employed a qualitative approach, using interpretive phenomenological analysis (IPA) as the guiding methodological framework. IPA aims to provide the detailed account of personal lived experiences of the participants (Jonathan Smith, Paul Flowers, & Michael Larkin, 2009). This approach is viewed as a co-construction of meaning between participants and investigators, as understanding of the patients' perspectives can only be gained through interpretive analytic work of the investigators (J. Smith, 1995). IPA is particularly well-suited for topics which are complex, ambiguous and emotionally laden (J. Smith & Osborn, 2015), such as pain, spirituality and their relationship. In this study, the IPA approach included in-depth semi-structured interviews and open coding thematic analysis. Institutional Review Board approval was obtained before beginning the research.

Participants and Setting

Women were recruited based on the following criteria – Inclusion: 1) age ≥ 21 years; 2) documented diagnosis of stage III or IV breast cancer; 3) able to speak English; 4) access to telephone; 5) able to hear normal conversation; 6) cognitively oriented; 7) living ≤ 40 miles from recruiting location; and 8) pain ≥ 2 on a 0-10 scale. Exclusion: 1) diagnosis of major mental illness (such as schizophrenia or bipolar disorder) which could impact ability to participate.

Recruitment included sending mailings via the tumor registry at a community-based cancer center. Potentially eligible women were identified based on a search through the tumor registry using the inclusion criteria. Mailings included a letter from the investigators, a flyer with study information, and a pre-stamped post card which was to be sent back to indicate interest in participation. Women were offered a \$25 gift card as compensation for their participation.

Mailings were sent out to 140 women with an 23% return rate. Primary reasons for non-participation included: Too busy, Not interested, Not currently experiencing pain.

Data Collection

Data were gathered through nine in-depth semi-structured interviews which were primarily completed in participants' homes. Using IPA methods, data collection continued until additional interviews did not result in new themes (saturation), which generally occurs within 6–12 interviews (Guest, Bunce, & Johnson, 2006). The interview process included developing rapport, conducting informed consent, conducting the in-depth semi-structured interviews and then completing standardized interview forms. Interview forms contained self-report questions about demographics, pain intensity and spirituality. Participants were asked to complete each form with pen and paper. Pain was assessed using a 0-10 rating scale, including “worst pain over the last 24 hours” and “average pain over the last 7 days”. This assessment was based on the Patient Reported Outcomes Measurement Information System (PROMIS) – 29 Profile v1.0 pain intensity item. Extensive testing of reliability and validity has been conducted on the entire PROMIS-29 Profile v1.0, yielding strong evidence of validity and $\alpha = 0.92\text{--}0.96$ in a large study with cancer patients (R. Jensen et al., 2015). Spirituality was assessed using the Long-Term Quality of Life [LTQL] Philosophical/Spiritual subscale. The LTQL spirituality assessment includes 11 items reflecting increased insight and appreciation since cancer diagnosis (connection with self/others/higher power/nature, meaning and heightened awareness of mortality) on a 0-4 rating scale, where higher scores reflect higher self-reported spirituality (Wyatt & Friedman, 1996; Wyatt et al., 1996). This assessment uses a broad existential approach to spirituality which can apply to all women regardless of religiosity (Wyatt & Friedman, 1996; Wyatt et al., 1996). The LTQL philosophical/spiritual subscale has established evidence of

validity (Wyatt et al., 1996) and high reliability ($\alpha=.80$) (Kamp et al., 2019). This information on demographics, pain intensity and spirituality was used to characterize the sample.

Following IPA procedures developed by J. Smith (1995), an interview guide was created to outline areas of interest to be discussed in the interview. This interview guide was developed in collaboration with content experts and experienced qualitative researchers, using the theory of ST and the accompanying model for conceptual grounding (P. Reed, 2015). Beginning with a broad question to explore women's experiences with advanced breast cancer, the emphasis of the interview was then on encouraging participants to discuss their experiences with pain and spirituality to gain insights into the nature of these phenomena and their potential relationship. This was done by posing broad open-ended questions and then offering more specific follow-up questions. The interview guide was not meant to be prescriptive; questions were adapted as necessary throughout the interview process to fit the exact context and to gain greater depth and clarity when necessary (J. Smith, 1995). See Table 4.1 for an overview of the questions included in the interviews.

Table 4. 1 Interview Questions

Primary Questions	Follow-Up Questions
Tell me about your journey with breast cancer.	
Please describe your experience with pain.	How does pain impact your experience? What are your painful sensations like? What are your thoughts like when you're experiencing pain? What are your emotions like when you're experiencing pain? When do you most feel pain? - If you're feeling pain, how long does it usually last? Do you experience pain on a regular basis? What types of things help you when you feel pain? - Do your activities vary by the level of pain? How do you cope with your pain/illness?

Table 4.1 (cont'd)

How does spirituality impact your experience?	What does spirituality look like for you? Do you engage in any spiritual practices? If so, how would you describe them? How do you express/connect with spirituality? [How] Has your spirituality changed since your breast cancer diagnosis? [How] Has your awareness of your beliefs/values/dreams changed since your breast cancer diagnosis? - What role does intuition (or “inner guidance”) have? [How] Have your relationships with others changed since your breast cancer diagnosis? [How] Has your relationship with nature/the environment changed since your breast cancer diagnosis? Could you describe any connection(s) you feel with a higher power, or anything beyond the ordinary/observable world? When you think about your past experiences and your future, what gives your life meaning?
[How] do you see your spirituality as impacting your pain?	Please describe your thoughts/beliefs about the relationship between your spirituality and pain. How would you describe your thoughts/beliefs about the purpose/meaning of your pain?
Are there any final thoughts you would like to share?	

Preparation for interviewing included consultation with experienced phenomenological researchers and review of landmark phenomenological texts (Benner, 1994; J. Smith, 1995; Van Manen, 1997) to gain understanding of broad and inclusive ways to explore the phenomena of interest. The first author conducted all interviews, accompanied by a research assistant. Interviews were audio recorded and transcribed by a hired transcription service. Field notes were completed after each interview and throughout the research process.

Data Analysis

Qualitative data analysis commenced as soon as data collection began. Data were confidentially transcribed verbatim and coded by hand. Following the analytic traditions of IPA,

an inductive, interpretive analysis approach was used, where themes were allowed to emerge from the data, rather than applying preconceived constructs (J. Smith & Osborn, 2015). Verbatim transcripts of the qualitative interviews served as raw data and the analysis followed IPA procedures outlined by J. Smith (1995). Based on these pre-defined procedures, analysis included the following steps: 1) Interview transcripts were read and re-read multiple times to ensure a thorough understanding of the entire interview; notes were taken, but no codes or themes were applied during this stage; 2) Starting at the beginning of each interview transcript, the text was re-read and initial codes were identified, hand-writing them in the margins; 3) Attention was then focused on the themes, applying definitions and establishing interrelationships; following additional readings, emergent codes were condensed, and themes were developed; definitions were organized into a codebook and data were then sorted electronically; 4) Themes were organized into consistent and meaningful statements about the data; representative participant quotes were selected for each theme.

For the first four interviews, two investigators independently reviewed the data. These investigators met to discuss the analysis, develop preliminary codes and determine areas which required further exploration. Throughout the data collection and analysis process, the two investigators met regularly to discuss the data and emerging themes. As with other studies following IPA procedures, this process was not intended to produce a single definitive analysis or a certain inter-rater reliability score, but rather to verify that the analysis presented by the first author was systematically achieved and supported by the data (Osborn & Smith, 1998). Finally, the refined list of themes and representative participant quotations was reviewed by all investigators.

For qualitative work, attention to trustworthiness (including credibility, dependability, confirmability, transferability and authenticity) is paramount (Connelly, 2016; Noble & Smith, 2015), and was built into this study at multiple points. Trustworthiness was maintained by creating a codebook throughout the data analysis process which linked each emerging code and theme to its intended meaning (Lincoln & Guba, 1985), discussing findings between two separate coders at multiple points throughout the analysis process (McAlister et al., 2017; Noble & Smith, 2015; J. Smith, 1995), and cross-checking each major code with data collected from multiple participants (triangulation) (Guion, 2002). Further, trustworthiness was facilitated with the use of meticulous field notes after each interview, maintaining analytic memos throughout the data analysis process, describing details about the context of the research in this published report (Glesne, 2015; Holloway, 1997) and presenting verbatim evidence along with each proposed theme (J. Smith, 1995). Each of these measures were taken to ensure optimal trustworthiness of results.

To characterize the sample of women in this study, descriptive statistics were examined. This analysis was conducted using SPSS Version 25.0. Analysis included calculating means for relevant personal characteristics, level of pain and level of spirituality.

Results

Nine women with advanced breast cancer were interviewed individually in early 2020. Duration of the interviews ranged from 45-60 minutes each. Eight of interviews were completed at the participants' homes and one was completed in a private room at the College of Nursing research office, according to participant preference. Participants in this study were predominantly Caucasian, married women with high levels of education. Mean age was 61. Women had Stage III or IV breast cancer and most were receiving hormonal treatment. In this

sample of women, average pain over the last 7 days was 3.5 out of 10, indicating moderate levels of pain (B. Given et al., 2008). Mean spirituality was 3.1 out of 4, indicating relatively high levels of spirituality (Wyatt et al., 1996). See Table 4.2 for an overview of participant characteristics and Table 4.3 for means of relevant variables in this sample of women.

Table 4. 2 Participant Characteristics

Characteristic	(N =), n (%)
Stage of cancer	
III	3 (33)
IV	6 (67)
Treatment type	
Chemotherapy or targeted therapy (with or without hormonal)	3 (33)
Hormonal therapy only	4 (44)
Unknown	2 (22)
Race	
Caucasian	9 (100)
Black or African American	0 (0)
Other	0 (0)
Ethnicity	
Hispanic or Latina	0 (0)
Not Hispanic or Latina	9 (100)
Employment	
Full time	2 (22)
Part time	1 (11)
Unable to work	2 (22)
Retired	4 (44)
Education	
High school graduate (or GED) or some high school	0 (0)
Some college or 2-year degree	3 (33)
4-year college graduate	4 (44)
More than 4-year college degree	2 (22)
Marital Status	
Never married	1 (11)
Married or living with partner	5 (55)
Divorced/separated	2 (22)
Widowed	1 (11)
Spiritual/Religious Preference	
Christian	9 (100)
Jewish	0 (0)
Buddhist	0 (0)
Hindu	0 (0)
Other	0 (0)
None	0 (0)

Table 4. 3 Means of Relevant Variables

Variable	Mean
Pain level (average over 7 days; 0-10)	3.5
Pain level (worst over 24 hours; 0-10)	5.6
Spirituality level (0-4)	3.1

Overall, findings from this study support the complex, multidimensional nature of both pain and spirituality. Pain was described as a broad, dynamic experience that impacted many other areas of life. Some women experienced ongoing pain, while others had a more cyclical relationship with this symptom. Participants often specified if they were referring to “physical” or “emotional” pain, while some women seemed to talk about these aspects interchangeably. Many women described pain as being intertwined with other symptoms and discussed how their symptom experiences changed throughout their advanced breast cancer journey.

The phenomenology of spirituality was described in broad and encompassing ways. Overall, spirituality was experienced as a sense of embodied presence (being in the present moment), often including feelings of appreciation. Spirituality was lived out through connection to one’s own sense of a higher power, family, nature, pets and community; each seen as useful resources when facing pain. For some women, spirituality also encompassed specific spiritual practices and service activities which helped women cope with pain. Themes were identified to characterize how spirituality impacted the experience of pain for these women. Themes included: 1) Spirituality provides positive cognitive framing to help women face pain; 2) Spirituality brings about positive emotions such as peace and tranquility despite pain; 3) Spiritual practices serve as pain self-management tools; and 4) Connection with others and service activities (aspects of spirituality) help women cope with pain. Overall, depth and breadth were provided

around the phenomenon of spirituality and how it can impact experiences of pain among women with advanced breast cancer.

Theme 1: Spirituality provides positive cognitive framing to help women face pain

Participants shared how spirituality provided a positive frame of mind in which to interpret their experiences with breast cancer, and specifically with their pain. Women described how this positive mental frame altered their relationship with pain. One participant shared that her bone metastases were so painful around her diagnosis that she lost nearly all function, including her ability to stand and walk. Her recovery, despite continued pain, has been supported by her spirituality, which she described as bringing about positive framing on the situation and a sense of gratitude.

“I’ll talk about God a little bit... You go through life and you’re always saying in your prayers, what you want... “Well God, I’d like to have a good day today and well, God, I’d like for you to bless my daughter so that she can get a new job or I would like you to bless my”— you’re always asking for something... What I found is that when you have nothing, you can’t even get up and go to the bathroom, when you have nothing, you become very grateful for what you have... There comes up an acceptance, it’s like I’m grateful. I stand upright. I’m grateful that I walk. I am grateful that I can sit in my chair for more than 15 minutes. I’m grateful that like, I don’t have my back brace on right now. I’m grateful that I’m getting better. I’m grateful for my home, my family, my improving health, and I’m grateful for any time I have left. I refuse to waste one minute being upset about what might happen.”

Women often talked about how spirituality brought about a positive mindset for them during challenging times, allowing women to let go of fears and worries. This positive mindset was described as an asset when facing pain.

“If you work it up, that’s going to be terrible. It is. I’m a firm believer that whatever your mind believes every fiber in your body makes it come true. It is a self-fulfilling prophecy and so it’s very important to check your mindset. Like when you get up in the morning, it’s like today’s going to be a good day. I don’t try to trick myself into saying there will be no pain because I know there will be, but it’s going to be a good day... I’ve [studied a lot about] how Christ has come, and He has freed you from the chains of sin and bondage. That’s a great gift embrace it. Use your freedom. He says, I’ll take care of burden, okay,

go give to you. He says, don't worry about tomorrow, okay, I won't. I don't need to do those things."

Overall, spirituality was found to serve as a positive resource which helped women frame their experiences with pain. With this positive frame, women were able to better face various difficult experiences associated with their cancer diagnoses, including pain.

Theme 2: Spirituality brings about positive emotions such as peace and tranquility despite pain

Participants reported that their sense of spirituality provided moments of peace and tranquility amidst their challenging circumstances, including their pain. Women described feeling a presence of something greater than themselves, providing solace during difficult painful times.

"I just feel like if you're in a better mental headspace... I mean, I talked today about God, but I really believe that there are some people that it could be Buddha or any level of spirituality if you just have that connection and can help calm yourself. I think anxiety and being overwhelmed or just feeling anxious can make pain worse."

Intentionally connecting with a higher power, however this was understood, was seen as a way to tap into this peaceful, calm state, even in the midst of discomfort. Women primarily accessed feelings like calm and tranquility through connection with a higher power, often by practicing prayer or meditation.

"They [family] see me in pain or discomfort or when I can't do something, which I can do a whole lot more than I could before, but it still—and I think, "Thank you, God, for getting me this far." Then I start havin' conversations [with God]. It reduces my fear of the unknown. It reduces my pain, physical pain, considerably. It's like it just eases up."

Overall, women described positive emotional effects of their spirituality on their experiences with pain. These included feelings of peace, tranquility, acceptance and calm amidst challenges such as facing advanced breast cancer and pain. Women accessed these positive

emotional effects in many ways, including intentional connection with their sense of a higher power.

Theme 3: Spiritual practices serve as pain self-management tools

Various spiritual practices were cited as important for women when coping with pain. Spiritual practices were seen as activities which allowed participants time and space to quiet the mind, explore habitual ways of thinking and connect with a sense of something greater. Prayer, meditation, visualization, reading spiritual texts and creating art were discussed as spiritual practices that women employed which could impact their experiences with pain. Prayer was seen as a way to connect with a sense of something greater than oneself and to ask for help.

“You pray because like I said, I don’t want to be hooked on any drugs. I don’t want to take drugs. I would prefer not to. You just pray that God will relieve that pain and that’s pretty much what I do. Sometimes He does. Sometimes He doesn’t.”

Women described prayer and meditation as providing a focus which could quiet the mind of worries and ruminations, which brought about a sense of comfort amidst pain. These spiritual practices also provided positive distraction from pain, redirecting negative thoughts and emotions which tend to exacerbate this symptom.

“I found, all of a sudden, it’s like, wow, this really works, this deep breathing, concentrating on in and out, breathing deep. I started realizing that I was doing that at the same time that I was praying in my head, or even sometimes, if it [the pain] got bad, I’d start sayin’ it out loud...”

Visualization practices were common techniques that women used to cope with pain, which some considered an aspect of their spirituality. Women employed various visualization techniques and often reported relief from their use.

“For me, at that time in my life, especially when I was first diagnosed and not feeling great [experiencing pain] and all the uncertainty, spirituality was a big help for me. I did a lot of visualization, and so I visualized that at night, I was sleeping in God’s hands. I was sleeping in his hands, and I was sleeping in his radiant light. That’s how I would fall

asleep at night. Every night, I would be like, I'm in God's hands, and he's gonna heal me. That was just my visualization and my mantra."

"If you focus on your pain, that's what you are focused on, that's what's going on and the receptors are yelling at you. I think it's real important not to focus on pain. It's almost like, a block. If you can build a little brick wall up there, and go okay pain's over here and the rest of my life's over here, I guess I do a lot of mental imagery to control pain and to let God's help come in.... I think it's very important, the coping mechanisms of shutting the pain away and building a block, a wall, and trying to stay physically active and listening to God, I think all of that is very important for pain control."

Spiritual practices such as prayer, meditation and visualization were found to be important activities which helped women cope with challenges such as pain. These practices, among others, were used in the moment of facing pain and were experienced as providing inner quiet and comfort.

Theme 4: Connection with others and service activities (aspects of spirituality) help women cope with pain

Connection and service activities each had the capacity to positively impact pain for some women. Participants described focusing on connection to family, friends, pets, and other people with cancer as a source of strength when facing advanced breast cancer and dealing with pain.

"If you aren't healthy mentally that can translate into having more body pain... I think spirituality and just having that connection typically brings you to a circle of people that can help with that, too, so that gives me more of a tribe, so I have people to talk to and connect with. I think that also makes you feel better so you're not alone... So having that spirituality then leads to connection with other women and other people."

When asked about how spirituality plays out in their lives, many participants talked about engaging in service activities. Women described how participation in varied types of service activities (which many considered part of their spirituality) was beneficial when facing pain. Service activities such as volunteering and sharing knowledge with others provided a broader

perspective on their individual lives and contributed to their sense of purpose. Participating in these service activities also brought positive distraction to women when they were facing pain.

“That week I’m [leading the survivorship retreat], it’s not about my cancer or my pain. You know what the craziest thing is? This is gonna sound crazy, but seriously, that week I was there... I did not have pain. I remember thinking, this is gonna be scary. I’m in charge, and I’m gonna be up early and stay up late. I hope that my body can do this, and it did. I flew away thinking, I really didn’t have pain. I think ‘cause I was so focused on helping everybody else and making sure that they were having an amazing time.”

Overall, connection with others and engagement in service activities were found to be significant aspects of spirituality that were helpful for women when they faced pain. These connections took many forms, including connection with family, friends, pets and other people with cancer. Service activities also varied but seemed to provide numerous benefits. Overall, experiences of connecting with others and engaging in service activities (described as aspects of spirituality) provided women with a sense of purpose and positive distraction, both beneficial when facing pain.

Discussion

Women in this study discussed pain as a dynamic experience that impacted many aspects of their lives. Participants experienced pain as being intertwined with other symptoms to create an inclusive experience that they often referred to broadly as “pain”. Overall, this study highlights how spirituality can serve as a positive resource to help women face experiences of pain in advanced disease. Many women in this study experienced spirituality as an asset when facing pain; although, spirituality was lived out differently by each participant. These women with advanced breast cancer often experienced spirituality as a sense of present moment awareness, appreciation and connection with something greater than oneself. Spirituality was lived out in broad and encompassing ways, including connection to one’s own sense of a higher power, family, nature, pets and community. For some women, spirituality also encompassed

service activities and spiritual practices, which helped bring about present-moment awareness, quiet the mind, reframe thoughts and connect to a sense of meaning when facing pain. The phenomenological view of spirituality uncovered in this study aligns closely with the conceptual approach to spirituality described in current literature (Steinhauser et al., 2017; Sun et al., 2017; Weathers et al., 2016).

Women in this study consistently described a deeper integration of their spirituality into their lives since diagnosis of advanced breast cancer, which was seen as an asset when facing pain. Prior research supports the finding that spirituality can become more salient after a diagnosis of serious illness (Krigel et al., 2014; Mosher et al., 2013). Women who were able to integrate their spirituality into their lives seemed to have a stronger foundation from which to face their cancer and their pain. For example, participants talked about the importance of incorporating their experience of spirituality into their daily lives, rather than compartmentalizing it into only one day a week. These findings support the idea that spirituality is a phenomenon which is broader than following a specific religious tradition (Lazenby, 2018); it is a unique, dynamic experience of embodied presence (being in the present moment) that can be beneficial for women when they are experiencing pain.

Spirituality was found to be a powerful cognitive reframing technique, which positively altered emotional states, and therefore positively impacted the experience of pain for many women. Previous research supports the idea that the frame or meaning ascribed to pain can alter the painful experience (Arntz & Classens, 2004; Peters, 2015). Some women seemed to automatically tend toward positive framing of their advanced breast cancer diagnoses and pain experiences through spirituality, others described continually working toward this positive view,

while a few women in the study did not seem to align as strongly with a spiritual framing on their circumstances.

