A Multimethod Approach to Understanding the Biopsychosocial Underpinnings of Chronic Cancer-Related Pain in Cancer Survivors

By:

Katie Fitzgerald Jones

A Dissertation

Presented to

Boston College William F. Connell School of Nursing

in partial fulfillment of the requirement for the degree of

Doctor of Philosophy

Copyright Notice

A Multimethod Approach to Understanding the Biopsychosocial Underpinnings of Chronic Cancer-Related Pain in Cancer Survivors

By: Katie Fitzgerald Jones

Dissertation Advisor/Chair: Lisa Wood Magee

Abstract

Background: Chronic cancer-related pain is a considerable problem in cancer survivors. The incidence of chronic pain in cancer survivors is nearly double the rate in the general population. Chronic cancer-related pain reduces quality of life and results in higher healthcare utilization. Due to a lack of alternative treatments, the management of chronic cancer-related pain relies on a biomedical model, with opioids being the cornerstone of cancer-related pain management. As concerns about the risks of long-term opioid therapy rise, there is a need to understand the factors that influence chronic cancer-related pain experience. This manuscript dissertation aims to answer the overarching question, "What are the unique factors that inform the chronic cancer-related pain experience in cancer survivors?"

Methods: First, an integrative review aimed to examine the evidence of long-term opioid use in cancer-survivors. Next, a qualitative study using descriptive phenomenology was conducted to develop a deeper understanding of the daily lived experience of chronic cancer-related pain. And finally, a prospective cross-section quantitative study was completed to quantify the contribution of unique cancer-specific factors to the chronic cancer-related pain experience in cancer survivors.

Results: The integrative review shed light on the biopsychosocial factors associated with the transition to long-term opioid therapy (LTOT), including the role of cancer type, medical comorbidities, mental health diagnoses, and socioeconomic factors. No studies examined pain

severity, pain interference, or cancer-specific psychosocial factors in cancer survivors prescribed LTOT. Second, cancer survivors describe living with chronic cancer-related pain as the cost of survival. Yet, their suffering was often invisible to others. The role of opioids in chronic cancer-related pain leads to strained communication with clinicians and the need to self-navigate a treatment plan characterized by 'trying everything'. And finally, select cancer-specific psychosocial factors explained relatively little variance in the pain experience compared to non-cancer specific factors of multisite pain and pain catastrophizing.

Conclusions: The constellation of the finding from this body of work demonstrates unique factors that inform the chronic cancer-related pain experience in cancer survivors, and several areas of overlap with other chronic pain syndromes.

Table of Contents

Chapter I
Introduction to the Dissertation

Introduction

Advances in early detection and treatment have dramatically improved cancer survival (