The current study uncovered how spirituality can bring about positive emotional states (such as peace and tranquility), which many women found beneficial when facing pain. Prior evidence suggests that aspects of spirituality, such as connection with a higher power and meaning, may provide a sense of safety and security in the face of difficulty (Gregg, 2011; Yeager et al., 2016), and that emotional states can significantly impact pain experiences (Lumley et al., 2011; Raphael et al., 2010). Women in this study talked about how spirituality provided solace when facing fear, anxiety or feelings of overwhelm, which then helped decrease their pain. This finding is supported by prior work showing that activation of fear, anxiety and anger can exacerbate pain while positive emotions such as relaxation and calm can lessen this symptom (Bushnell et al., 2013; Peters, 2015). Findings from this study support the idea that pain has interconnected physical, cognitive and emotional components which work together to create the total painful experience (Bushnell et al., 2013; Wang et al., 2016; Williams & Craig, 2016).

Previous research supports the use of practices such as meditation, prayer and visualization as components of comprehensive pain management (Eilami, Moslemirad, Naimi, Babuei, & Rezaei, 2019; Kwekkeboom, Cherwin, Lee, & Wanta, 2010; Wren et al., 2019; Zeidan & Vargo, 2016). Women in this study reported finding comfort in these practices, seeing them as opportunities to redirect negative thoughts and provide positive distraction, which is supported by prior research (Kwekkeboom et al., 2010). Alterations in emotions and opportunities for distraction can both be powerful in the modulation of pain experiences (Bushnell et al., 2013). In this study, women employed varying spiritual practices (with a main

focus on prayer, meditation and visualization) when facing pain, and described a sense of relief from their use.

Women in this study also described connection with others and service activities as important aspects of their spirituality, which played a role in coping with their pain. Various types of social support have been found to be important to the experience of pain in women with breast cancer (Hughes et al., 2014) and prior research highlights the importance of social support when facing pain (Davis, 2020; Galloway, Meadors, Boselli, & Walsh, 2019). Women in this study described the importance of service activities in their experience of pain, which is aligned with prior findings that chronic pain sufferers who engaged in volunteer work reported a greater sense of purpose and decreased pain (Salt, Crofford, & Segerstrom, 2017). Overall, the sense of safety, comfort and positive distraction provided by connection to others and service activities can be important for women with advanced breast cancer when facing pain.

Participants in this study described varying degrees and interpretations of spirituality. Despite most women in this study relaying a strong personal sense of how spirituality impacted their pain experiences, a few participants seemed to experience less connection to this phenomenon. Further, a recent study quantitatively examined the impact of spirituality on pain among women with advanced breast cancer and identified no significant association (Miller et al., 2020, under review). These seemingly conflicting findings may reflect the fact that all women with advanced breast cancer experience varying perceptions of, and experiences with, spirituality. Women in this prior study reported relatively high levels of self-reported spirituality (Miller et al., 2020, under review); therefore it may have been difficult to detect significant quantitative associations. Further, this previous study employed a 1-item pain intensity item (Miller et al., 2020, under review). This approach may not be able to fully capture intricacies of

how spirituality impacts the overall painful experience in the way that qualitative inquiry could. Finally, women in the current study were enrolled based on their interest in talking about the potential benefits of their spirituality on their pain, thus, women who were interested in this topic were likely more inclined to enroll. Because the findings of the current qualitative study reflect potential benefits of spirituality for some women when facing pain, further research is needed to examine methods for facilitating lived experiences of spirituality among patients with advanced cancer who experience pain. Additionally, findings support further exploration into the factors which may contribute to formation of spiritual beliefs and practices among a more diverse sample of women with advanced breast cancer.

The Theory of ST, which guided this work, was partially supported by the findings. Many women described an enhanced sense of spirituality subsequent to their advanced breast cancer diagnosis. This aligns with Reed's view of vulnerability facilitating ST (P. Reed, 2015). ST theory was also supported in that spirituality was seen as a positive resource, having the capacity to impact experiences of pain. This is aligned with Reed's description of ST leading to enhanced well-being (P. Reed, 2015). One finding that was not aligned with ST theory was that some women also described their experiences with pain as impacting their relationship with spirituality (in both positive and negative ways). Women described how experiences with pain opened them up to seek something greater in an effort to self-manage this symptom. On the negative side of this relationship, women talked about how their pain often impeded their ability to connect with others and to attend their regular spiritual and religious activities. These findings extend ST theory, with the added dimension that well-being (operationalized as pain in this study) may have the capacity to alter spirituality (ST) among women with advanced breast cancer.

Limitations

As with all studies, limitations exist. First, this sample of women were extremely homogenous, with the majority identifying as Caucasian, Christian and married. Due to the nature of the study, women who had a greater connection to spirituality and a greater sense of how spirituality impacted their pain experiences may have been more likely to voluntarily participate. These results may not reflect the experiences of spirituality and pain of women from different racial, ethnic and religious backgrounds. Since participants were recruited from one community-based cancer center, this center's management of pain and spirituality likely play a role in the reports from their patients. These findings may not be carried over to other women with advanced breast cancer receiving treatment elsewhere. Because these findings reflect the interpretation of the phenomena of interest (pain, spirituality, and the impact of spirituality on pain) as experienced by a specific subset of women, results cannot be directly transferred to other populations.

Implications for Practice

These findings have the potential to expand nurses' understanding of pain and spirituality for women with advanced breast cancer. This enhanced understanding can facilitate improved management of pain, which may include addressing spirituality. Based on these findings, nurses are encouraged to use multidimensional or open-ended assessments of pain. Further, nurses can explore the unique nature of spirituality in their patients by assessing spiritual needs, with the understanding that pain and spirituality may mean different things to different patients. By encouraging patients to explore their own unique spirituality, patients may experience alterations in their thoughts and emotions, and therefore changes in their symptom experience. Nurses can employ interventions to enhance spirituality, such as meditative practices (Mackenzie et al.,

2007), meaning-centered therapy (Breitbart et al., 2012) or music therapy (Cook & Silverman, 2013), even for women who do not already align with a strong sense of spirituality. These evidence-based interventions may be adapted based on individual preferences and potentially included as part of comprehensive symptom management.

Further Research

Additional research is needed which can further explore how spirituality may impact pain through the alteration of cognitive and emotional states. Research which specifically examines the mechanisms underlying spirituality's positive effects on thoughts and emotions is warranted. Although many women in this study described positive effects of spirituality on their pain experiences, not all participants aligned as strongly with this view. Additional research is needed which can explore individual characteristics and/or other factors that may contribute to women's sense of spirituality, and therefore the capacity for spiritual beliefs and practices to impact their pain.

Further work is needed which can phenomenologically explore pain and spirituality in women of varying racial, ethnic and religious backgrounds. Future research may also continue to examine the role of spiritual practices such as prayer, meditation and visualization in comprehensive pain management, since women in this study found these self-management practices helpful in their daily lives. It must also be acknowledged that some women may benefit from other belief systems to cope with cancer-related pain, so future work can explore additional cognitive and emotional routes to alter pain experiences. Research focused on developing and testing interventions based on individual preferences in spiritual practices, or practices rooted in other belief systems, may be useful.

Conclusion

Returning to the purpose of this study, *Exploring the meaning of pain and spirituality for women with advanced breast cancer, and examining the lived connection between spirituality and pain*, four major themes emerged. These themes lay the foundation for further exploration of the link between spirituality and pain. Pain was seen as a dynamic, multidimensional experience that impacted many aspects of women's lives. Spirituality was unique to each participant, but overall included a sense of present moment awareness, appreciation and connection with something greater than oneself. Spirituality was lived out through connection with a higher power, family, nature, pets and community. Many women in this study described how spirituality served as a positive mental framing technique, which was able to alter their relationship with pain. Women's sense of spirituality was able to support them emotionally, offering a sense of peace and tranquility despite challenges such as advanced breast cancer and pain. For women in this study, spiritual practices were important activities to offer comfort and provide support in self-management of pain. Participants also described the importance of connection to others and service activities for coping with pain. ST theory (P. Reed, 2015) served as a theoretical guide, grounding the focus of the study on the contribution of spirituality to the lived pain experience. Overall, women who had a strong sense of their own unique spirituality were able to experience greater support when facing pain, which positively impacted their experiences with this symptom. This study highlights the importance of integrating spirituality throughout one's life in order to experience ongoing benefits. Further research is needed to explore how these broad aspects of spirituality may be harnessed as part of comprehensive symptom management.

CHAPTER 5: CONCLUSIONS

This dissertation employed a multiple manuscript approach to address a central theme: The impact of spirituality on pain among women with advanced breast cancer. The Theory of Self-Transcendence (ST) was used as the guiding conceptual framework (P. Reed, 2015). Manuscript 1 (Chapter 2) is a scoping literature review exploring how both pain and spirituality have been conceptualized, assessed, and addressed, and how they may be related. Manuscript 2 (Chapter 3) describes a secondary data analysis examining demographic and clinical factors associated with pain and spirituality, the impact of spirituality on pain, and how spirituality and pain relate to engagement with a Complementary and Integrative Health (CIH)-based reflexology intervention. Manuscript 3 (Chapter 4) reports on a phenomenological qualitative study which explored how women with advanced breast cancer describe their experiences of pain and spirituality, as well as their perceptions of how spirituality impacts their pain. Overall, this work highlights the complex, multidimensional nature of both pain and spirituality, as well as the potential value of spirituality for supporting women with advanced breast cancer who are facing pain.

The Theory of ST and the accompanying model (P. Reed, 2015) served as the conceptual underpinning for each of the three manuscripts in this dissertation. This theory and its accompanying model include the concepts of vulnerability (awareness of mortality), ST (expanding boundaries on multiple personal levels), well-being (subjective sense of health or wholeness), and personal/contextual factors (P. Reed, 2015). Modified for this study, advanced breast cancer is the condition which contributes to vulnerability, spirituality is conceptually aligned with ST, and the experience of pain is the outcome which indicates one aspect of well-being. With modifications, ST theory indicates that spirituality may impact the way pain is

experienced in women with advanced breast cancer. As each manuscript is discussed below, aspects of ST Theory will be highlighted which provided the foundation for each component of the overall dissertation.

Summary of the Three-Manuscript Dissertation

Prior research has suggested the potential value of spirituality when facing advanced breast cancer and pain, yet the impact of spirituality on pain in this population had not been examined, leading to this three-manuscript dissertation work. Since pain is constructed of interacting sensory, cognitive and emotional components, altering any of these carries potential to modulate the pain experience (Zeidan & Vargo, 2016). Spirituality may have the capacity to alter negative thoughts and emotions associated with pain, modulating both the cognitive and emotional components and transforming the painful experience. Previous studies support this idea, indicating that thoughts and emotions play a profound role in how pain is experienced (Keefe et al., 2004; Wiech et al., 2009); Spirituality may offer a route to accessing positive thoughts and emotions, such as a sense of safety and security, when facing difficult circumstances (Gregg, 2011; Yeager et al., 2016). Spirituality may also impact pain through a lesser-studied behavioral route, potentially enhancing the uptake of pain management interventions, thus indirectly influencing pain. Research suggests that those with higher self-reported spirituality report using more self-management interventions (Harvey, 2008; Hsiao et al., 2008; B. Smith et al., 2008b; Zarei et al., 2015). Therefore, spirituality may directly impact pain through alterations in thoughts and emotions, and indirectly impact pain by enhancing the uptake of a pain self-management interventions. Building on this prior research, the current dissertation explored the impact of spirituality on pain among women with advanced breast cancer through a three-manuscript approach.

Manuscript 1 is a scoping literature review characterizing how pain and spirituality have been conceptualized, assessed, and addressed, as well as how these concepts may be related, among women with advanced breast cancer. According to ST theory, vulnerability (awareness of mortality, often brought about by a life-threatening diagnosis) can lead to enhanced ST, and ST is seen as a resource to alter well-being. Findings from this review aligned with ST theory in two main ways: 1) Women described a deepening sense of spirituality (ST) after their advanced breast cancer diagnoses (vulnerability); and 2) Results suggested that spirituality (ST) may serve to modulate pain experiences (the aspect of well-being that was assessed, whereas lower pain indicates higher well-being). A gap in understanding spirituality and its influence on pain in this population was identified, which led to the work completed in the next two manuscripts of the dissertation.

Although literature was identified in the scoping review which suggested the importance of spirituality when facing pain, no studies were identified which quantitatively examined the impact of spirituality on pain, leading to Manuscript 2 of this dissertation. Manuscript 2 is a secondary analysis based on a National Cancer Institute-funded randomized controlled trial of home-based, caregiver-delivered foot reflexology (Wyatt et al., 2011-2016). This study found that various demographic and clinical factors were associated with pain and/or spirituality among this sample of women. ST theory proposes that demographic and clinical factors (personal/contextual factors) can impact both spirituality (ST) and pain (well-being), thus, the theory was supported. Based on ST theory, it was hypothesized that spirituality (ST) would significantly impact pain (well-being), yet this hypothesis was not supported. Null findings could have been a result of the especially high level of self-reported spirituality within this sample, and thus, little variation in spirituality levels. Overall, this manuscript yielded the conclusion that

additional work is needed which can explore pain and spirituality with more depth and breadth. This led to the work completed in Manuscript 3 of the dissertation.

Since pain and spirituality are both highly individual phenomena, understanding these concepts in a broad context offers unique insight into how (or if) spirituality impacts the experience of pain. Yet the impact of spirituality on pain had not yet been examined as a lived experience among women with advanced breast cancer. To address this gap, Manuscript 3 describes a phenomenological qualitative study examining pain and spirituality in women with advanced breast cancer, as well as perceived relationships between these concepts. Results revealed that pain was seen as a complex, multidimensional experience that was often intertwined with other symptoms. Spirituality was experienced as a sense of present moment awareness, appreciation and connection with something greater than oneself, lived out in broad and encompassing ways including connection with a higher power, family, nature, pets and community, engagement in service activities and spiritual practices. Themes included: 1) Spirituality provides positive cognitive framing to help women face pain; 2) Spirituality brings about positive emotions such as peace and tranquility despite pain; 3) Spiritual practices serve as pain self-management tools; 4) Connection with others and service activities (aspects of spirituality) help women cope with pain. Although women in this study described positive effects of spirituality on their pain experiences, all women experienced varying degrees and interpretations of spirituality, warranting further research. ST theory was supported by these findings in two main ways: 1) Women described a deepening sense of spirituality (ST) since their diagnosis (vulnerability); and 2) Women described various routes whereby their spirituality (ST) served to positively alter their experiences with pain (the aspect of well-being focused on in this work). These findings are aligned with ST theory in that Reed proposes vulnerability can be

an experience leading to greater ST, and that ST is a resource to enhance overall well-being. ST theory was potentially extended in that some women also described their pain (an aspect of well-being) as impacting their experience with spirituality (ST), in both positive and negative ways. This work sets the stage for future research exploring cognitive and emotional modulation of pain, as well as eventual development and testing of comprehensive pain management interventions, which may include spiritual components.

Seemingly conflicting findings between Manuscript 2 and Manuscript 3 can likely be attributed to the differing study designs and purposes. While Manuscript 2 quantitatively examined impact of spirituality on pain among women with advanced breast cancer, Manuscript 3 phenomenologically explored how women described their lived experiences with spirituality and pain. Manuscript 2 identified no significant relationship between spirituality and pain, while Manuscript 3 reported various routes by which spirituality contributed to lived experiences of pain among participants. These seemingly differing findings may reflect the fact that participants in Manuscript 2 were all enrolled in a CIH intervention trial and had relatively high levels of self-reported spirituality, yielding little variation in spirituality ratings and limited ability to detect a significant association. Further, examining spirituality's impact on pain intensity using a 1-item numerical rating may not have captured the intricacies of how spirituality alters the overall painful experience, while the qualitative study offered a more comprehensive assessment of these phenomena. In Manuscript 3, women were voluntarily enrolled in the study based on their interest in talking about the potential benefits of their spirituality on pain, thus, women who had experienced this were likely more inclined to enroll. Overall, findings from these two manuscripts speak to the promising potential of spirituality to impact pain experiences for some

women with advanced breast cancer, although additional work is needed to explore this phenomenon more thoroughly.

The overall purpose of this dissertation was to examine the impact of spirituality on pain experiences among women with advanced breast cancer. With the theory of ST (P. Reed, 2015) employed as a guiding framework, findings from the three manuscripts advance nursing science by providing new insight into the nature of pain and spirituality among women with advanced breast cancer, and by offering a unique perspective on how spirituality may impact perceptions of pain. The complex and multidimensional nature of pain was highlighted throughout all three manuscripts, with a focus on how cognitive and emotional factors contribute to the experience of this symptom. In this work, women with advanced breast cancer perceived spirituality as being an important aspect of coping with their disease, which also has the potential to impact their symptom experiences. With women reporting moderate pain on average, all three manuscripts in this dissertation reinforce the need for further research to advance comprehensive pain management for women with advanced breast cancer. The Theory of ST was supported, and potentially extended, through findings from each of these manuscripts. This work is the first step in an incremental program of research focused on improving comprehensive pain management for people with advanced cancer.

Limitations

As with all research, limitations must be noted. In Manuscript 1, review methods could have limited the findings. Publications which reported outcomes for different stages of breast cancer together (i.e., stage I–III or I–IV) or which reported outcomes on various types of cancer were excluded. Due to this reporting approach, relevant data may have been embedded in reports and missed in the review. Additionally, although grey literature was screened through multiple

databases for this scoping review, due to the vast and varied nature of this content, some relevant publications may have been missed.

In Manuscript 2, the sample of women included in the secondary analysis had low diversity and all women were enrolled in a CIH intervention trial, limiting generalizability of the findings. Due to the nature of the secondary analysis, available measurements were limited. Using the PROMIS pain intensity item (a one-item pain assessment) is not optimal when examining a complex concept, so specific intricacies of women's pain experiences may have been missed. Specific types of pain (acute, chronic, somatic, visceral, neuropathic, etc.) were not assessed in this study, and should be considered in future work. Next, a lay caregiver-delivered intervention was used to examine spirituality's effect on intervention engagement, which is less ideal. In the parent study, the women with advanced breast cancer likely had a high degree of control over practicing reflexology, but the effect of the caregiver's willingness to engage in the intervention could not be accounted for in this study.

In Manuscript 3, a main limitation is that the sample of women were extremely homogenous. With the majority identifying as Caucasian, Christian and married, findings cannot be transferred to other populations. Since participants were recruited from one community-based cancer center, this center's management of pain and spirituality likely played a role in the reports from their patients. Additionally, participants were enrolled based on their interest in talking about the potential benefits of their spirituality on pain, thus, women who had significant experiences with this phenomenon were likely more inclined to enroll. Thus, these findings may not be directly transferred into other women with advanced breast cancer.

Overall, this dissertation was limited by a lack of racial, ethnic and socioeconomic diversity among participants. Future work which can examine pain and spirituality across more

diverse samples of cancer patients is needed. Further, the use of one-item measures for quantitative assessments of pain is not optimal for a study of this nature. Future research should incorporate broad and multidimensional pain assessments, including assessment of pain type, intensity, severity, interference, along with cognitive and emotional aspects of this symptom. Despite the noted limitations, this dissertation contributes novel insights that may be built upon to enhance nursing care for women with advanced breast cancer.

Implications

Despite numerous advancements in cancer care, women with advanced breast cancer experience significant levels of pain (Flanigan et al., 2019). Spirituality is one area that had not been investigated for its potential to positively impact the experience of pain in this population. This dissertation began addressing the identified gap, exploring the impact of spirituality on pain through a scoping literature review (Flanigan et al., 2019), a quantitative secondary analysis (Miller et al., 2020, under review) and a qualitative study (Miller et al., 2020, in preparation). This dissertation work has implications for nursing research, education, practice and policy, each discussed below.

Nursing Research

This dissertation impacts nursing research by providing a unique approach to examining the concepts of pain and spirituality among women with advanced breast cancer, as well as how spirituality may be employed as a resource for altering how pain is experienced. With the advent of new targeted therapies and new supportive medications, there is likely to be a growing population of women living with advanced breast cancer (Krigel et al., 2014) as well as a growing number of people with different types of cancer (Centers for Disease Control and Prevention, 2019). All three manuscripts in this dissertation revealed that women with advanced

breast cancer experience moderate pain, on average, that spirituality is important to their disease experiences, and that spirituality may alter how pain is experienced. Exploration of the impact of spirituality on pain can now be expanded into broader cancer populations, examining the complex dimensions of pain and how spiritual support may play a role in comprehensive symptom management.

This dissertation approached pain as a complex symptom having physical, cognitive and emotional components. This work adds to the evidence base regarding spirituality's impact on pain, partially supporting the idea that spirituality can alter pain experiences through cognitive and emotional mechanisms. The scoping literature review (Manuscript 1) suggested that spirituality may help women cope with pain, the secondary analysis (Manuscript 2) revealed no significant relationship between spirituality and pain, and the qualitative study (Manuscript 3) uncovered that many women perceive their spirituality as positively impacting their pain through various routes (cognitive and emotional modulation, implementation of spiritual practices and social support through a sense of connection with others). Future nursing research can build on this dissertation by designing studies which explore specific cognitive and emotional mechanisms underlying spirituality's impact on pain in broader samples of people with advanced cancer. This future research may include mixed-methods work to assess the contribution of various thoughts and emotions to experiences of pain, and to explore specific aspects of spirituality which patients may find beneficial.

Manuscript 2 of this dissertation identified certain demographic and clinical characteristics which were associated with pain (younger, not married/living with a partner, not employed, or were receiving hormonal therapy were associated with higher pain) and spirituality (older, non-Caucasian or Christian were associated with higher spirituality) in a sample of

women with advanced breast cancer who were enrolled in a CIH intervention trial. Future research can explore these demographic and clinical characteristics in more depth, potentially leading to the design of targeted interventions to support cancer patients who are experiencing issues with pain and/or spirituality.

Regular engagement with CIH self-management interventions can be an important aspect of pain control. Manuscript 2 found that spirituality was not associated with CIH intervention engagement among women enrolled in a lay caregiver-provided foot reflexology intervention study. Nursing research focused on engagement with CIH interventions is growing (Frambes et al., 2017; Rottman et al., 2020; Wyatt, Sikorskii, Rahbar, Victorson, & Adams, 2010), yet more research is needed to understand which factors are associated with engagement in pain self-management interventions. The null finding in this dissertation could be attributed to the relatively high level of self-reported spirituality in this sample of women (3.2/4), as well as unknown variables related to the lay caregiver's willingness to engage in the reflexology intervention. Thus, future research to explore other factors which may be associated with CIH intervention use is warranted.

Manuscript 3 reported how women qualitatively discussed perceptions of how spirituality impacted their pain, yet some women did not seem to align as strongly with a personal sense of spirituality. This unexpected finding warrants further investigation, as women with a stronger personal sense of spirituality seemed to experience more positive impacts on their symptom experience. Future research is needed to explore factors contributing to formation of spiritual beliefs and practices, or lack of spiritual beliefs and practices, among more diverse samples of people with advanced cancer. Future research can also explore the application of spirituality-enhancing interventions such as meditative practices (Mackenzie et al., 2007), meaning-centered

therapy (Breitbart et al., 2012) or music therapy (Cook & Silverman, 2013) across various groups of cancer patients.

Manuscript 3 also revealed that many women consider their use of CIH interventions as spiritual practices, and that women employ these interventions as pain self-management techniques. Ultimately, this program of research aims to develop holistic pain management interventions, which may include spirituality. Since a high proportion of women with breast cancer are using variations of CIH therapies (Boon et al., 2007; Voi, Höxtermann, Dobos, & Cramer, 2020), continued exploration of CIH-based interventions as holistic pain management tools in this population is needed. Mind-body interventions such as mindfulness meditation (Wren et al., 2019), prayer (Eilami et al., 2019), visualization (Kwekkeboom et al., 2010), yoga (Carson et al., 2017; Carson et al., 2007), variations of cognitive-behavioral therapy (Maindet et al., 2019) and therapeutic use of art (Ettun, Schultz, & Bar-Sela, 2014) each warrant additional research for their efficacy in supporting patients who are facing pain. Psychedelic-assisted therapy is another intervention which may have positive effects on spirituality, and thus, impact pain through cognitive and emotional routes (Agin-Liebes et al., 2020; Griffiths et al., 2016; Ross et al., 2016), warranting further research. Overall, this dissertation work provides a strong foundation from which to build and sustain a program of nursing research focused on CIH-based comprehensive pain management, including spiritual components.

Nursing Education

This dissertation can have impacts on nursing education at various levels. Findings from all three manuscripts related to the multidimensional nature of pain and spirituality can be incorporated into training programs for undergraduate and graduate nurses, along with education on the use of various evidence based CIH interventions. Nurses currently experience barriers to

effective pain management, including lack of comprehensive training (Lohman, Schleifer, & Amon, 2010). Nurses also face barriers to the implementation of evidence based nonpharmacologic interventions to support pain management (Blackburn, Abel, Green, Johnson, & Panda, 2019). Since nurses now require continuing education on pain, opportunities exist for disseminating current knowledge on pain management to both nursing students and practicing nurses. Training programs should be developed which explore the intertwined sensory, cognitive and emotional aspects of this symptom. Successful education regarding pain may include discussion and practice of non-pharmacologic pain management approaches in foundational nursing courses, a flipped-classroom approach which allows students to explore and discuss literature describing current best practices for management of various types of pain, and simulations focused on multi-modal pain management.

Programs should also include education on evidence based CIH interventions that can be employed in clinical settings as part of comprehensive pain management. To incorporate CIH intervention use in nursing education, trainees should have opportunities to practice various interventions independently (such as mindfulness meditation, aromatherapy and art therapy) and with peers (such as reflexology, guided imagery and therapeutic touch). While exploring each CIH intervention, nursing students or practicing nurses should have opportunities for self-reflection and direct feedback on their implementation of each therapy.

While the support of spirituality by clinical nurses can have positive impacts for patients with cancer, nurses have reported a lack of training in providing spiritual care (Farahani et al., 2019) and a desire to receive more comprehensive training focused on spirituality (Moosavi, Rohani, Borhani, & Akbari, 2019). Educational programs which support nursing students and practicing nurses in exploring their own unique sense of spirituality (such as brief in-house

retreats for undergraduate nursing students, practice of CIH interventions and reflective writing assignments which encourage exploration specific aspects of spirituality) could result in more holistic care being provided to patients. Taken together, the findings of this dissertation could contribute to the development of nursing curriculum and continuing education courses related to comprehensive pain management and the facilitation of spirituality in people with advanced cancer.

Nursing Practice

Pain can impact all areas of QOL (Paice & Ferrell, 2011; Rodriguez et al., 2019) and can result in cancer treatment dose delays and interruptions (Wyatt et al., 2015), making management of this symptom a top priority for clinical nurses. All three manuscripts in this dissertation underscore the importance of approaching pain in a comprehensive way. Clinical nurses could be well-served to extend the traditional 0-10 pain assessment to also include questions about cognitive and emotional aspects of this symptom, along with perceptions of pain interference with daily life. Multidimensional pain assessment in clinical settings may begin to capture the complexity of this symptom and may continue to extend pain management to include nonpharmacologic and CIH interventions alongside the use of pharmacologic agents.

Manuscript 2 identified demographic and clinical characteristics which were associated with pain (younger, not married/living with a partner, not employed, and/or were receiving hormonal therapy associated with higher pain) and spirituality (older, non-Caucasian and/or Christian associated with higher spirituality). These findings impact nursing practice because they highlight the importance of conducting comprehensive assessments of pain and spirituality for each patient. By understanding that individual differences may contribute to patients' experiences of pain and spirituality, nurses can identify those who may require additional support

in these areas. Ultimately, this can result in individualized care which is more closely tailored to each individual patient.

This dissertation highlights the significance of addressing spirituality as part of comprehensive care for women with advanced breast cancer. All three manuscripts supported the idea that spirituality is an important phenomenon for women which can impact their disease experience. Prior research has found that cancer patients and their caregivers perceive oncology nurses as in a role to support spirituality (Taylor, 2003). Clinical nurses can explore spirituality with their patients through employing inclusive spirituality assessments. These assessments should include a broad, existential approach to spirituality, with dimensions such as connection to a higher power, self, family, nature, pets, community and a sense of meaning. Findings from this dissertation also highlight that spirituality is a unique phenomenon that is not necessarily equated with religion. Thus, practicing nurses can employ open-ended spirituality assessments to learn how to best support their patients' spirituality.

Clinical nurses can also offer evidence based CIH interventions as part of comprehensive pain management, which some women in Manuscript 3 considered to be spiritual practices. Practicing nurses must be knowledgeable about the evidence base (including safety, efficacy and proper use) of CIH therapies for pain, which often have spiritual underpinnings. Interventions such as mindfulness meditation (Wren et al., 2019), prayer (Eilami et al., 2019), visualization (Kwekkeboom et al., 2010) have spiritual underpinnings and may also have the capacity to alter pain. These interventions can be simple to learn and easily employed in clinical settings. Further expansion of CIH interventions as part of standard oncology care may mean the creation of new care delivery systems such as home visits from trained CIH practitioners, wellness clinics and retreat centers for cancer patients. Overall, a shift in nursing practice toward more holistic care,

including greater focus on non-pharmacologic pain management, spiritual support and the use of CIH interventions, is needed.

Policy Implications

With women experiencing moderate pain, on average (as reported in all three manuscripts), this work highlights the need for more comprehensive pain management. Policies are needed which urge clinicians to employ non-pharmacological pain management approaches alongside pharmacological approaches (when indicated), aligning with current clinical guidelines (Centers for Disease Control and Prevention, 2016; National Coalition for Hospice and Palliative Care, 2018).

A high proportion of women are using CIH interventions to support self-management of this symptom, yet insurance reimbursement for evidence based CIH interventions is lacking. Policies which support the availability of evidence based CIH interventions for people with advanced cancer could be an important step in providing more comprehensive pain management. Since many CIH interventions have spiritual underpinnings, this policy change could also help in enhancing spirituality for people with advanced cancer. Funding for additional research into nonpharmacologic pain management approaches, including CIH interventions, is also needed. Overall, policies which support more comprehensive pain management, along with further research and insurance reimbursement for CIH interventions, warranted.

Contributions to Science

Overall, this work offers broader thinking about pain in advanced disease, considering the complex aspects of this symptom which are often overlooked. The research described in the preceding chapters enhances the science in three main ways: 1) Synthesis and identification of gaps in the literature related to the impact of spirituality on pain among women with advanced

breast cancer (Manuscript 1/Chapter 2); 2) Examination of demographic and clinical factors in relation to pain and spirituality, the impact of spirituality on pain and the impact of spirituality on engagement with a CIH pain management intervention among women with advanced breast cancer (Manuscript 2/Chapter 3); 3) Qualitative exploration of the lived experience of pain, spirituality and the impact of spirituality on pain among women with advanced breast cancer (Manuscript 3/Chapter 4). The findings from this dissertation serve to build the science by underscoring the complex and multidimensional nature of both pain and spirituality, uncovering factors which may identify women who require additional support with pain and spirituality, and offering qualitative understanding on the phenomena of pain and spirituality. Understanding pain and spirituality among women with advanced breast cancer may provide a more holistic view on how to optimally address complex symptom experiences and provide comprehensive care for these women.

These findings highlight the importance of re-integrating spirituality into nursing care. Women in all three manuscripts reported the importance of spirituality to their disease experience, and potentially their symptoms. In an increasingly technological world, acknowledging spirituality can have far-reaching impacts on how cancer care is approached. Focusing on spirituality can bring about present-moment awareness and non-judgmental acceptance, both especially important for clinicians and for patients who are facing pain near the end of life. The use of CIH interventions can be especially powerful for bringing a deeper level humanity back into nursing care, encouraging caring presence and physical touch between patients and caregivers.

This dissertation work began exploring a holistic approach to cancer care, yet much more work is needed to build on these findings. Future research will continue to explore cognitive and

emotional aspects of symptom experiences, as well as how CIH interventions may be integrated into care. The future of nursing education must prepare nurses to assess and address pain and spirituality in comprehensive ways. Future cancer care may include comprehensive assessments of pain and spirituality across cancer trajectory, routine application of CIH interventions (in cancer centers, free-standing wellness centers and at home), as well as insurance reimbursement for CIH therapies. This dissertation work is a first step in a program of research aimed at improving pain management through spirituality via a ST lens for patients with advanced cancer.

In conclusion, this dissertation found that women with advanced breast cancer experience significant pain, and spirituality may be one overlooked resource which can aid in comprehensive management of this symptom for some women. This dissertation contributes to the science by examining the complex concepts of pain and spirituality from multiple views: A scoping literature review, a quantitative secondary analysis and a qualitative study. Continued exploration of cognitive and emotional influences on pain, possibly considering spirituality, could yield significant advancements in the area of pain management for patients with advanced cancer.

APPENDICES

Appendix A: PRISMA ScR Checklist

Table. PRISMA-ScR Checklist

Section	Item	PRISMA-ScR Checklist Item
Title	1	Identify the report as a scoping review.
Abstract Structured summary	2	Provide a structured summary that includes (as applicable) background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.
Introduction Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.
Methods Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).
Summary measures	13	Not applicable for scoping reviews.
Synthesis of results	14	Describe the methods of handling and summarizing the data that were charted.
Risk of bias across studies	15	Not applicable for scoping reviews.
Additional analyses	16	Not applicable for scoping reviews.
Results Selection of sources of evidence	17	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.
Characteristics of sources of evidence	18	For each source of evidence, present characteristics for which data were charted and provide the citations.
Critical appraisal within sources of evidence	19	If done, present data on critical appraisal of included sources of evidence (see item 12).
Results of individual sources of evidence	20	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.
Synthesis of results	21	Summarize and/or present the charting results as they relate to the review questions and objectives.
Risk of bias across studies	22	Not applicable for scoping reviews.
Additional analyses	23	Not applicable for scoping reviews.
Discussion Summary of evidence	24	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.
Limitations	25	Discuss the limitations of the scoping review process.
Conclusions	26	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.
Funding	27	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

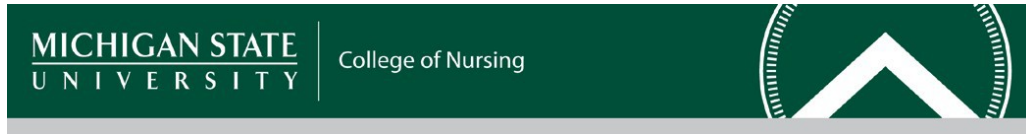
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy documents).

Tricco, A., Lillie, E., W., Z., O'Brien, K., Colquhoun, H., Levac, D., . . . Straus, S. (2018). PRISMA Extension for Scoping

Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*, 169(7), 467-473. doi:10.7326/M18-0850

Appendix B: Parent Study Informed Consent and Enrollment Form



Home-Based Symptom Management via Reflexology for Breast Cancer Patients (Patient)

Nursing Care for Breast Cancer
1355 Bogue Street Room C360M
College of Nursing
Michigan State University
East Lansing, Michigan

Explanation of the Study and Consent Form

You are being invited to participate in a study that will look at the possible benefits of a complementary therapy for breast cancer patients. The purpose of this research is to learn if a complementary therapy, called Reflexology (a specialized foot massage), provided by a friend or family member will help you feel better physically and/or emotionally during cancer therapy. Whether or not you participate ***will not*** change the care you receive from your doctors. If you agree to participate, you will be randomized (like the flip of a coin) to one of two groups (**Group A or B**). Regardless of which group you are in, you will be asked to participate in seven telephone calls. There will be 4 brief telephone calls (5 minutes each) that occur four weeks in a row, where we will be asking you about any symptoms you may be experiencing, and 3 phone calls (30-40 minutes each) at study weeks 1, 5, and 11, where we will be asking you about your symptoms, functioning, general health perception, and social support. You will be in the study for approximately 11 weeks.

You will be randomly assigned to **one** of the following two groups:

Group A : If you are in Group A, the Reflexology group, in addition to participating in the phone calls described above, you will receive a specialized 30 minute foot reflexology session by a trained friend or family member of your choice. The friend or family member will be trained by a certified reflexology practitioner. You will receive a minimum of 1 reflexology session per week for 4 weeks at home plus the telephone calls mentioned above. This special type of massage is used primarily to reduce stress and promote deep relaxation to help all systems of the body function more efficiently.

OR

Group B: If you are assigned to this group, you will be asked to complete only the telephone calls described above. At the end of your participation in the study, you will be offered a session of reflexology for yourself or a training session for your friend or family member to express appreciation for your time.



ACCESS TO INFORMATION

We ask your permission to review your medical chart for information such as stage of your cancer, symptoms you may experience, and cancer treatment information, so we can better understand your overall health status.

Information from all participants in this research will be grouped together without names, and you will not be personally identified in any way in reports of the research. Information about you will be seen only by the research staff, the Institutional Review Boards (IRB) of your participating hospital, and the Human Research Protection Program at Michigan State University. Hard copy data that is collected will be stored in a locked file in the research office without your name. Electronic data will be stored on a secure server without your name and managed by personnel who have been trained to protect your confidentiality. All data will be stored for a minimum of 3 years after the study is completed. Please check with your institution, as they may require longer record retention. Your confidentiality will be protected to the maximum extent allowable by law.

ALTERNATIVE OPTIONS

You do not have to take part in this study to receive treatment for your condition.

BENEFITS

Preliminary research suggests that women who participate in Group A may experience an improved perception of their quality of life. However, there are no implied benefits to participation in this study.

RISKS

Your involvement in this study is voluntary, and there are minimal risks, but you will be allowed to discontinue participation at any time. It is possible that massage to an existing sore point on the foot could result in additional irritation. You will be encouraged to disclose any preexisting foot soreness prior to the interventions. It is also possible that you may feel uncomfortable with having your feet touched. As in all studies in which medical records are reviewed, there is the possibility that confidentiality may be breached, however numerous safeguards are in place to prevent this. Finally, there is a very minimal psychological risk that you may become upset when answering the interview questions about symptoms and quality of life. Past research indicates that few people are upset by these kinds of questions. If this should occur and you request assistance with your feelings, you will be provided with a list of local counseling services which you may choose to contact on your own. The physicians and practitioners involved in your care will not be provided with your responses to these interviews.

A research injury is any physical injury or illness caused by the medications, devices, or procedures required by the study which are administered, used, or performed appropriately. These medications, devices, or procedures are different from the medical treatment you would have received if you had not taken part in the study.



If you are injured as a result of your participation in this research project, Michigan State University will assist you in obtaining emergency care, if necessary, for your research related injuries. If you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. As with any medical insurance, any costs that are not covered or are in excess of what are paid by your insurance, including deductibles, will be your responsibility. The University's policy is not to provide financial compensation for lost wages, disability, pain or discomfort, unless required by law to do so. This does not mean that you are giving up any legal rights you may have. You may contact Dr. Gwen Wyatt at 517-432-5511 (or toll free at 1-877-752-6136) with any questions or to report an injury

STOPPING STUDY PARTICIPATION

You may ask questions about this research at any time. Participation is voluntary, and you can stop taking part at any time without affecting the medical care you receive and without penalty or loss of benefits to which you are otherwise entitled. Your participation in this study may be stopped by the study clinician or study sponsor, without your consent, for any reason, which will be explained to you.

Examples include:

- The study medication or procedures appear to be medically harmful to you.
- You fail to follow directions for participating in the study.
- It is discovered you do not meet the study requirements.
- The study is canceled.
- It is determined to be in your best interest (for example, your disease has progressed despite treatment).

If you have questions or concerns about your role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503 or e-mail irb@msu.edu or regular mail at 408 West Circle Drive, Room 207 Olds Hall, MSU, East Lansing, MI 48824.

If you have any questions, if you would like to speak with someone about how you are feeling, or to report an injury, you may contact Dr. Gwen Wyatt via phone at 517-432-5511; fax 517-353-4587; email (gwyatt@msu.edu); or regular mail: 1355 Bogue Street Room C345, East Lansing, MI 48824



Statement of Consent

Home-Based Symptom Management via Reflexology for Breast Cancer Patients

I have read this form. I have been given the opportunity to ask questions, and my questions have been answered to my satisfaction. My signature below indicates my voluntary agreement to participate in this study. I have been told that I will be given a copy of the fully signed and dated informed consent form.

☐ **I VOLUNTARILY AGREE TO BOTH STUDY PARTICIPATION AND CHART REVIEW**

☐ **I AGREE TO ONLY CHART REVIEW**

Name: (please print) _____

Address: _____

Telephone number: (area code) () _____ - _____

Patient Signature **Date:** ____/____/____

Printed Name of Person Conducting the Informed Consent Discussion

Signature of Person Conducting the Informed Consent Discussion **Date:** ____/____/____

Research Office:
Phone number: (517) 432-5511
Toll Free: 1-877-752-6136
Fax number: (517) 353-4587

ID# _____

REFLEXOLOGY ENROLLMENT FORM

Patient Demographics

Medical Record # _____ Recruitment Location _____

Name: _____ Age: _____

Address: _____
Street Apt. # City State Zip

Phone: (home) () _____ - _____ (work) () _____ - _____ (other) () _____ - _____

Best day(s) to call: ___Monday ___Tuesday ___Wednesday ___Thursday ___Friday ___Saturday ___Sunday

Best time of day to call: _____

Marital Status: ☐Never Married, ☐Married or Living with a Partner, ☐Divorced/Separated, ☐Widowed, ☐Refused

Occupation: ☐Full-time, ☐Part-time, ☐Not Employed, ☐Retired, ☐Disabled, ☐Homemaker, ☐Refused

Ethnicity: ☐Hispanic or Latino, ☐Not Hispanic or Latino, ☐Refused

Race: ☐American Indian or Alaskan Native, ☐Asian, ☐Black or African American, ☐Native Hawaiian or Pacific Islander,
☐White, ☐Refused

Current Stage of Disease:

Clinical: ___3, ___4 Pathology: ___3, ___4 Recurrent* ___yes ___no Metastasis** ___yes ___no

*Recurrence: a second or subsequent diagnosis of cancer in either breast.

**Metastasis: a previous diagnosis of breast cancer that has now spread beyond the breast and regional axillary lymph nodes.

Treatment Type

Chemotherapy only _____ Chemotherapy and Hormonal Therapy _____ Hormonal Therapy Only _____

Inclusion/Exclusion Criteria

Patient Inclusion Criteria:

- ___ Woman, 21 years of age or older
- ___ Diagnosis of breast cancer, Stage III, IV or Stage I or II with metastasis or recurrence
- ___ Able to perform basic ADLs
- ___ Undergoing chemotherapy and/or hormonal therapy for breast cancer
- ___ Able to speak and understand English
- ___ Have access to a telephone
- ___ Able to hear a normal conversation
- ___ Cognitively oriented to time, place, and person (determined via recruiter)

Patient Exclusion Criteria:

- ___ Diagnosis of major mental illness on the medical record and verified by the recruiter
- ___ Residing in a nursing home
- ___ Bedridden
- ___ Currently receiving regular reflexology
- ___ Diagnosis of symptoms of deep vein thrombosis or painful foot neuropathy, which will require medical approval

Friend/Family Member Inclusion Criteria:

- ___ 18 or older
- ___ Able and willing to provide reflexology
- ___ Able to speak and understand English
- ___ Have access to a telephone
- ___ Able to hear normal conversation
- ___ Cognitively oriented to time, place, and person (determined via recruiter)

Friend/Family Member Exclusion Criteria:

- ___ Unwilling to perform return demonstration with 90% accuracy

Version Date: 8/7/2013

ID# _____

Patient Enrollment Information

Patient consented to study:

- ☐ Consent attached
- ☐ Date consent signed ____/____/____
Cognitively oriented to time, place, & person ☐ Yes ☐ No
- ☐ Patient will send consent on: ____/____/____

☐ Patient refused to participate due to:

- ☐ Too busy ☐ No reason given
- ☐ Too sick
- ☐ Physician refused
- ☐ Overwhelmed by prospect of research
- ☐ Specifically not interested in CTs
- ☐ Specifically not interested in research
- ☐ Does not want to be interviewed
- ☐ Foot Concerns
- ☐ Caregiver not available **
- ☐ Lives too far away
- ☐ Other

Date of 1st contact: ____/____/____

Time required: _____minutes

Location: ☐ Phone call ☐ Clinic ☐ Patient's home

Follow-up contact date: ____/____/____

Time required with participants: _____minutes

Location: ☐ Phone call ☐ Clinic ☐ Patient's home

Follow-up contact date: ____/____/____

Time required with participants: _____minutes

Location: ☐ Phone call ☐ Clinic ☐ Patient's home

Follow-up contact date: ____/____/____

Time required with participants: _____minutes

Location: ☐ Phone call ☐ Clinic ☐ Patient's home

**** If patient refuses because caregiver is not available, please indicate the reason that the caregiver was not available:**

- a. Patient could not identify a caregiver
- b. An identified caregiver did not want to participate
- c. The patient does not want to bother a caregiver to ask them to participate
- d. The identified caregiver wants to participate, but cannot due time, distance, etc.

Please then send this page (Page 2) of the patient enrollment form with the patient ID at the top to the study office via fax.
Please do not include any identifying information.

Appendix C: Parent Study Data Collection Instruments – Demographics Form, PROMIS, LTQL Spiritual/Philosophical Subscale, Weekly Call Form and Debriefing Form

ID# _____

PATIENT DEMOGRAPHICS

I will begin this first set of questions by asking you some questions about yourself.

1. What is your highest level of education completed?
 - ☐ 8th Grade or Less
 - ☐ Some high school, but did not graduate
 - ☐ High school graduate or GED
 - ☐ Some college or 2-year degree
 - ☐ 4-year college graduate
 - ☐ More than a 4-year college degree
 - ☐ Refused/NA
2. What is your ethnic background?
 - ☐ Hispanic or Latino
 - ☐ Not Hispanic or Latino
 - ☐ Refused/NA
3. What is your racial background?
 - ☐ American Indian or Alaska Native
 - ☐ Asian
 - ☐ Black or African American
 - ☐ Native Hawaiian or Other Pacific Islander
 - ☐ White
 - ☐ Refused/NA
4. What is your spiritual preference?
 - ☐ Christian
 - ☐ Jewish
 - ☐ Buddhist
 - ☐ Hindu
 - ☐ Muslim
 - ☐ Other (specify:)
 - ☐ None
 - ☐ Refused/NA
5. What is your marital status?
 - ☐ Never married
 - ☐ Married/living with partner
 - ☐ Divorced/separated
 - ☐ Widowed
 - ☐ Refused/NA

6. The person with whom you are participating in this study is:
☐ Male
☐ Female
7. What is your relationship to the person with whom you are participating in this study?
 He or she is your:
☐ Spouse or partner
☐ Parent or step-parent
☐ Brother/step-brother or Sister/step-sister
☐ Cousin
☐ Daughter-in-law or son-in-law
☐ Aunt or uncle
☐ Niece or Nephew
☐ Daughter/step-daughter or Son/step-son
☐ Friend
☐ Other (specify _____)
8. How close are you to the person with whom you are participating in this study? Please refer to the Blue Five Point Response Guide C1.
☐ Not at all close (0)
☐ A little bit close (1)
☐ Somewhat close (2)
☐ Quite a bit close (3)
☐ Very much close (4)
9. What is your current menopausal status?
☐ Premenopausal
☐ Perimenopausal
☐ Postmenopausal
☐ Unknown
10. What is your employment status?
☐ Employed full time
☐ Employed part time
☐ Not employed
☐ Retired
☐ Disabled
☐ Homemaker
☐ Other (specify:)
☐ Refused/NA

11. (Skip if #10 is other than employed full or part time)

What is the annual income from your job, before taxes? (Circle the letter)

- | | | |
|------------------------|-------------------------|---------------------------|
| a. \$1 - \$999 | m. \$12,000 - \$12,999 | y. \$40,000 - \$44,999 |
| b. \$1,000 - \$1,999 | n. \$13,000 - \$13,999 | z. \$45,000 - \$49,999 |
| c. \$2,000 - \$2,999 | o. \$14,000 - \$14,999 | aa. \$50,000 - \$74,999 |
| d. \$3,000 - \$3,999 | p. \$15,000 - \$15,999 | bb. \$75,000 - \$99,999 |
| e. \$4,000 - \$4,999 | q. \$16,000 - \$16,999 | cc. \$100,000 - \$149,999 |
| f. \$5,000 - \$5,999 | r. \$17,000 - \$17,999 | dd. \$150,000 - \$199,999 |
| g. \$6,000 - \$6,999 | s. \$18,000 - \$18,999 | ee. \$200,000 - \$299,999 |
| h. \$7,000 - \$7,999 | t. \$19,000 - \$19,999 | ff. \$300,000 - \$499,999 |
| i. \$8,000 - \$8,999 | u. \$20,000 - \$24,999 | gg. \$500,000 - \$999,999 |
| j. \$9,000 - \$9,999 | v. \$25,000 - \$29,999 | hh. \$1,000,000 or more |
| k. \$10,000 - \$10,999 | w. \$30,000 - \$34,999. | ii. Prefer not to answer |
| l. \$11,000 - \$11,999 | x. \$35,000 - \$39,999 | |

PROMIS-29 Profile v1.0

This is the last set of questions for this interview. There are 29 questions total in this set. For this section, please refer to the blue five-point response guide C4.

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1. Are you able to do chores such as vacuuming or yard work?	0	1	2	3	4
2. Are you able to go up and down stairs at a normal pace?	0	1	2	3	4
3. Are you able to go for a walk of at least 15 minutes?	0	1	2	3	4
4. Are you able to run errands and shop?	0	1	2	3	4

For this section, please refer to the blue five-point response guide C5.

In the past 7 days	Never	Rarely	Sometimes	Often	Always
5. I felt fearful	0	1	2	3	4
6. I found it hard to focus on anything other than my anxiety	0	1	2	3	4
7. My worries overwhelmed me	0	1	2	3	4
8. I felt uneasy	0	1	2	3	4
In the past 7 days...	Never	Rarely	Sometimes	Often	Always
9. I felt worthless	0	1	2	3	4
10. I felt helpless	0	1	2	3	4
11. I felt depressed	0	1	2	3	4
12. I felt hopeless	0	1	2	3	4

PROMIS-29 Profile v1.0

For this section, please refer to the blue five-point response guide C1.

In the past 7 days ...	Not at all	A little bit	Somewhat	Quite a bit	Very much
13. I feel fatigued	0	1	2	3	4
14. I have trouble <u>starting</u> things because I am tired	0	1	2	3	4
15. How run-down did you feel on average?	0	1	2	3	4
16. How fatigued were you on average?	0	1	2	3	4

For this section, please refer to the blue five point response guide C6.

In the past 7 days...	Very poor	Poor	Fair	Good	Very good
17. My sleep quality was...	0	1	2	3	4

For this section, please refer to the blue five point response guide C1.

In the past 7 days...	Not at all	A little bit	Somewhat	Quite a bit	Very much
18. My sleep was refreshing	0	1	2	3	4
19. I had a problem with my sleep	0	1	2	3	4
20. I had difficulty falling asleep	0	1	2	3	4
In the past 7 days...	Not at all	A little bit	Somewhat	Quite a bit	Very much
21. I am satisfied with how much work I can do (including work at home)	0	1	2	3	4
22. I am satisfied with my ability to work (including work at home)	0	1	2	3	4
23. I am satisfied with my ability to do regular personal and household responsibilities	0	1	2	3	4
24. I am satisfied with my ability to perform my daily routine	0	1	2	3	4
25. How much did pain interfere with your day to day activities?	0	1	2	3	4
26. How much did pain interfere with work around the home?	0	1	2	3	4

In the past 7 days...	Not at all	A little bit	Somewhat	Quite a bit	Very much
27. How much did pain interfere with your ability to participate in social activities?	0	1	2	3	4
28. How much did pain interfere with your enjoyment of life?	0	1	2	3	4

For this section, please refer to the green ten point response guide G1.

For this section, please refer to the green ten point response guide G1.											
In the past 7 days...	No Pain									Worst Imaginable Pain	
29. How would you rate your pain on average?	0	1	2	3	4	5	6	7	8	9	10

**Spiritual QOL
LTQL Subscale**

The next set of questions has to do with your philosophical or spiritual views on life. Please refer to the blue five-point response guide C2 and indicate to what extent each of these statements apply to you.					
	No extent at all	Small extent	Some extent	Great extent	Very great extent
1. I have a better idea about what serious illness is since having had cancer.....	0	1	2	3	4
2. I feel a guiding energy in my life which has my best interest in mind.....	0	1	2	3	4
3. Since having had cancer, I have a greater appreciation for the time I spend with my friends and family	0	1	2	3	4
4. I follow my inner voice when making health decisions	0	1	2	3	4
5. I have intuitive experiences that reassure me about my health care choices	0	1	2	3	4
6. I receive subtle cues that give me confidence in my health decisions	0	1	2	3	4
7. I am sympathetic with family/friends who have major illnesses, such as heart or kidney disease since my cancer.....	0	1	2	3	4
8. Since having had cancer, I tend to notice things in nature more, such as sunsets, raindrops and spring flowers	0	1	2	3	4
9. I feel an inner direction that helps me make wise decisions	0	1	2	3	4
10. I have become closer with some family members/friends since having had cancer	0	1	2	3	4
11. Since having had cancer, I don't take life's little things for granted.....	0	1	2	3	4

ID# _____

REFLEXOLOGY PATIENT CALL FORM
(used by Education Coordinator)

Patient Name _____

Patient Home Phone _____ Best time to call ____am or ____pm

Phone call _____ Date ____/____/____
1 2 3 4
(circle one)

Day of Week: ____Su ____Mo ____Tu ____We ____Th ____Fr ____Sa

Time of Day: ____am ____pm

Reason unable to complete call:

- ____ patient too tired
- ____ hospitalized
- ____ too sick
- ____ too busy
- ____ had company
- ____ unable to reach

voice mail left:

↓
____ date
____ time

____ date
____ time

____ date
____ time

no answer (make 3 attempts)

↓
____ date (1st attempt)
____ time (1st attempt)

____ date (2nd attempt)
____ time (2nd attempt)

____ date (3rd attempt)
____ time (3rd attempt)

1. Did your home provider give you the Weekly session?

____ YES
↓

____ NO
↓

____ # of full
sessions
(30 minutes
each)

____ I was too tired
____ I was in the hospital
____ I felt too sick
____ I was too busy
____ Other (Describe)

2. On a 1 - 7 scale, please rate the home environment during this week's scheduled session (1 is very peaceful and 7 is hectic with many interruptions)

1 2 3 4 5 6 7
very peaceful hectic with many interruptions

3. Administer Symptom Inventory (MDASI) Each Week.

Did patient attrite?

____ YES ____ NO

↓
____ Date

Reason (Describe): _____

Patient ID: _____

REFLEXOLOGY PATIENT ATTRITION FORM

(Used by Education Coordinator)

Did patient attrite?

_____ YES

_____ NO

1

Date _____

Reason (Check one):

_____ Patient too sick

_____ Patient too busy

_____ Patient overwhelmed

_____ Changed mind/no longer interested

_____ Didn't like the interview questions

_____ Not reached via telephone

_____ Didn't like being in Control Group without foot sessions

_____ Didn't want to be interviewed

_____ Didn't like foot sessions

☐ Prefer not to provide a reason

Other (Describe): _____

Weekly Symptom Call 1_____

Weekly Symptom Call 2_____

Weekly Symptom Call 3_____**Weekly Symptom Call 4_____**

****You have the right not to tell us why you do not wish to continue your participation, but we are interested in learning your reason (for research data purposes) if you are willing to provide us with that information.**

NOTE: Give these data to the Project Manager

Reflexology

Study ID # _____

DEBRIEFING TOOL
(Overall Study Satisfaction)

Now, I'd like to ask you a few questions about the period of time that you have been in the study.

1. Did you see or hear any information on reflexology during the study?

____ Yes (If Yes, Check What Media Below) ____ No ____ N/A

Check All That Apply:

Magazine ____

Television ____

Internet ____

Other (Please describe Media)

2. For this question, please refer to the light blue six point response scale D2.
How satisfied were you overall in taking part in this study?

____ Very Dissatisfied

____ Moderately Dissatisfied

____ Slightly Dissatisfied

____ Slightly Satisfied

____ Moderately Satisfied

____ Very Satisfied

3. Have you had any additional reflexology sessions by your friend or family home provider (who took part in this study) since your second interview 6 weeks ago?

____ Yes ____ No

If yes, how many? _____

Appendix D: Secondary Data Analysis IRB Determination

MICHIGAN STATE **U N I V E R S I T Y**

DETERMINED NOT "HUMAN SUBJECTS"

April 13, 2018

To: Gwen Wyatt

Re: **MSU Study ID:** STUDY00000664
Principal Investigator: Gwen Wyatt
Determination Date: 4/13/2018

Title: Examining the Interconnectedness of Pain & Spiritual Quality of Life Among Women with Advanced Breast Cancer

The activity described in this submission was determined not to meet the definition of "human subjects" as defined by the U.S. Department of Health and Human Services (DHHS) regulations for the protection of human research subjects.

Definition of Human Subject

For DHHS, "human subject" means "a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Data through intervention or interaction with the individual, or (2) Identifiable private information." [45 CFR 46.102(f)].

Determination

The data set you will receive will not contain identifiable data.
Hence, the activity does not involve human subjects.

Therefore, the federal regulations for the protection of human subjects would not apply to this project and Michigan State University (MSU) IRB approval is not needed to proceed. However, please note that while MSU IRB approval is not required, other federal, state, or local regulations or requirements or ethical or professional standards may still be applicable based on the activity.

Modifications: If any of the activities described in this submission change, please contact the IRB office as the activity may involve human subject research and require IRB approval. For example, this determination is not applicable to activities that may be regulated by U.S. Food & Drug Administration (FDA), such as those involving drugs, medical devices, human food additives, color additives, electronic products, or any other test articles regulated by the FDA.

Modifications to Project Funding: Changes in project funding may alter this determination. For example, MSU IRB review and approval is required if MSU receives an award through a grant, contract, or cooperative agreement directly from a federal agency, even where all non-exempt research involving human subjects are carried out by employees or agents of another institution.



**Office of
Regulatory Affairs
Human Research
Protection Program**

4000 Collins Road
Suite 136
Lansing, MI 48910

517-355-2180
Fax: 517-432-4503
Email: irb@msu.edu
www.hrpp.msu.edu

MSU is an affirmative-action,
equal-opportunity employer.

Appendix E: Qualitative Study Recruitment Materials



Women with breast cancer often experience uncomfortable symptoms, and nursing care can help. As nurse researchers at the Michigan State University (MSU) College of Nursing, we are hoping to learn more about these symptoms so we can help improve the quality of life of women who have advanced breast cancer.

You are being asked to take part in this research study because you have indicated that you experience pain. Up to 80% of women with advanced breast cancer have reported experiencing pain, which can have impact all areas of life.

Some research suggests that our thoughts and beliefs can impact the way we experience and cope with pain, so we are conducting a research study to better understand this. Spirituality (including, but not limited to, things like insight, appreciation for life, meaning in life or religious beliefs) has the potential to play a role in how we experience pain. We value your insights on these topics. As part of this study, we are interested in learning more about your perceptions of pain and spirituality.

By choosing to participate in this study you should not experience any negative physical or emotional effects. In fact, reflecting and responding to some of the questions may provide increased insight into your experiences. Your confidentiality will be protected to the maximum extent allowable by law and you will not be personally identified in any way as part of this research. Your participation is completely voluntary, and you may withdraw from the study at any time. You will be provided with a \$25 gift card for your participation.

We encourage you to take part in this study. The information you provide will help us understand how to better support women with advanced breast cancer.

A handwritten signature in black ink, appearing to read 'M. Miller'.

Megan Miller, BSN, RN, PhD Student

A handwritten signature in black ink, appearing to read 'Gwen Wyatt'.

Gwen Wyatt, PhD, RN, FAAN



- **Who:**
 - Women who have advanced breast cancer and rate their pain at a 2 or greater out of 10
- **What:**
 - The participation process includes meeting in person to review the consent form and answer any questions, then completing an informal interview.
 - The entire process should take about an hour and a half.
 - You will be provided with a \$25 gift card for your participation.
- **When:**
 - At a time that's convenient for you.
- **Where:**
 - In your home or in a private room at the Michigan State University College of Nursing.
- **How:**
 - If you meet the above criteria and are interested in participation, please fill out the included post card and return in the pre-stamped envelope.
 - If you have any questions, please contact Megan Miller (formerly Flanigan) at Flanig21@msu.edu or 586-604-5862.

☐

Yes, I would like to participate.

The best phone number to reach me at is:

The best time to call is:

☐

No, I'm not able to participate.

___ I am too busy

___ I don't feel well

___ Other reason:

☐

Yes, I would like to participate.

The best phone number to reach me at is:

The best time to call is:

☐

No, I'm not able to participate.

___ I am too busy

___ I don't feel well

___ Other reason:

Appendix F: Qualitative Study Informed Consent and Enrollment Form



Research Participant Information and Consent Form

You are being asked to participate in a research study. Researchers are required to provide a consent form to inform you about the research study, to convey that participation is voluntary, to explain risks and benefits of participation, and to empower you to make an informed decision. You should feel free to ask the researchers any questions you may have.

Study Title: Examining the Interconnectedness of Pain & Spiritual Quality of Life Among Women with Advanced Breast Cancer

1. PURPOSE OF RESEARCH

The purpose of this research study is to learn more about women's perceptions of pain and spirituality in order to provide better care in the future. Women with advanced breast cancer often experience significant pain and often have spiritual concerns.

You are being asked to take part in this research study because you have indicated that you experience pain. We value your insights and are interested in learning more about your perceptions.

2. WHAT YOU WILL DO

If you choose to take part in this study, a nursing PhD student will contact you to schedule a time that is convenient to conduct an interview. The interview will last about 30-60 minutes and can be done in your home if you wish, or in a private room at the study office (Michigan State University College of Nursing). You will be asked to discuss your perception about connections between your pain and spirituality. Questions will be asked to help you think about this topic. You may stop your participation in the interview at any time.

Your participation in the study will last through the duration of the interview process. This will be about an hour, including time to explain the study, answer questions, review and sign the consent form, complete the survey form and complete the interview. You will first be asked to fill out a short survey form telling us a little about yourself. It will not include your name. The interview itself will take about 30-60 minutes and will be audio recorded. You may talk as much or as little as you would like, and you may end the interview at any time. You are free to skip any questions if you would prefer not to answer.

3. POTENTIAL BENEFITS

The potential benefits of participation in this study include exploring your pain and spirituality, better understanding how you relate to your pain, sharing your story, and potentially improving pain management in the future for women who have advanced breast cancer.

4. POTENTIAL RISKS

Participation in this study has minimal foreseen risks. Answering the interview questions may bring up some emotions, which you will be free to express. Any new information related to risks and/or benefits of this research study will be made available.



5. PRIVACY, CONFIDENTIALITY & AUTHORIZATION (HIPAA)

We are committed to protecting the confidentiality of information obtained about you in connection with this research study.

- Information about you will be kept confidential to the maximum extent allowable by law.
- Only the research team and the Michigan State University Human Research Protection Program will have access to research study records. Staff members at the Michigan State University Human Research Protection Program may see your name in the process of reviewing the data to ensure that the research team is carrying out the project properly.
- Study data (recordings and transcriptions of the interview & survey forms) will not include your name or personal information. You will be assigned a study ID number which will be used to identify you in study records. All persons working on the project will only see a study ID number that cannot identify you.
- Recording devices and all study forms will be stored in a locked box when not in use.
- Electronic data will be stored on a secure, password protected computer in a locked office. The study investigators will be responsible for maintaining data security.
- Your name or personal information will never be shared.
- Your personal information will be kept in a locked cabinet until the end of the study. After the study it will be de-identified and/or destroyed.
- Data will be stored for at least 3 years after study completion (without your personal information).
- If the results of this study are made public, information that identifies you will not be used.

By signing this form, you authorize and request Michigan State University and Sparrow Hospital to make a disclosure of your protected health information ("PHI"), including

- Name
- Address
- Phone number
- Information about my cancer diagnosis
- Information about my pain
- And, as applicable,
 - Alcohol and drug use and mental health treatment information protected under the regulations in Title 42 of Code of Federal Regulations Part II.
 - Information about human immunodeficiency virus-HIV, acquired immunodeficiency syndrome-AIDS, and AIDS related complex-ARC, as defined by Department of Community Health rules (1989 Public Act 174)

During this research, information about your health will be collected. Under Federal law, called the HIPAA and HITECH Rule, health information is private. However, there are exceptions to this rule and you should know who may be able to see, use, and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this study without your written permission. By signing this form, you are providing that permission.

- Health information may be collected about you from:
 - Tumor registry (for screening purposes)
 - Research procedures (survey and interview)



Why will this information be used and/or given to others?

- To do the research
 - To report the results
 - To see if the research was done correctly
- If the results of this study are made public, information that identifies you will not be used.

With whom may your health information be shared?

- The Michigan State University Institutional Review Board that oversees the research
- Sparrow Clinical Research Institute (SCRI)
- A group that oversees the data (study information) and safety of this research

Information disclosed may contain mental healthcare records (except psychotherapy notes that are not kept within the medical records) alcohol/substance abuse treatment records, and any AIDS/HIV status. Limited data gathered could imply this type of treatment; such as a medication list with medications used to treat the above conditions. (This sensitive information has special protections under title 42 of the Code of Federal Regulations Part II and the 1989 Public Act 174)

Is your health information protected after it has been shared with others?

- We ask anyone who receives your health information from us to protect your privacy; however, once your information is shared, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

6. YOUR RIGHTS TO PARTICIPATE, SAY NO, OR WITHDRAW

It is up to you to decide whether or not being on this study is the right choice for you, and if you decide to participate you can change your mind at any time. You have the right to say no and the right not to sign this form. If you do not sign the form, you cannot take part in this research study. If you choose to sign and participate, you can stop at any time after the study has already started. If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used. There will be no consequences if you stop and you will not be criticized. You will not lose any benefits that you normally receive.

7. COSTS AND COMPENSATION FOR BEING IN THE STUDY

Taking part in this study does not include any additional costs to you or your healthcare insurer. The interview will be scheduled over the telephone and conducted in your home or at a private room in the Michigan State University (MSU) study office if you prefer. If you choose to conduct the interview at MSU, you will be responsible for costs of transportation and parking. You will be provided with a \$25 gift card at the conclusion of your participation.

8. ALTERNATIVE OPTIONS

You are free to decide whether you would like to participate or not. If you choose not to take part in this study, there will be no influence on your current care.



9. CONTACT INFORMATION

If you have concerns or questions about this study, such as scientific issues, how to do any part of it, or to report an injury, please contact the researcher (Megan Flanigan, BSN, RN, PhD Student, 1355 Bogue St. East Lansing, MI 48824, flanig21@msu.edu, 586-604-5862 OR Dr. Gwen Wyatt, 1355 Bogue St. East Lansing, MI 48824, gwyatt@msu.edu, 517-432-5511).

If you have questions or concerns about your role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503, or e-mail irb@msu.edu or regular mail at 4000 Collins Rd, Suite 136, Lansing, MI 48910.

If you have any questions or complaints regarding your research activity at Sparrow Health System, please contact the SCRI Office at SCRI@sparrow.org or 517-364-5760.

10. DOCUMENTATION OF INFORMED CONSENT.

Before signing this form below, make sure that you:

- Have read the entire consent form
- Know that your participation is voluntary
- Know that you may choose to discontinue your participation at any time
- Have taken your time to think about your decision to participate
- Have had all of your questions answered



Your signature below means that you voluntarily agree to participate in this research study.

Printed Name _____ / /
Date

Signature

You will be given a copy of this form to keep.

Person obtaining consent

- I have explained the research study to the participant
- I have answered all questions about this research to the best of my ability

Printed Name and Title _____ / /
Date

Signature

ID# _____

ENROLLMENT FORM

Recruitment Location _____

Name: _____ Age: _____

Address: _____
Street Apt. # City State Zip

Phone: (home) () _____ - _____ (work) () _____ - _____ (other) () _____ - _____

Current Stage of Disease: __3, __4 Recurrent* _____yes __no Metastasis** __yes __no

*Recurrence: a second or subsequent diagnosis of cancer at the same site as a previous cancer diagnosis

**Metastasis: a previous diagnosis of cancer that has now spread beyond the primary site.

Treatment Type: Chemotherapy Only _____
Chemotherapy and Hormonal Therapy _____

Hormonal Therapy Only _____
Targeted Therapy _____

On a scale from 0 to 10, how would you **rate your pain on average in the last 7 days?**

No pain
0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐ Worst Imaginable pain

Inclusion/Exclusion Criteria

Patient Inclusion Criteria:

- ☐ Age $\geq$ 21 years
- ☐ Diagnosis of stage III or IV breast cancer, or stage II with recurrence or metastasis
- ☐ Able to speak and understand English
- ☐ Access to telephone
- ☐ Able to hear normal conversation
- ☐ Cognitively oriented
- ☐ Living $\leq$ 40 miles from recruiting location
- ☐ Pain $\geq$ 2 on a 0-10 scale

Patient Exclusion Criteria:

- ☐ Diagnosis of major mental illness

Patient Enrollment Information

ID#: _____

Patient consented to study:

Consent attached? Yes ____ No ____

Date consent signed: ____/____/____

Refused to participate due to:

- ☐ No reason given
- ☐ Too busy
- ☐ Too sick
- ☐ Other: _____

Appendix G: Qualitative Study Forms

Date: ____ / ____ / ____

Study ID #: _____

Demographics Survey

*We appreciate your time in answering these questions!
Please respond to each to the best of your ability.*

Place a check mark in the box next to your response.

On a scale from 0 to 10, how would you rate your average pain in the last 7 days?

No pain												Worst imaginable pain
0	1	2	3	4	5	6	7	8	9	10		

On a scale from 0 to 10, how would you rate your pain at its worst in the last 24 hours?

No pain												Worst imaginable pain
0	1	2	3	4	5	6	7	8	9	10		

Place a check mark in the box next to your response.

Which of the following best describes your marital status?

- ☐ Never married
- ☐ Married
- ☐ Divorced/separated
- ☐ Widowed
- ☐ A member of an unmarried couple
- ☐ Prefer not to answer

Date: ____ / ____ / ____

Study ID #: _____

What is the highest level of education you've completed?

- ☐ 8th Grade or Less
- ☐ Some high school, but did not graduate
- ☐ High school graduate or GED
- ☐ Some college or 2-year degree
- ☐ 4-year college graduate
- ☐ More than a 4-year college degree
- ☐ Prefer not to answer

How would you describe your spiritual preference?

- ☐ Christian
- ☐ Jewish
- ☐ Buddhist
- ☐ Hindu
- ☐ Muslim
- ☐ Other (specify: _____)
- ☐ None
- ☐ Refused/NA

Which one of these groups would you say best represents your race?

- ☐ White
- ☐ Black or African American
- ☐ American Indian or Alaskan Native
- ☐ Asian or Pacific Islander
- ☐ Other (Please specify): _____
- ☐ Prefer not to answer

Are you Hispanic, Latino, or of Spanish origin?

- ☐ Yes
- ☐ No
- ☐ Prefer not to answer

1.14.20

2

Date: ____ / ____ / ____

Study ID #: _____

What is your current menopausal status?

- ☐ Premenopausal (before menopause; having regular periods)
- ☐ Perimenopausal (changes in periods but have not gone 12 months in a row without a period)
- ☐ Postmenopausal (after menopause)
- ☐ Unknown
- ☐ Prefer not to answer

What is your current employment status?

- ☐ Employed full time
- ☐ Employed part time
- ☐ Not employed
- ☐ Retired
- ☐ Unable to work
- ☐ Homemaker
- ☐ Other (specify: _____)
- ☐ Prefer not to answer

Thank you for completing this survey!

Please flip over this sheet and complete the final page.

*This set of questions has to do with your philosophical views on life.
Please indicate to what extent each of these statements apply to you.*

*Also, please note that there are no "correct" answers here –
we are only interested in learning about your beliefs and experiences.*

	No extent at all	Small extent	Some extent	Great extent	Very great extent
1. I have a better idea about what serious illness is since having had cancer..... 0	1	2	3	4	
2. I feel a guiding energy in my life which has my best interest in mind..... 0	1	2	3	4	
3. Since having had cancer, I have a greater appreciation for the time I spend with my friends and family 0	1	2	3	4	
4. I follow my inner voice when making health decisions..... 0	1	2	3	4	
5. I have intuitive experiences that reassure me about my health care choices 0	1	2	3	4	
6. I receive subtle cues that give me confidence in my health decisions 0	1	2	3	4	
7. I am sympathetic with family/friends who have major illnesses, such as heart or kidney disease since my cancer..... 0	1	2	3	4	
8. Since having had cancer, I tend to notice things in nature more, such as sunsets, raindrops and spring flowers 0	1	2	3	4	
9. I feel an inner direction that helps me make wise decisions 0	1	2	3	4	
10. I have become closer with some family members/friends since having had cancer 0	1	2	3	4	
11. Since having had cancer, I don't take life's little things for granted..... 0	1	2	3	4	

1.14.20

Appendix H: Qualitative Study Interview Protocol

Qualitative Interview Guide

I am talking with women who have advanced breast cancer about their experiences with pain, and how spirituality may impact their experience. This information will be important for helping support women with breast cancer who are experiencing pain. Please note that there are no “correct” answers to these questions – We are interested in learning about your beliefs and experiences.

Primary Questions	Follow-Up Questions
Tell me about your journey with breast cancer.	
Please describe your experience with pain.	How does pain impact your experience? What are your painful sensations like? What are your thoughts like when you’re experiencing pain? What are your emotions like when you’re experiencing pain? When do you most feel pain? - If you’re feeling pain, how long does it usually last? Do you experience pain on a regular basis? What types of things help you when you feel pain? - Do your activities vary by the level of pain? How do you cope with your pain/illness?
How does spirituality impact your experience?	What does spirituality look like for you? Do you engage in any spiritual practices? If so, how would you describe them? How do you express/connect with spirituality? [How] Has your spirituality changed since your breast cancer diagnosis? [How] Has your awareness of your beliefs/values/dreams changed since your breast cancer diagnosis? - What role does intuition (or “inner guidance”) have? [How] Have your relationships with others changed since your breast cancer diagnosis? [How] Has your relationship with nature/the environment changed since your breast cancer diagnosis? Could you describe any connection(s) you feel with a higher power, or anything beyond the ordinary/observable world? When you think about your past experiences and your future, what gives your life meaning?
[How] do you see your spirituality as impacting your pain?	Please describe the relationship between your spirituality and pain. How would you describe about the purpose/meaning of your pain?
Are there any final thoughts you would like to share?	

Appendix I: Qualitative Study IRB Approval

MICHIGAN STATE UNIVERSITY

Initial Study APPROVAL

October 2, 2018

To: Gwen Wyatt

Re: **MSU Study ID:** STUDY00001138
IRB: Biomedical and Health Institutional Review Board Social Science
Principal Investigator: Gwen Wyatt
Category: Expedited 5 & 7
Submission: Initial Study STUDY00001138
Submission Approval Date: 10/2/2018
Effective Date: 10/2/2018
Study Expiration Date: 10/1/2019

Title: Qualitative Exploration of Pain & Spirituality in Women with Advanced Breast Cancer

Funding Title: Examining the Interconnectedness of Pain & Spiritual Quality of Life Among Women with Advanced Breast Cancer
Agency: Amer Nurses Foundation Inc
Status: Funded



**Office of
Regulatory
Affairs
Human Research
Protection Program**

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Suite 136
Lansing, MI 48910

517-355-2180
Fax: 517-432-4503
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www.hrpp.msu.edu

This submission has been approved by the Michigan State University (MSU) Biomedical and Health Institutional Review Board Social Science. The submission was reviewed by the Institutional Review Board (IRB) through Non-Committee Review procedure. The IRB has found that this study protects the rights and welfare of human subjects and meets the requirements of MSU's Federal Wide Assurance (FWA00004556) and the federal regulations for the protection of human subjects in research (e.g., 45 CFR 46, 21 CFR 50, 56, other applicable regulations).

This project falls under the Reliance agreement between MSU and Sparrow Hospital.

How to Access Final Documents

To access the study's final materials, including those approved by the IRB such as consent forms, recruitment materials, and the approved protocol, if applicable, please log into the Click™ Research Compliance System, open the study's workspace, and view the "Documents" tab. To obtain consent form(s) stamped with the IRB watermark, select the "Final" PDF version of your consent form(s) as applicable in the "Documents" tab. Please note that the consent form(s) stamped with the IRB watermark must typically be used.

Continuing Review: IRB approval is valid until the expiration date listed above. If the research continues to involve human subjects, you must submit a Continuing Review request at least one month before expiration.

Modifications: Any proposed change or modification with certain limited exceptions discussed below must be reviewed and approved by the IRB prior to implementation of the change. Please submit a Modification request to have the changes reviewed. If changes are made at the time of continuing review, please submit a Modification and Continuing Review request.

Immediate Change to Eliminate a Hazard: When an immediate change in a research protocol is necessary to eliminate a hazard to subjects, the proposed change need not be reviewed by the IRB prior to its implementation. In such situations, however, investigators must report the change in protocol to the IRB immediately thereafter.

Reportable Events: Certain events require reporting to the IRB. These include:

- Potential unanticipated problems that may involve risks to subjects or others
- Potential noncompliance
- Subject complaints
- Protocol deviations or violations
- Unapproved change in protocol to eliminate a hazard to subjects
- Premature suspension or termination of research
- Audit or inspection by a federal or state agency
- New potential conflict of interest of a study team member
- Written reports of study monitors
- Emergency use of investigational drugs or devices
- Any activities or circumstances that affect the rights and welfare of research subjects
- Any information that could increase the risk to subjects

Please report new information through the study's workspace and contact the IRB office with any urgent events. Please visit the Human Research Protection Program (HRPP) website to obtain more information, including reporting timelines.

Personnel Changes: Key study personnel must be listed on the MSU IRB application for expedited and full board studies and any changes to key study personnel must be submitted as modifications. Although only key study personnel need to be listed on a non-exempt application, all other individuals engaged in human subject research activities must receive and maintain current human subject training, must disclose conflict of interest, and are subject to MSU HRPP requirements. It is the responsibility of the Principal Investigator (PI) to maintain oversight over all study personnel and to assure and to maintain appropriate tracking that these requirements are met (e.g. documentation of training completion, conflict of interest). When non-MSU personnel are engaged in human research, there are additional requirements. See HRPP Manual Section 4-10, Designation as Key Project Personnel on Non-Exempt IRB Projects for more information.

Prisoner Research: If a human subject involved in ongoing research becomes a prisoner during the course of the study and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for

research involving prisoners under subpart C of 45 CFR part 46, the investigator must promptly notify the IRB.

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Closure: If the research activities no longer involve human subjects, please submit a Continuing Review request, through which study closure may be requested. Human subject research activities are complete if there is no further interactions or interventions with human subjects and/or no further analysis of identifiable private information.

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increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

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(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

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Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

Expedited 4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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MICHIGAN STATE UNIVERSITY

Continuing Review APPROVAL Pre-2018 Common Rule

July 17, 2019

To: Gwen Wyatt

Re: **MSU Study ID:** STUDY00001138
IRB: Biomedical and Health Institutional Review Board
Principal Investigator: Gwen Wyatt
Category: Expedited 5 & 7
Submission: Continuing Review CR00000776
Submission Approval Date: 7/11/2019
Effective Date: 7/11/2019
Study Expiration Date: 7/10/2020

Title: Qualitative Exploration of Pain & Spirituality in Women with Advanced Breast Cancer

This submission has been approved by the Michigan State University (MSU) Biomedical and Health Institutional Review Board. The submission was reviewed by the Institutional Review Board (IRB) through the Non-Committee Review procedure. The IRB has found that this study protects the rights and welfare of human subjects and meets the requirements of MSU's Federal Wide Assurance (FWA00004556) and the federal regulations for the protection of human subjects in research (e.g., pre-2018 45 CFR 46, 28 CFR 46, 21 CFR 50, 56, other applicable regulations).



**Office of
Regulatory
Affairs
Human Research
Protection Program**

4000 Collins Road
Suite 136
Lansing, MI 48910

517-355-2180
Fax: 517-432-4503
Email: irb@msu.edu
www.hrpp.msu.edu

How to Access Final Documents

To access the study's final materials, including those approved by the IRB such as consent forms, recruitment materials, and the approved protocol, if applicable, please log into the Click™ Research Compliance System, open the study's workspace, and view the "Documents" tab. To obtain consent form(s) stamped with the IRB watermark, select the "Final" PDF version of your consent form(s) as applicable in the "Documents" tab. Please note that the consent form(s) stamped with the IRB watermark must typically be used.

Continuing Review: IRB approval is valid until the expiration date listed above. If the research continues to involve human subjects, you must submit a Continuing Review request at least one month before expiration.

Modifications: Any proposed change or modification with certain limited exceptions discussed below must be reviewed and approved by the IRB prior to implementation of the change. Please submit a Modification request to have the changes reviewed. If changes are made at the time of continuing review, please submit a Modification and Continuing Review request.

New Funding: If new external funding is obtained to support this study, a Modification request must be submitted for IRB review and approval before new funds can be spent on human research activities, as the new funding source may have additional or different requirements.

Immediate Change to Eliminate a Hazard: When an immediate change in a research protocol is necessary to eliminate a hazard to subjects, the proposed change need not be reviewed by the IRB prior to its implementation. In such situations, however, investigators must report the change in protocol to the IRB immediately thereafter.

Reportable Events: Certain events require reporting to the IRB. These include:

- Potential unanticipated problems that may involve risks to subjects or others
- Potential noncompliance
- Subject complaints
- Protocol deviations or violations
- Unapproved change in protocol to eliminate a hazard to subjects
- Premature suspension or termination of research
- Audit or inspection by a federal or state agency
- New potential conflict of interest of a study team member
- Written reports of study monitors
- Emergency use of investigational drugs or devices
- Any activities or circumstances that affect the rights and welfare of research subjects
- Any information that could increase the risk to subjects

Please report new information through the study's workspace and contact the IRB office with any urgent events. Please visit the Human Research Protection Program (HRPP) website to obtain more information, including reporting timelines.

Personnel Changes: Key study personnel must be listed on the MSU IRB application for expedited and full board studies and any changes to key study personnel must be submitted as modifications. Although only key study personnel need to be listed on a non-exempt application, all other individuals engaged in human subject research activities must receive and maintain current human subject training, must disclose conflict of interest, and are subject to MSU HRPP requirements. It is the responsibility of the Principal Investigator (PI) to maintain oversight over all study personnel and to assure and to maintain appropriate tracking that these requirements are met (e.g. documentation of training completion, conflict of interest). When non-MSU personnel are engaged in human research, there are additional requirements. See HRPP Manual Section 4-10, Designation as Key Project Personnel on Non-Exempt IRB Projects for more information.

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1200 E. Michigan Ave, Suite 550
Lansing, Michigan 48912
Phone: 517-364-5760

September 28, 2018

Gwen Wyatt RN, PhD, FAAN
1355 Bogue St, Room C345
MSU College of Nursing
gwyatt@msu.edu

Re: MSU IRB # 1138
Study Title: Qualitative Exploration of Pain & Spirituality in Women with Advanced Breast Cancer

Dear Dr. Wyatt

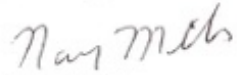
Sparrow Health System through Sparrow Clinical Research Institute is pleased to notify you that your request to conduct the above mentioned research study has been approved as follows:

- MSU IRB approval is pending. *Reminder that MSU IRB approval is required separate from Sparrow approval.*
- Location (s): Sparrow Cancer Center – Tumor Registry, Breast Cancer Support Group (presentation), SCRI office located in the Sparrow Professional Building Suite 550 (if needed to assemble mailings).
- MSU research staff applications have been completed for Megan Flanigan. Please complete an MSU research staff application for any staff added throughout the study that will involve coming to a Sparrow location.
- Access to Subject medical records is NA.
- Badge access is NA.
- Protocol Summary was received. Please provide updated version if revised.
- Copy of the IRB approved consent and Patient HIPPA Waiver are on file. Please provide updated versions if revised.
- Schedule of Events occurring at Sparrow is NA.
- A signed contract is on file. Any study changes that affect this agreement may require a revision.
- There are no research related subject events that require billing to MSU or subject insurance.
- SCRI will be provided with copies of any study amendments related to any activities at Sparrow, when Sparrow or new Sparrow records are no longer being utilized for the study, or when the study is closed with the MSU IRB.

- If you plan to use any study provided and/or personal equipment or supplies (ie ECG Machines, tablets, laptops, blood draw kits if used by person not employed by Sparrow at the date and time used) on any subjects they must be approved by SCRI.
- We request that Sparrow Health System be acknowledged in any publications.
- As a reminder, you as the Principal Investigator, must adhere to the Sparrow policies for research. SCRI reserves the right to withdraw this approval if any Sparrow research policies or conditions of this letter are violated.

We look forward to the successful completion of your study. If you have any further questions or need any assistance, please contact SCRI at (517) 364-5760.

Sincerely,

A handwritten signature in cursive script, appearing to read "Nancy Miller".

Nancy Miller
Director of Research

REFERENCES

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- Abernethy, A., Herndon, J., Coan, A., Staley, T., Wheeler, J., Rowe, K., & Lyerly, H. (2010). Phase 2 Pilot Study of Pathfinders: A Psychosocial Intervention for Cancer Patients. *Support Care Cancer*, 18(7), 893-898. doi:10.1007/s00520-010-0823-z
- Abernethy, A. P., Herndon, J. E., 2nd, Coan, A., Staley, T., Wheeler, J. L., Rowe, K., . . . Lyerly, H. K. (2010). Phase 2 Pilot Study of Pathfinders: A Psychosocial Intervention for Cancer Patients. *Supportive Care in Cancer*, 18(7), 893-898. doi:10.1007/s00520-010-0823-z
- Agin-Liebes, G., Malone, T., Yalch, M., Mennenga, S., Ponte, K., Guss, J., . . . Ross, S. (2020). Long-Term Follow-Up of Psilocybin-Assisted Psychotherapy for Psychiatric and Existential Distress in Patients With Life-threatening Cancer. *Journal of Psychopharmacology*, 34(2), 155-166. doi:10.1177/0269872320917161
- Ahmad, F., Muhammad, M., & Abdullah, A. (2011). Religion and Spirituality in Coping with Advanced Breast Cancer: Perspectives from Malaysian Muslim Women. *J Relig Health*, 50(1), 36-45. doi:10.1007/s10943-010-9401-4
- Akbari, M. E., Kashani, F. L., Ahangari, G., Pornour, M., Hejazi, H., Nooshinfar, E., . . . Hosseini, L. (2016). The Effects of Spiritual Intervention and Changes in Dopamine Receptor Gene Expression in Breast Cancer Patients. *Breast Cancer*, 23(6), 893-900. doi:10.1007/s12282-015-0658-z
- Al-Natour, A., Al Momani, S., & Qandil, A. (2017). The Relationship Between Spirituality and Quality of Life of Jordanian Women Diagnosed with Breast Cancer. *J Relig Health*, 56(5), 2096-2108. doi:10.1007/s10943-017-0370-8
- Al-Natour, A., Al Momani, S., & Qandil, A. (2017). The Relationship Between Spirituality and Quality of Life of Jordanian Women Diagnosed with Breast Cancer. *J Religion Health*, 56(6), 2096-2108. doi:10.1007/s10943-017-0370-8
- Albabbainm, H., Alwhaibi, M., Alburaikan, K., & Asiri, Y. (2018). Quality of Life and Complementary and Alternative Medicine Use Among Women with Breast Cancer. *Saudi Pharmaceutical Journal*, 26(3), 416-421. doi: 10.1016/j.jsps.2017.12.020.
- Alves, M. L., Vieira, J. E., Mathias, L. A., & Gozzani, J. L. (2013). Preoperative Coping Mechanisms Have No Predictive Value for Postoperative Pain in Breast Cancer. *Rev Bras Psiquiatr*, 35(4), 364-368. doi:10.1590/1516-4446-2012-0934

- American Cancer Society. (2019). *Cancer Facts and Figures: 2019*. Retrieved from <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf>
- Aneja, S., & Yu, J. (2016). The Effect of Marital Status on Health-Related Quality of Life in Elderly Patients Undergoing Radiation Therapy. *Int J Radiat Oncol Biol Phys*, 96(2S), S161. doi:10.1016/j.ijrobp.2016.06.389
- Arathuzik, M. D. (2009). Living with Suffering: The Process of Coping with Metastatic Breast Cancer Pain. *Oncol Nurs Forum*, 36(3), 34-34.
- Arksey, H., & O'Malley, L. (2005). Scoping Studies: Towards a Methodological Framework. *Int J Soc Res Methodol*, 8(1), 19-32. doi:10.1080/1364557032000119616
- Arnstein, P. (2018). Adult Cancer Pain: An Evidence-Based Update. *Journal of Radiology Nursing*, 37, 15-20. doi:10.1016/j.jradnu.2017.10.009
- Arntz, A., & Classens, L. (2004). The Meaning of Pain Influences its Experienced Intensity. *Pain*, 109(1-2), 20-25. doi: 10.1016/j.pain.2003.12.030
- Atahan, L., Yildiz, F., Cengiz, M., Kaplan, B., Ozkan, M., Yazici, G., . . . Hayran, M. (2010). Zoledronic Acid Concurrent with Either High- or Reduced-Dose Palliative Radiotherapy in the Management of the Breast Cancer Patients with Bone Metastases: A Phase IV Randomized Clinical Study. *Support Care Cancer*, 18(6), 691-698. doi:10.1007/s00520-009-0663-x
- Auvray, M., Myin, E., & Spence, C. (2010). The Sensory-Discriminative and Affective-Motivational Aspects of Pain. *Neuroscience and Biobehavioral Reviews*, 34, 214-223. doi:10.1016/j.neubiorev.2008.07.008
- Bai, J., Brubaker, A., Meghani, S., Bruner, D., & Yeager, K. (2018). Spirituality and Quality of Life in Black Patients with Cancer Pain. *Journal of Pain and Symptom Management*, [Epub](3), 390-398. doi:10.1016/j.jpainsymman.2018.05.020
- Balboni, T., Balboni, M., Paulk, M. E., Phelps, A., Wright, A., Peteet, J., . . . Prigerson, H. (2011). Support of Cancer Patients' Spiritual Needs and Associations With Medical Care Costs at the End of Life. *Cancer*, 117(23), 5383-5391. doi:10.1002/cncr.26221
- Balducci, L. (2019). Geriatric Oncology, Spirituality, and Palliative Care. *J Pain Symptom Manage*, 57(1), 171-175. doi: 10.1016/j.jpainsymman.2018.05.009
- Barkwell, D. (1991). Ascribed Meaning: A Critical Factor in Coping and Pain Attenuation Inpatients With Cancer-Related Pain. *Journal of Palliative Care*, 7(3), 5-14.

- Barnes, P. M., Bloom, B., & Nahin, R. (2008). Centers for Disease Control. Complementary and Alternative Medicine use Among Adults and Children: United States, 2007. National Health Statistics Reports. *National Health Statistics Reports*, 12, 1-24.
- Barragan-Campos, H. M., Le Faou, A. L., Rose, M., Livartowski, A., Doz, M., Astagneau, P., . . . Chiras, J. (2014). Percutaneous Vertebroplasty in Vertebral Metastases from Breast Cancer: Interest in Terms of Pain Relief and Quality of Life. *Interv Neuroradiol*, 20(5), 591-602. doi:10.15274/inr-2014-10084
- Belfer, I., Schreiber, K., Shaffer, J., Shnol, H., Blaney, K., Morando, A., . . . Bovbjerg, D. (2013). Persistent Postmastectomy Pain in Breast Cancer Survivors: Analysis of Clinical, Demographic, and Psychosocial Factors. *Journal of Pain*, 14(10), 1185-1195. doi:10.1016/j.jpain.2013.05.002
- Bell, T., Crown, J. P., Lang, I., Bhattacharyya, H., Zanotti, G., Randolph, S., . . . Slamon, D. (2016). Impact of Palbociclib Plus Letrozole on Pain Severity and Pain Interference with Daily Activities in Patients with Estrogen Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer as First-Line Treatment. *Curr Med Res Opin*, 32(5), 959-965. doi:10.1185/03007995.2016.1157060
- Benner, P. (1994). *Interpretive Phenomenology: Embodiment, Caring, and Ethics in Health and Illness*: SAGE Publications. doi: <http://dx.doi.org/10.4135/9781452204727>
- Blackburn, L., Abel, S., Green, L., Johnson, K., & Panda, S. (2019). The Use of Comfort Kits to Optimize Adult Cancer Pain Management. *Pain Manag Nurs*, 20, 25-31. doi:10.1016/j.pmn.2018.01.004
- Boon, H., Olatunde, F., & Zick, S. (2007). Trends in Complementary/Alternative Medicine use by Breast Cancer Survivors: Comparing Survey Data from 1998 and 2005. *BMC Womens Health*, 7(4). doi: 10.1186/1472-6874-7-4
- Brant, J., Dudley, W., Beck, S., & Miaskowski, C. (2016). Evolution of the Dynamic Symptoms Model. *Oncol Nurs Forum*, 43(5), 651-654. doi:10.1188/16.ONF.651-654
- Breitbart, W., Poppito, S., Rosenfeld, B., Vickers, A. J., Li, Y., Abbey, J., . . . Cassileth, B. R. (2012). Pilot Randomized Controlled Trial of Individual Meaning-Centered Psychotherapy for Patients with Advanced Cancer. *J Clin Oncol*, 30(12), 1304-1309. doi:10.1200/JCO.2011.36.2517
- Bushnell, C., Ceko, M., & Low, L. (2013). Cognitive and Emotional Control of Pain and its Disruption in Chronic Pain. *Nature Reviews Neuroscience*, 14(7). doi: 10.1038/nrn3516

- Butler, L. D., Koopman, C., Neri, E., Giese-Davis, J., Palesh, O., Thorne-Yocam, K. A., . . . Spiegel, D. (2009). Effects of Supportive-Expressive Group Therapy on Pain in Women With Metastatic Breast Cancer. *Health Psychol*, 28(5), 579-587. doi:10.1037/a0016124
- Byers, D. (2001). *Better Health With Foot Reflexology: The Ingham Method* (Rev. ed. ed.). St. Petersburg, FL: Ingham Publishing Inc.
- Caldeira, S., Timmins, F., de Carvalho, E. C., & Vieira, M. (2016). Nursing Diagnosis of "Spiritual Distress" in Women With Breast Cancer: Prevalence and Major Defining Characteristics. *Cancer Nurs*, 39(4), 321-327. doi:10.1097/ncc.0000000000000310
- Carson, J., Carson, K., Olsen, M., Sanders, L., & Porter, L. (2017). Mindful Yoga for Women With Metastatic Breast Cancer: Design of a Randomized Controlled Trial. *BMC Complement Altern Med*, 17(1), 153. doi:10.1186/s12906-017-1672-9
- Carson, J., Carson, K., Porter, L., Keefe, F., Shaw, H., & Miller, J. (2007). Yoga for Women with Metastatic Breast Cancer: Results from a Pilot Study. *Journal of Pain and Symptom Management*, 33(3), 331-341. doi:10.1016/j.jpainsymman.2006.08.009
- Castel, L., Saville, B., DePuy, V., Godley, P., Hartmann, K., & Abernethy, A. (2007). Racial Differences in Pain During 1 Year Among Women With Metastatic Breast Cancer. *Cancer*, 112(1), 162-170. doi: 10.1002/cncr.23133
- Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., . . . Hays, R. (2010). Initial Item Banks and First Wave Testing of the Patient-Reported Outcomes Measurement Information System (PROMIS) Network: 2005-2008. *J Clin Epidemiol.*, 63(11), 1179-1194. doi:10.1016/j.jclinepi.2010.04.011
- Cella, D., Yount, S., Rothrock, N., Gershon, R., Cook, K., Reeve, B., . . . Rose, M. (2007). The Patient-Reported Outcomes Measurement Information System (PROMIS): Progress of an NIH Roadmap Cooperative Group During its First Two Years. *Med Care*, 45(5), S3-S11. doi: 10.1097/01.mlr.0000258615.42478.55
- Centers for Disease Control and Prevention. (2016). Guideline for Prescribing Opioids for Chronic Pain. Retrieved from https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fmmwr%2Fvolumes%2F65%2Frr%2Frr6501e1er.htm
- Centers for Disease Control and Prevention. (2019). Expected New Cancer Cases and Deaths in 2020. Retrieved from https://www.cdc.gov/cancer/dcpc/research/articles/cancer_2020.htm

- Chen, S., & Walsh, S. (2009). Effect of a Creative-Bonding Intervention on Taiwanese Nursing Students' Self-Transcendence and Attitudes Toward Elders. *Res Nurs Health*, 32(2), 204-216. doi:10.1002/nur.20310.
- Clark, D. (1999). 'Total Pain', Disciplinary Power and the Body in the Work of Cicely Saunders, 1958–1967. *Social Science & Medicine*, 49(6), 727-736. doi:http://dx.doi.org/10.1016/S0277-9536(99)00098-2
- Cleeland, C. S., Body, J. J., Stopeck, A., von Moos, R., Fallowfield, L., Mathias, S. D., . . . Chung, K. (2013). Pain Outcomes in Patients With Advanced Breast Cancer and Bone Metastases: Results from a Randomized, Double-Blind Study of Denosumab and Zoledronic Acid. *Cancer*, 119(4), 832-838. doi:10.1002/cncr.27789
- Closs, S. J., & Briggs, M. (2013). Religious Identity and the Experience and Expression of Chronic Pain: A Review. *Journal of Religion, Disability & Health*, 17, 91–124. doi:10.1080/15228967.2013.778515
- Connelly, L. (2016). Trustworthiness in Qualitative Research. *Medsurg Nursing*, 25(6), 435-436.
- Cook, E., & Silverman, M. J. (2013). Effects of Music Therapy on Spirituality with Patients on a Medical Oncology/ Hematology Unit: A Mixed-Methods Approach. *The Arts in Psychotherapy*, 40(2), 239-244. doi: 10.1016/j.aip.2013.02.004
- Cooper, R. S. (2011). Case Study of a Chaplain's Spiritual Care for a Patient with Advanced Metastatic Breast Cancer. *J Health Care Chaplain*, 17(1/2), 19-37. doi:10.1080/08854726.2011.559832
- Coward, D. (2003). Facilitation of Self-Transcendence in a Breast Cancer Support Group: II. *Oncology Nursing Forum*, 30(2), 291-300. doi:10.1188/03.ONF.291-300
- Coward, D., & Kahn, D. (2004). Resolution of Spiritual Disequilibrium by Women Newly Diagnosed with Breast Cancer. *Oncol Nurs Forum*, 31, E1-E8. doi:10.1188/04.ONF.E24-E31
- Cronfalk, B., Strang, P., & Ternstedt, B. (2009). Inner Power, Physical Strength and Existential Well-Being in Daily Life: Relatives' Experiences of Receiving Soft Tissue Massage in Palliative Home Care. *J Clin Nurs*, 18(15), 2225-2233. doi: 10.1111/j.1365-2702.2008.02517.x.
- Davis, C. (2020). Greater Social Support May Help Alleviate Pain in Patients with Cancer. *Oncology Nurse*, 13(1), 14.

- Deandrea, S., Corli, O., Consonni, D., Villani, W., Greco, M. T., & Apolone, G. (2014). Prevalence of Breakthrough Cancer Pain: A Systematic Review and a Pooled Analysis of Published Literature. *J Pain Symptom Manage*, 47(1), 57-76. doi:10.1016/j.jpainsymman.2013.02.015
- Delgado-Guay, M. O., Chisholm, G. B., Williams, J., Frisbee-Hume, S., Ferguson, A., & Bruera, E. (2016). Frequency, Intensity, and Correlates of Spiritual Pain in Advanced Cancer Patients Assessed in a Supportive/Palliative Care Clinic. *Palliative & Supportive Care*, 14(4), 341-348. doi:10.1017/S147895151500108X
- Di Franco, R., Falivene, S., Ravo, V., Mammucari, M., Sarli, E., Baffini, S., . . . Muto, P. (2014). Management of Painful Bone Metastases: Our Experience According to Scientific Evidence on Palliative Radiotherapy. *Anticancer Res*, 34(2), 1011-1014.
- Eilami, O., Moslemirad, M., Naimi, E., Babuei, A., & Rezaei, K. (2019). The Effect of Religious Psychotherapy Emphasizing the Importance of Prayers on Mental Health and Pain in Cancer Patients. *Journal of Religion and Health*, 58, 444-451. doi: 10.1007/s10943-018-0696-x.
- Ersek, M., & Ferrell, B. (1994). Providing Relief From Cancer Pain by Assisting in the Search for Meaning. *Journal of Palliative Care*, 10(1), 15-22.
- Ettun, R., Schultz, M., & Bar-Sela, G. (2014). Transforming Pain into Beauty: On Art, Healing, and Care for the Spirit. *Evidence-Based Complementary and Alternative Medicine*, 1-7. doi: 10.1155/2014/789852
- Farahani, A., Rassouli, M., Salmani, N., Mojen, L., Sajjadi, M., Heidarzadeh, M., . . . Khademi, F. (2019). Evaluation of Health-Care Providers' Perception of Spiritual Care and the Obstacles to its Implementation. *Asia-Pacific Journal of Oncology Nursing*, 6(2), 122-129. doi: 10.4103/apjon.apjon_69_18.
- Ferrell, B. (2000). The Cost of Comfort: Economics of Pain Management in Oncology. *ONE*, 1(9), 56-61. doi: https://doi.org/10.1016/0885-3924(94)90099-X
- Ferrell, B., Grant, M., Padilla, G., Vemuri, S., & Rhiner, M. (1991). The Experience of Pain and Perceptions of Quality of Life: Validations of a Conceptual Model. *The Hospice Journal*, 7(3), 9-24. doi: 10.1080/0742-969x.1991.11882702
- Flanigan, M., & Cui, Y. (2019). Does Reflexology Use Impact Spirituality? [unpublished data analysis]. Michigan State University.

- Flanigan, M., Wyatt, G., & Lehto, R. (2019). Spiritual Perspectives on Pain in Advanced Breast Cancer: A Scoping Review. *Pain Manag Nurs*, 18, S1524-9042. doi:10.1016/j.pmn.2019.04.002
- Frambes, D., Lehto, R., Sikorskii, A., Tesnjak, I., Given, B., & Wyatt, G. (2017). Fidelity Scorecard: Evaluation of a Caregiver-Delivered Symptom Management Intervention. *Journal of Advanced Nursing*, 73(8), 2012-2021. doi:10.1111/jan.13266
- Gagliese, L., Gauthier, L., & Rodin, G. (2007). Cancer Pain and Depression: A Systematic Review of Age-Related Patterns. *Pain Res Manag J Can Pain Soc.*, 12, 205-211. doi: 10.1155/2007/150126
- Galloway, S., Meadors, D., Boselli, D., & Walsh, D. (2019). *Anxiety, Depression, Pain, and Social Support in a Large Representative Cancer Population*. Paper Presented at the American Society for Clinical Oncology 2019 Annual Meeting. Retrieved from: <https://meetinglibrary.asco.org/record/180885/abstract>
- Ganz, P. A., Schag, C., & Sim, M. (1992). The CARES: A Generic Measure of Health-Related Quality of Life for Patients with Cancer. *Qual Life Res*, 1, 19-29. doi: 10.1007/bf00435432
- Gaston-Johansson, F., Haisfield-Wolfe, M., Reddick, B., Goldstein, N., & Lawal, T. (2013). The Relationships Among Coping Strategies, Religious Coping, and Spirituality in African American Women With Breast Cancer Receiving Chemotherapy. *Oncol Nurs Forum*, 40(2), 120-131. doi: 10.1188/13.ONF.120-131.
- Gauthier, L., Dworkin, R. H., Warr, D., Pillai-Riddell, R., Macpherson, A., Rodin, G., . . . Gagliese, L. (2018). Age-Related Patterns in Cancer Pain and Its Psychosocial Impact: Investigating the Role of Variability in Physical and Mental Health Quality of Life. *Pain Med*, 19(4), 658–676. doi:proxy1.cl.msu.edu/10.1093/pm/pnx002
- Given, B., Given, C., Sikorskii, A., Jeon, S., McCorkle, R., Champion, V., & Decker, D. (2008). Establishing Mild, Moderate, and Severe Scores for Cancer-Related Symptoms: How Consistent and Clinically Meaningful Are Interference-Based Severity Cut-Points? *Journal of pain and symptom management*, 35(2), 126-135. doi: 10.1016/j.jpainsymman.2007.03.012
- Given, C., Given, B., Azzouz, F., Kozachik, S., & Stommel, M. (2001). Predictors of Pain and Fatigue in the Year Following Diagnosis Among Elderly Cancer Patients. *J Pain Symptom Manage*, 21(6), 456-466. doi:10.1016/s0885-3924(01)00284-6
- Glesne, C. (2015). *Becoming Qualitative Researchers: An Introduction, 5th Edition*. MA: Longman.

- Grady, P., & Lucio-Gough, L. (2014). Self-Management: A Comprehensive Approach to Management of Chronic Conditions. *Am J Public Health, 104*(8), e25–e31. doi:10.2105/AJPH.2014.302041
- Grealish, L., Lomasney, A., & Whiteman, B. (2000). Foot Massage: A Nursing Intervention to Modify the Distressing Symptoms of Pain and Nausea in Patients Hospitalized With Cancer. *Cancer Nurs, 23*(3), 237-243. doi: 10.1097/00002820-200006000-00012
- Gregg, G. (2011). I'm A Jesus Girl: Coping Stories of Black American Women Diagnosed with Breast Cancer. *J Relig Health, 50*(4), 1040–1053. doi:10.1007/s10943-010-9395-y
- Griffiths, R., Johnson, M., Carducci, M., Umbricht, A., Richards, W., Richards, B., . . . Klinedinst, M. (2016). Psilocybin Produces Substantial and Sustained Decreases in Depression and Anxiety in Patients With Life-Threatening Cancer: A Randomized Double-Blind Trial. *Journal of Psychopharmacology, 30*(12), 1181-1197. doi:10.1177/0269881116675513
- Guest, G., Bunce, A., & Johnson, L. (2006). How Many Interviews Are Enough? An Experiment With Data Saturation and Variability. *Field Methods, 18*(1), 59-82. doi: <https://doi.org/10.1177/1525822X05279903>
- Guion, L. (2002). Triangulation: Establishing the Validity of Qualitative Studies. . *University of Florida Cooperative Extension Service, Institute of Food and Agricultural Sciences, EDIS*.
- Harvey, I. (2008). Assessing Self-Management and Spirituality Practices Among Older Women. *American Journal of Health Behavior, 32*(2), 157-168. doi: 10.5555/ajhb.2008.32.2.157
- HealthMeasures. (2018). Available PROMIS® Measures for Adults. Retrieved from <http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/list-of-adult-measures>
- Holloway, I. (1997). *Basic Concepts for Qualitative Research*. London: Blackwell Science.
- Hospice and Palliative Nurses Association. (2007). Position Paper: Spiritual Care. *Journal of Hospice & Palliative Nursing, 9*(1), 15-16.
- Hsiao, A., Wong, M., Miller, M., Ambs, A., Goldstein, M., Smith, A., . . . Wenger, n. (2008). Role of Religiosity and Spirituality in Complementary and Alternative Medicine Use Among Cancer Survivors in California. *Integrative Cancer Therapies, 7*(7), 139-146. doi:10.1177/1534735408322847

- Hughes, S., Jaremka, L., Alfano, C., Glaser, R., Povoski, S., Lipari, A., . . . Kiecolt-Glaser, J. (2014). Social Support Predicts Inflammation, Pain, and Depressive Symptoms: Longitudinal Relationships Among Breast Cancer Survivors. *Psychoneuroendocrinology*, 42, 38-44. doi: 10.1016/j.psyneuen.2013.12.016
- Hui, D., De La Cruz, M., Thorney, S., Parsons, H. A., Delgado-Guay, M. O., & Bruera, E. (2011). The Frequency and Correlates of Spiritual Distress Among Patients With Advanced Cancer Admitted to an Acute Palliative Care Unit. *American Journal of Hospice & Palliative Care*, 28(4), 264-270. doi: 10.1177/1049909110385917.
- International Association for the Study of Pain. (1979). IASP pain terms - 1979. *Pain*, 6, 247-252.
- International Association for the Study of Pain. (2009). Mechanisms of Cancer Pain. Retrieved from https://www.iasp-pain.org/files/AM/Images/GYAP/CancerPain_Final.pdf
- JadidMilani, M., Ashktorab, T., AbedSaeedi, Z., & AlaviMajd, H. (2015). The Impact of Self-Transcendence on Physical Health Status Promotion in Multiple Sclerosis Patients Attending Peer Support Groups. *International Journal of Nursing Practice*, 21, 725-732. doi: 10.1111/ijn.12186
- Jensen, M., Smith, D., Ehde, D., & Robinson, L. (2001). Pain Site and the Effects of Amputation Pain: Further Clarification of the Meaning of Mild, Moderate, and Severe Pain. *Pain*, 317-322. doi: 10.1016/s0304-3959(00)00459-0
- Jensen, M., Tome-Pires, C., de la Vega, R., Galan, S., Sole, E., & Miro, J. (2017). What Determines Whether a Pain is Rated as Mild, Moderate, or Severe? The Importance of Pain Beliefs and Pain Interference. *Clin J Pain*, 33(5), 414-421. doi:10.1097/AJP.0000000000000429
- Jensen, R., Potosky, A., Reeve, B., Hahn, E., Cella, D., Fries, J., . . . Moinpour, C. (2015). Validation of the PROMIS Physical Function Measures in a Diverse U.S. Population-Based Cohort of Cancer Patients. *Qual Life Res*, 24(10), 2333-2344. doi:10.1007/s11136-015-0992-9
- Jeon, S., Given, C., Sikorskii, A., & Given, B. (2009). Do Interference-Based Cut-Points Differentiate Mild, Moderate, and Severe Levels of 16 Cancer-Related Symptoms Over Time? *J Pain Symptom Manage*, 37(2), 220-232. doi: 10.1016/j.jpainsymman.2008.01.010
- Jugali, R., Yodchai, K., & Thaniwattananon, P. (2018). Factors Influencing Spiritual Well-Being in Patients Receiving Haemodialysis: A Literature Review. *Renal Society of Australasia Journal*, 14(3), 90-95.

- Kamp, K., Flanigan, M., Thana, K., Terpstra, J., Wyatt, G., & Sikorskii, A. (2019). Expanding Application of the Long-Term Quality of Life (LTQL) Instrument to the Population of Women Undergoing Treatment for Advanced Breast Cancer. *[Epub]. Cancer Nurs.* doi: 10.1097/NCC.0000000000000768
- Keefe, F., Rumble, M., Scipio, C., Giordano, L., & Perri, L. (2004). Psychological Aspects of Persistent Pain: Current State of the Science. *The Journal of Pain*, 5(4), 195-211. doi:10.1016/j.jpain.2004.02.576
- Kokkonen, K., Saarto, T., Makinen, T., Pohjola, L., Kautio, H., Jarvenpaa, S., & Puustjarvi-Sunabacka, K. (2017). The Functional Capacity and Quality of Life of Women With Advanced Breast Cancer. *Breast Cancer*, 24(1), 128-136. doi:10.1007/s12282-016-0687-2
- Krigel, S., Myers, J., Befort, C., Krebill, H., & Klemp, J. (2014). 'Cancer Changes Everything!' Exploring the Lived Experiences of Women With Metastatic Breast Cancer. *Int J Palliat Nurs.*, 20(7), 334-342. doi:10.12968/ijpn.2014.20.7.334
- Kumar, N., Bhatnagar, S., Velpandian, T., Patnaik, S., Menon, G., Mehta, M., . . . Surajpal. (2013). Randomized Controlled Trial in Advance Stage Breast Cancer Patients for the Effectiveness on Stress Marker and Pain through Sudarshan Kriya and Pranayam. *Indian J Palliat Care*, 19(3), 180-185. doi:10.4103/0973-1075.121537
- Kwekkeboom, K., Cherwin, C., Lee, J., & Wanta, B. (2010). Mind-Body Treatments for the Pain-Fatigue-Sleep Disturbance Symptom Cluster in Persons with Cancer. *Journal of Pain and Symptom Management*, 39, 126-138. doi: 10.1016/j.jpainsymman.2009.05.022
- Kwok, W., & Bhuvanakrishna, T. (2014). The Relationship Between Ethnicity and the Pain Experience of Cancer Patients: A Systematic Review. *Indian J Palliat Care*, 20(3). doi:10.4103/0973-1075.138391
- Laroche, F., Coste, J., Medkour, T., Cottu, P., Pierga, J., Lotz, J., . . . Perrot, S. (2014). Classification of and Risk Factors for Estrogen Deprivation Pain Syndromes Related to Aromatase Inhibitor Treatments in Women With Breast Cancer: A Prospective Multicenter Cohort Study. *The Journal of Pain*, 15(3), 293-303. doi: 10.1016/j.jpain.2013.11.004
- Lazenby, M. (2018). Understanding and Addressing the Religious and Spiritual Needs of Advanced Cancer Patients. *Seminars in Oncology Nursing*, 34(3). doi:10.1016/j.soncn.2018.06.008
- Lazenby, M., McCorkle, R., & Sulmasy, D. (2014). *Safe passage: A Global Spiritual Sourcebook for Care at the End of Life*. New York: Oxford University Press.

- Lee, C. E., Kim, S., Kim, S., Joo, H. M., & Lee, S. (2017). Effects of a Mindfulness-Based Stress Reduction Program on the Physical and Psychological Status and Quality of Life in Patients With Metastatic Breast Cancer. *Holist Nurs Pract*, 31(4), 260-269. doi:10.1097/hnp.0000000000000220
- Levine, E., Aviv, C., Yoo, G., Ewing, C., & Au, A. (2009). The Benefits of Prayer on Mood and Well-Being of Breast Cancer Survivors. *Support Care Cancer*, 17, 295–306. doi: 10.1007/s00520-008-0482-5
- Levine, E., Yoo, G., Aviv, C., Ewing, C., & Au, A. (2007). Ethnicity and Spirituality in Breast Cancer Survivors. *J Cancer Surviv*, 1(3), 212-225. doi:10.1007/s11764-007-0024-z
- Leysen, L., Adriaenssens, N., Nijs, J., Lahousse, A., & Beckwee, D. (2018). Chronic Pain in Breast Cancer Survivors: Nociceptive, Neuropathic, or Central Sensitization Pain? *Pain Practice*, 19(2), 183-195. doi: 10.1111/papr.12732
- Li, K., Harris, K., Hadi, S., & Chow, E. (2007). What Should be the Optimal Cut Points for Mild, Moderate, and Severe Pain? *Journal of Palliative Medicine*, 10(6), 1338-1346. doi:10.1089/jpm.2007.0087
- Lincoln, Y. S., & Guba, E. G. (1985). *Naturalistic Inquiry*. Newbury Park, CA: Sage Publications.
- Lohman, D., Schleifer, R., & Amon, J. (2010). Access to Pain Treatment as a Human Right. *BMC Medicine*, 8(8).
- Lumley, M., Cohen, J., Borszcz, G., Cano, A., Radcliffe, A., Porter, L., . . . Keefe, F. (2011). Pain and Emotion: A Biopsychosocial Review of Recent Research. *J Clin Psychol*, 67(9), 942–968. doi:10.1002/jclp.20816
- Luo, Q., & Asher, G. (2017). Complementary and Alternative Medicine Use at a Comprehensive Cancer Center. *Integrative Cancer Therapies*, 16(1), 104-109. doi:10.1177/1534735416643384
- Mackenzie, M., Carlson, L., Munoz, M., & Specia, M. (2007). A Qualitative Study of Self-Perceived Effects of Mindfulness-Based Stress Reduction (MBSR) in a Psychosocial Oncology Setting. *Stress and Health*, 23, 59-69. doi: https://doi.org/10.1002/smi.1120
- Maindet, C., Burnod, A., Mainello, C., George, B., Allano, G., & Lemaire, A. (2019). Strategies of Complementary and Integrative Therapies in Cancer-Related Pain: Attaining Exhaustive Cancer Pain Management. *Supportive Care in Cancer*, 27, 3119–3132. doi:10.1007/s00520-019-04829-7

- Matthews, E., & Cook, P. (2009). Relationships Among Optimism, Well-Being, Self-Transcendence, Coping, and Social Support in Women During Treatment for Breast Cancer. *Psychooncology*, 18(7), 716-726. doi:10.1002/pon.1461.
- Mazor, M., Cataldo, J., Lee, K., Dhruva, A., Paul, S., Smoot, B., . . . Miaskowski, C. (2018). Influence of Menopausal Status on the Symptom Experience of Women Before Breast Cancer Surgery. *Cancer Nurs*, 41(4), 265-278. doi: 10.1097/NCC.0000000000000545
- McAlister, M., Clemson, D., Ehlert, K., Kajfez, R., Faber, C., & Kennedy, M. (2017). Qualitative Coding: An Approach to Assess Inter-Rater Reliability. *American Society for Engineering Education*. doi: 10.18260/1-2--28777
- McCabe, R., Murray, R., Austin, P., & Siddall, P. (2018). Spiritual and Existential Factors Predict Pain Relief in a Pain Management Program With a Meaning-Based Component. *Journal of Pain Management*, 11(2), 163-170.
- McCaffery, M. (1968). *Nursing Practice Theories Related to Cognition, Bodily Pain, and Man-Environment Interactions*. Los Angeles: University of California at Los Angeles Students' Store.
- McCarthy, V., Hall, L., Crawford, T., & Connelly, J. (2018). Facilitating Self-Transcendence: An Intervention to Enhance Well-Being in Late Life. *Western Journal of Nursing Research*, 40(6), 854-873. doi: 10.1177/0193945917690731
- McGrady, A., & Moss, D. (2018). *Integrative Pathways: Navigating Chronic Illness with a Mind-Body-Spirit Approach*. Cham, Switzerland: Springer.
- McPherson, C. J., Hadjistavropoulos, T., Lobchuk, M. M., & Kilgour, K. N. (2013). Cancer-Related Pain in Older Adults Receiving Palliative Care: Patient and Family Caregiver Perspectives on the Experience of Pain. *Pain Res Manag*, 18(6), 293-300. doi:dx.doi.org/15227
- McVicar, A., Greenwood, C., Fewell, F., D'Arcy, V., Chandrasekharan, S., & Alldridge, L. (2007). Evaluation of Anxiety, Salivary Cortisol and Melatonin Secretion Following Reflexology Treatment: A Pilot Study in Healthy Individuals. *Complement Ther Clin Pract*, 13(1), Complement Ther Clin Pract. doi: 10.1016/j.ctcp.2006.11.001
- Meriggiola, M. C., Nanni, M., Bachiocco, V., Vodo, S., & Aloisi, A. (2012). Menopause Affects Pain Depending on Pain Type and Characteristics. *Menopause*, 19(5), 517-523. doi: 10.1097/gme.0b013e318240fe3d.

- Miller, M., Greenwalt, K., Lehto, R., Wu, H.-S., Moser, J., & Wyatt, G. (2020, in preparation). Pain and Spirituality in Women with Advanced Breast Cancer: Insights from a Phenomenological Qualitative Study.
- Miller, M., Xu, D., Lehto, R., Moser, J., Wu, H.-S., & Wyatt, G. (2020, under review). Pain and Spirituality Outcomes in Women with Advanced Breast Cancer within a Randomized Controlled Trial of Foot Reflexology.
- Mohammed, S., Brookes, M., & Eldabe, S. (2012). Ziconotide for Severe Neuropathic Pain in Metastatic Breast Cancer. *Journal of Pain & Palliative Care Pharmacotherapy*, 26, 286–288. doi: 10.3109/15360288.2012.703296
- Moher, D., Liberati, A., & Altman, D. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*, 6(7), e1000097. doi:10.1371/
- Moosavi, S., Rohani, C., Borhani, F., & Akbari, M. (2019). Factors Affecting Spiritual Care Practices of Oncology Nurses: A Qualitative Study. *Supportive Care in Cancer*, 27, 901–909. doi: <https://doi.org/10.1007/s00520-018-4378-8>
- Mosher, C., Johnson, C., Dickler, M., Norton, L., Massie, M., & HDuHamel, K. (2013). Living with Metastatic Breast Cancer: A Qualitative Analysis of Physical, Psychological, and Social Sequelae. *Breast J*, 19(3), 285–292. doi:10.1111/tbj.12107
- Mystakidou, K., Tsilika, E., Parpa, E., Hatzipli, I., Smyrnioti, M., Galanos, A., & Vlahos, L. (2008). Demographic and Clinical Predictors of Spirituality in Advanced Cancer Patients. *Journal of Clinical Nursing*, 17(13), 1779–1785. doi:10.1111/j.1365-2702.2008.02327.x
- National Cancer Institute. (2017). Hormone Therapy for Breast Cancer. Retrieved from <https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet#q6>
- National Cancer Institute. (2018). Cancer Pain PDQ - Health Professional Version. Retrieved from <https://www.cancer.gov/about-cancer/treatment/side-effects/pain/pain-hp-pdq>
- National Cancer Institute. (2019). NCI Dictionary of Cancer Terms. Retrieved from <https://www.cancer.gov/publications/dictionaries/cancer-terms>
- National Center for Complementary and Alternative Medicine. (2000). *Expanding Horizons of Healthcare: Five-Year Strategic Plan 2001 - 2005*. Retrieved from <https://nccih.nih.gov/sites/nccam.nih.gov/files/about/plans/fiveyear/fiveyear.pdf>
- National Center for Complementary and Integrative Health. (2018). Complementary, Alternative, or Integrative Health: What's In a Name? Retrieved from <https://nccih.nih.gov/health/integrative-health#hed5>

- National Coalition for Hospice and Palliative Care. (2018). *Clinical Practice Guidelines for Quality Palliative Care, 4th ed.* Retrieved from <https://www.nationalcoalitionhpc.org/ncp/>
- National Comprehensive Cancer Network. (2018). *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Adult cancer pain [v.1.2018]*. Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf
- Nelson, C., & Breitbart, W. (2002). Spirituality, Religion, and Depression in the Terminally Ill. *Psychosomatics, 43*(3). doi: 10.1176/appi.psy.43.3.213
- Noble, H., & Smith, J. (2015). Issues of Validity and Reliability in Qualitative Research. *Evidence Based Nursing, 18*(2), 34-25. doi: <http://dx.doi.org/10.1136/eb-2015-102054>
- Osborn, M., & Smith, J. (1998). The Personal Experience of Chronic Benign Lower Back Pain: An Interpretive Phenomenological Analysis. *British Journal of Health Psychology, 3*, 65-83. doi: <https://doi.org/10.1111/j.2044-8287.1998.tb00556.x>
- Otis-Green, S., Sherman, R., Perez, M., & Baird, R. (2002). An Integrated Psychosocial-Spiritual Model for Cancer Pain Management. *Cancer Practice, 10*(Suppl 1), S58–S65. doi: 10.1046/j.1523-5394.10.s.1.13.x
- Pacsi, A. L. (2015). Understanding the Experience of Dominican American Women Living With Late-Stage Breast Cancer: A Qualitative Study. *Hisp Health Care Int, 13*(2), 86-96. doi:10.1891/1540-4153.13.2.86
- Paice, J. A., & Ferrell, B. (2011). The Management of Cancer Pain. *CA Cancer J Clin, 61*(3), 157-182. doi:10.3322/caac.20112
- Paul, S., Zelman, D., Smith, M., & Miaskowski, C. (2005). Categorizing the Severity of Cancer Pain: Further Exploration of the Establishment of Outpoints. *Pain, 113*, 37-44. doi: 10.1016/j.pain.2004.09.014
- Perroud, H. A., Alasino, C. M., Rico, M. J., Queralt, F., Pezzotto, S. M., Rozados, V. R., & Scharovsky, O. G. (2016). Quality of Life in Patients With Metastatic Breast Cancer Treated With Metronomic Chemotherapy. *Future Oncol, 12*(10), 1233-1242. doi:10.2217/fon-2016-0075
- Peters, M. (2015). Emotional and Cognitive Influences on Pain Experience. *Mod Trends Pharmacopsychiatry, 30*, 138-152. doi:10.1159/000435938

- Peterson, J., Pearce, P. F., Ferguson, L. A., & Langford, C. A. (2017). Understanding Scoping Reviews: Definition, Purpose, and Process. *J Am Assoc Nurse Pract*, 29(1), 12-16. doi:10.1002/2327-6924.12380
- Petpichetchian, W., & Brenner, P. (2004). Meanings Ascribed to the Cancer Pain Experience by Thai Patients. *Asian Journal of Nursing Studies*, 7(2), 51-63.
- Piderman, K. M., Kung, S., Jenkins, S. M., Euerle, T. T., Yoder, T. J., Kwete, G. M., & Lapid, M. I. (2015). Respecting the Spiritual Side of Advanced Cancer Care: A Systematic Review. *Curr Oncol Rep*, 17(2), 6. doi:10.1007/s11912-014-0429-6
- Pimenta, F., Maroco, J., Ramos, C., & Leal, I. (2014). Menopausal Symptoms: Is Spirituality Associated with the Severity of Symptoms. *J Relig Health*, 53, 1013-1024. doi:10.1007/s10943-013-9696-z
- Polzer, R., & Miles, M. (2005). Spirituality and Self-Management of Diabetes in African Americans. *Journal of Holistic Nursing*, 23(2), 230-250. doi:10.1177/1049732306297750
- Posternak, V., Dunn, L., Dhruva, A., Paul, S., Luce, J., Mastick, J., . . . Miaskowski, C. (2016). Differences in Demographic, Clinical, and Symptom Characteristics and Quality of Life Outcomes Among Oncology Patients with Different Types of Pain. *Pain*, 157(4), 892–900. doi:10.1097/j.pain.0000000000000456
- Puetzler, J., Feldmann, R. E., Brascher, A. K., Gerhardt, A., & Benrath, J. (2014). Improvements in Health-Related Quality of Life By Comprehensive Cancer Pain Therapy: A Pilot Study With Breast Cancer Outpatients Under Palliative Chemotherapy. *Oncol Res Treat*, 37(9), 456-462. doi:10.1159/000365537
- Raphael, J., Hester, J., Ahmedzai, S., Barrie, J., Farquhar-Smith, P., Williams, J., . . . Sparkes, E. (2010). Cancer Pain: Part 2: Physical, Interventional and Complimentary Therapies; Management in the Community; Acute, Treatment-Related and Complex Cancer Pain: A Perspective from the British Pain Society Endorsed by the UK Association of Palliative Medicine and the Royal College of General Practitioners. *Pain Medicine*, 11, 872–896. doi: 10.1111/j.1526-4637.2010.00841.x
- Reed, E., Simmonds, P., Haviland, J., Corner, J., Reed, E., Simmonds, P., . . . Corner, J. (2012). Quality of Life and Experience of Care in Women With Metastatic Breast Cancer: A Cross-Sectional Survey. *J Pain Symptom Manage*, 43(4), 747-758. doi:10.1016/j.jpainsymman.2011.05.005
- Reed, P. (1996). Transcendence: Formulating Nursing Perspectives. *Nursing Science Quarterly*, 9(1), 2-4. doi: <https://doi.org/10.1177/089431849600900102>

- Reed, P. (2015). Pamela Reed's Theory of Self-Transcendence. In M. Smith & M. Parker (Eds.), *Nursing Theories & Nursing Practice*. Philadelphia, PA: A. Davis Company.
- Reeve, B., Hays, R., Bjorner, J., Cook, K., Crane, P., Teresi, J., . . . Cella, D. (2007). Psychometric Evaluation and Calibration of Health-Related Quality of Life Item Banks. *Med Care*, 45, S22-S26.
- Reflexology Association of America. (2018). Defining Reflexology. Retrieved from <http://reflexology-usa.org/information/downloads-online-resources/defining-reflexology/>
- Reynolds, D. (2006). Examining Spirituality Among Women With Breast Cancer. *Holist Nurs Pract*, 20(3), 118-121. doi: 10.1097/00004650-200605000-00005
- Riley, W., Rothrock, N., Bruce, B., Christodolou, C., Cook, K., Hahn, E., & Cella, D. (2010). Patient-Reported Outcomes Measurement Information System (PROMIS) Domain Names and Definitions Revisions: Further Evaluation of Content Validity in IRT-derived Item Banks. *Qual Life Res*, 19(9), 1311-1321. doi:10.1007/s11136-010-9694-5
- Rodrigues, L., Nader, I., de Melo e Silva, A., dos Santos Tavares, D., & Fernandes Martins Molina, N. (2017). Spirituality and Religiosity Related to Socio-Demographic Data of the Elderly Population. *Rev Rene.*, 18(4), 429-436. doi: 10.15253/2175-6783.2017000400002
- Rodriguez, C., Ji, M., Wang, H., Padhya, T., & McMillan, S. (2019). Cancer Pain and Quality of Life. *Journal of Hospice & Palliative Nursing*, 21(2), 116-123. doi:10.1097/NJH.0000000000000507
- Rosenfield, R., & Stahl, D. (2006). Pain Management of Bone Metastases in Breast Cancer. *Journal of Hospice & Palliative Nursing*, 8(8), 233-244.
- Rosenzweig, M., Wiehagen, T., Brufsky, A., & Arnold, R. (2009). Challenges of Illness in Metastatic Breast Cancer: A Low-Income African American Perspective. *Palliative and Supportive Care*, 7, 143–152. doi: 10.1017/S1478951509000194.
- Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., . . . Schmidt, B. (2016). Rapid and Sustained Symptom Reduction Following Psilocybin Treatment for Anxiety and Depression in Patients with Life-Threatening Cancer: A Randomized Controlled Trial. *Journal of Psychopharmacology*, 30(12), 1165-1180. doi:10.1177/0269881116675512
- Rottman, B., Wyatt, G., Crane, T., & Sikorskii, A. (2020). Expectancy and Utilisation of Reflexology among Women with Advanced Breast Cancer. *Appl Psychol Health Well Being*, [Epub]. doi:10.1111/aphw.12194

- Rustøen, T., Fossa, S., Skarstein, J., & Moum, T. (2003). The Impact of Demographic and Disease-Specific Variables on Pain in Cancer Patients. *Journal of Pain and Symptom Management*, 26(2), 696-704. doi:10.1016/S0885-3924(03)00239-2
- Salt, E., Crofford, L., & Segerstrom, S. (2017). The Mediating and Moderating Effect of Volunteering on Pain and Depression, Life Purpose, Well-Being, and Physical Activity. *Pain Manag Nurs*, 18(4), 243-249. doi: 10.1016/j.pmn.2017.04.004
- Saunders, C. (1964). The Symptomatic Treatment of Incurable Malignant Disease. *Prescribers' Journal*, 4(4), 68-73.
- Schnoll, R. A., Harlow, L. L., & Brower, L. (2000). Spirituality, Demographic and Disease Factors, and Adjustment to Cancer. *Cancer Pract*, 8(6), 298-304.
- Schwadel, P. (2011). The Effects of Education on Americans' Religious Practices, Beliefs, and Affiliations. *Rev Relig Res*, 53, 161-182. doi:10.1007/s13644-011-0007-4
- Serlin, R., Mendoza, T., Nakamura, Y., Edwards, K., & C.S., C. (1995). When is Cancer Pain Mild, Moderate or Severe? Grading Pain Severity by its Interference With Function. *Pain*, 61, 277-284. doi: 10.1016/0304-3959(94)00178-h
- Sheean, P., Kabir, C., Rao, R., Hoskins, K., & Stolley, M. (2015). Exploring Diet, Physical Activity, and Quality of Life in Females with Metastatic Breast Cancer: A Pilot Study to Support Future Intervention. *J Acad Nutr Diet*, 115(10), 1690-1698. doi:10.1016/j.jand.2015.03.017
- Shen, M., Redd, W., Winkel, G., & Badr, H. (2014). Associations Among Pain, Pain Attitudes, and Pain Behaviors in Patients with Metastatic Breast Cancer. *J Behav Med*, 37(4), 595-606. doi:10.1007/s10865-013-9529-2
- Sherman, A., Merluzzi, T., Pustejovsky, J., Park, C., George, L., Fitchett, G., . . . Salsman, J. (2015). A Meta-Analytic Review of Religious or Spiritual Involvement and Social Health Among Cancer Patients. *Cancer*, 121, 3779-3788. doi: 10.1002/cncr.29352
- Shi, Q., Giordano, S., Lu, H., Saleeba, A., Malveaux, D., & Cleeland, C. (2013). Anastrozole-Associated Joint Pain and Other Symptoms in Patients With Breast Cancer. *The Journal of Pain*, 14(3), 290-296. doi: 10.1016/j.jpain.2012.11.010
- Sikorskii, A., Victorson, D., O'Connor, P., Hankin, V., Safikhani, A., Crane, T., . . . Wyatt, G. (2018). PROMIS and Legacy Measures Compared in a Supportive Care Intervention for Breast Cancer Patients and Caregivers: Experience from a Randomized Trial. *Psycho-Oncology*, 27(9), 2265-2273. doi:10.1002/pon.4825

- Sikorskii, A., Wyatt, G., Tamkus, D., Victorson, D., Rahbar, M., & Ahn, S. (2012). Concordance Between Patient Reports of Cancer-Related Symptoms and Medical Records Documentation. *Journal of Pain and Symptom Management*, 44(3), 362-372. doi:DOI: 10.1016/j.jpainsymman.2011.09.017
- Smith, B., Dalen, j., Wiggins, K., Christopher, P., Bernard, J., & Shelley, B. (2008a). Who is Willing to Use Complementary and Alternative Medicine? . *Explore(NY)*, 4(6), 359–367. doi:10.1016/j.explore.2008.08.001
- Smith, B., Dalen, j., Wiggins, K., Christopher, P., Bernard, J., & Shelley, B. (2008b). Who is Willing to Use Complementary and Alternative Medicine? *Explore(NY)*, 4(6), 359–367. doi:10.1016/j.explore.2008.08.001
- Smith, J. (1995). Semi-Structured Interviewing and Qualitative Analysis. In J. Smith, R. Harre, & L. Van Langenhove (Eds.), *Rethinking Methods in Psychology*. London: SAGE. doi: <http://dx.doi.org/10.4135/9781446221792.n2>
- Smith, J., Flowers, P., & Larkin, M. (2009). *Interpretative Phenomenological Analysis: Theory, Method and Research*. London: Sage.
- Smith, J., Flowers, P., & Larkin, M. (2009). *Interpretive Phenomenological Analysis: Theory, Method and Research*. London: SAGE.
- Smith, J., & Osborn, M. (2015). Interpretative Phenomenological Analysis as a Useful Methodology for Research on the Lived Experience of Pain. *British Journal of Pain*, 9(1), 41–42. doi: 10.1177/2049463714541642
- Smith, S., Herndon, J., Lyster, K., Coan, A., Wheeler, J., Staley, T., & Abernethy, A. (2011). Correlates of Quality of Life-Related Outcomes in Breast Cancer Patients Participating in the Pathfinders Pilot Study. *Psycho-Oncology*, 20(5), 559–564. doi:10.1002/pon.1770
- Smyth, E. N., Shen, W., Bowman, L., Peterson, P., John, W., Melemed, A., & Liepa, A. M. (2016). Patient-Reported Pain and Other Quality of Life Domains as Prognostic Factors for Survival in a Phase III Clinical Trial of Patients With Advanced Breast Cancer. *Health Qual Life Outcomes*, 14, 52. doi:10.1186/s12955-016-0449-z
- Soltow, D., Given, B., & Given, C. (2010). Relationship Between Age and Symptoms of Pain and Fatigue in Adults Undergoing Treatment for Cancer. *Cancer Nurs*, 33(4), 296-303. doi: 10.1097/NCC.0b013e3181ce5a1a
- Steinhauser, K., Fitchett, G., Handzo, G., Johnson, K., Koenig, H., Pargament, K., . . . Balboni, T. (2017). State of the Science of Spirituality and Palliative Care Research Part I:

- Definitions, Measurement, and Outcomes. *Journal of Pain and Symptom Management*, 54(3), 428-440. doi: 10.1016/j.jpainsymman.2017.07.028.
- Stephenson, N., & Dalton, J. (2003). Using Reflexology for Pain Management. *J Holist Nurs*, 21(4), 179-191. doi: 10.1177/0898010103021002007
- Stephenson, N., Swanson, M., Dalton, J., Keefe, F., & Engelke, M. (2007). Partner-Delivered Reflexology: Effects on Cancer Pain and Anxiety. *Oncol Nurs Forum*, 34(1), 127-132. doi: 10.1188/07.ONF.127-132
- Stinson, C., & Kirk, E. (2006). Structured Reminiscence: An Intervention to Decrease Depression and Increase Self-Transcendence in Older Women. *J Clin Nurs*, 15(2), 208-218. doi:10.1111/j.1365-2702.2006.01292.x
- Stuver, S. O., Isaac, T., Weeks, J. C., Block, S., Berry, D. L., Davis, R. B., & Weingart, S. N. (2012). Factors Associated With Pain Among Ambulatory Patients With Cancer With Advanced Disease at a Comprehensive Cancer Center. *J Oncol Pract*, 8(4), 17-23. doi:10.1200/JOP.2011.000388
- Sun, K., So Young, C., & Jin Sook, K. (2017). Evolutionary Concept Analysis of Spirituality. *Journal of Korean Academic Nursing*, 47(2), 242-256. doi:10.4040/jkan.2017.47.2.242
- Susan G. Komen. (2018). Breast Cancer Stages and Staging. Retrieved from <https://ww5.komen.org/BreastCancer/StagingofBreastCancer.html>
- Taylor, E. (2003). Nurses Caring for the Spirit: Patients With Cancer and Family Caregiver Expectations. *Oncol Nurs Forum*, 30(4), 585-590. doi: 10.1188/03.ONF.585-590
- Thomas, J., Burton, M., Quinn-Griffin, M., & Fitzpatrick, J. (2010). Self-Transcendence, Spiritual Well-Being, and Spiritual Practices of Women With Breast Cancer. *Journal of Holistic Nursing*, 28(2), 115-122. doi: 10.1177/0898010109358766.
- Tricco, A., Lillie, E., W., Z., O'Brien, K., Colquhoun, H., Levac, D., . . . Straus, S. (2018). PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*, 169(7), 467-473. doi:10.7326/M18-0850
- Twelves, C., Cortes, J., O'Shaughnessy, J., Awada, A., Perez, E. A., Im, S. A., . . . Rugo, H. S. (2017). Health-Related Quality of Life in Patients With Locally Recurrent or Metastatic Breast Cancer Treated With Etrinecan Pegol Versus Treatment of Physician's Choice: Results From the Randomised Phase III BEACON Trial. *Eur J Cancer*, 76, 205-215. doi:10.1016/j.ejca.2017.02.011

- Vachon, S., Fillion, L., & Achille, M. (2009). A Conceptual Analysis of Spirituality at the End of Life. *Journal of Palliative Medicine*, 12(1), 53-59. doi:10.1089/jpm.2008.0189
- Van den Beuken-van Everdingen, M., de Rijke, J., Kessels, A., Schouten, H., van Kleef, M., & Patijn, J. (2007). Prevalence of Pain in Patients With Cancer: A Systematic Review of the Past 40 Years. *Annals of Oncology*, 18, 1437–1449. doi:doi:10.1093/annonc/mdm056
- Van Manen, M. (1997). *Researching Lived Experience: Human Science for an Action Sensitive Pedagogy (2nd ed.)*. London, Ontario, Canada: Althouse Press.
- Visser, A., de Jager Meezenbroek, E., & Garssen, B. (2018). Does Spirituality Reduce the Impact of Somatic Symptoms on Distress in Cancer Patients? Cross-Sectional and Longitudinal Findings. *Social Science & Medicine*, 214, 57-66. doi:doi.org/10.1016/j.socscimed.2018.08.012
- Voi, B., Höxtermann, M., Dobos, G., & Cramer, H. (2020). Mind-Body Medicine Use By Women Diagnosed With Breast Cancer: Results of a Nationally Representative Survey. *Support Care Cancer*, 1077-1082. doi:10.1007/s00520-019-04914-x
- Von Moos, R., Body, J. J., Egerdie, B., Stopeck, A., Brown, J., Fallowfield, L., . . . Qian, Y. (2016). Pain and Analgesic Use Associated With Skeletal-Related Events in Patients With Advanced Cancer and Bone Metastases. *Support Care Cancer*, 24(3), 1327-1337. doi:10.1007/s00520-015-2908-1
- Wang, Y., Jackson, T., & Cai, L. (2016). Causal Effects of Threat and Challenge Appraisals on Coping and Pain Perception. *Eur J Pain*, 20(7), 1111-1120. doi:10.1002/ejp.835
- Wang, Y., & Lin, C. (2016). Spiritual Well-Being May Reduce the Negative Impacts of Cancer Symptoms on the Quality of Life and the Desire for Hastened Death in Terminally Ill Cancer Patients. *Cancer Nurs*, 39(4), E43-E50. doi: 10.1097/NCC.0000000000000298
- Weathers, E., McCarthy, G., & Coffey, A. (2016). Concept Analysis of Spirituality: An Evolutionary Approach. *Nursing Forum*, 51(2), 79-96. doi:10.1111/nuf.12128
- Wiech, K., Fairias, M., Kahane, G., Shackel, N., Tiede, W., & Tracey, I. (2009). An fMRI Study Measuring Analgesia Enhanced By Religion as a Belief System. *Pain*, 139, 467-476.
- Wilkinson, S., Lockhart, K., Gambles, M., & Storey, L. (2008). Reflexology for Symptom Relief in Patients With Cancer. *Cancer Nurs*, Sept-Oct(5), 354-360. doi:10.1097/01.NCC.0000305756.58615.81
- Williams, A. C., & Craig, K. D. (2016). Updating the Definition of Pain. *Pain*, 157(11), 2420-2423. doi:10.1097/j.pain.0000000000000613

- Willis, K., Lewis, S., Ng, F., & Wilson, L. (2015). The Experience of Living With Metastatic Breast Cancer—A Review of the Literature. *Health Care Women Int*, 36(5), 514-542. doi:10.1080/07399332.2014.896364
- Wren, A., Shelby, R., Soo, M., Huysmans, Z., Jarosz, J., & Keefe, F. (2019). Preliminary Efficacy of a Lovingkindness Meditation Intervention for Patients Undergoing Biopsy and Breast Cancer Surgery: A Randomized Controlled Pilot Study. *Support Care Cancer*, 27, 3583–3592. doi:10.1007/s00520-019-4657-z
- Wyatt, G., & Friedman, L. (1996). Long-Term Female Cancer Survivors: Quality of Life Issues and Clinical Implications. *Cancer Nurs*, 19(1), 1-7. doi: 10.1097/00002820-199602000-00001
- Wyatt, G., Kurtz, M., Friedman, L., Given, B., & Given, C. (1996). Preliminary Testing of the Long Term Quality of Life (LTQL) Instrument for Female Cancer Survivors. *J Nurs Meas*, 4(4), 153-170.
- Wyatt, G., Kurtz, M., & Liken, M. (1993). Breast Cancer Survivors: An Exploration of Quality of Life Issues. *Cancer Nurs*, 16(6), 440-448.
- Wyatt, G., Sikorskii, A., Holmstrom, A., & Luo, Z. (2006-2010). Reflexology: An Intervention for Advanced Breast Cancer. National Institutes of Health, National Cancer Institute grant # R01CA104883.
- Wyatt, G., Sikorskii, A., Holmstrom, A., & Luo, Z. (2011-2016). Home Based Symptom Management via Reflexology for Advanced Breast Cancer Patients. National Institutes of Health, National Cancer Institute grant # R01CA157459-01.
- Wyatt, G., Sikorskii, A., Rahbar, M., Victorson, D., & Adams, L. (2010). Intervention Fidelity: Aspects of Complementary and Alternative Medicine Research. *Cancer Nurs*(5), 331-342. doi: 10.1097/NCC.0b013e3181d0b4b7.
- Wyatt, G., Sikorskii, A., Rahbar, M., Victorson, D., & You, M. (2012). Health-Related Quality-of-Life Outcomes: A Reflexology Trial With Patients With Advanced-Stage Breast Cancer. *Oncol Nurs Forum*, 39(6), 568-577. doi:10.1188/12.ONF.568-577
- Wyatt, G., Sikorskii, A., Tamkus, D., & You, M. (2013). Quality of Life Among Advanced Breast Cancer Patients With and Without Distant Metastasis. *Eur J Cancer Care*, 22(2), 272-280. doi:10.1111/ecc.12028
- Wyatt, G., Sikorskii, A., Tesnjak, I., Frambes, D., Holmstrom, A., Luo, Z., . . . Tamkus, D. (2017). A Randomized Clinical Trial of Caregiver-Delivered Reflexology for Symptom

- Management During Breast Cancer Treatment. *Journal of Pain and Symptom Management*, 54(5), 670-679. doi: 10.1016/j.jpainsymman.2017.07.037
- Wyatt, G., Sikorskii, A., Tesnjak, I., Victorson, D., & Srkalovic, G. (2015). Chemotherapy Interruptions in Relation to Symptom Severity in Advanced Breast Cancer. *Support Care Cancer*, 23(11), 3183-3191. doi:10.1007/s00520-015-2698-5
- Yamanaka, M. (2018). A Concept Analysis of Self-Management of Cancer Pain. *Asia Pac J Oncol Nurs*, 5(3), 254–261. doi:10.4103/apjon.apjon_17_18
- Yeager, K., Sterk, C., Quest, T., Dilorio, C., Vena, C., & Bauer-Wu, S. (2016). Managing One's Symptoms: A Qualitative Study of Low-Income African Americans With Advanced Cancer. *Cancer Nurs*, 39(4), 303-312. doi: 10.1097/NCC.0000000000000284
- Zarei, B., Vagharseyyedin, S., & Gorganie, E. (2015). Relationship Between Spiritual Well-Being and Self-Management Among Iranian People With Multiple Sclerosis. *J Chronic Dis Care*, 4(4), 18-24. doi: 10.17795/jjcdc-30154
- Zeidan, F., & Vargo, D. (2016). Mindfulness Meditation–Based Pain Relief: A Mechanistic Account. *Ann N.Y. Acad Sci*, 1373, 114-127. doi: 10.1111/nyas.13153.
- Zhang, J., Wang, Y., Han, K., Tang, L., Hu, H., Wu, C., . . . Yao, Y. (2013). Percutaneous Vertebroplasty Combined With Zoledronic Acid for the Treatment of Painful Osteolytic Spinal Metastases in Patients With Breast Cancer. *J Vasc Interv Radiol*, 24(12), 1861-1867. doi:10.1016/j.jvir.2013.08.023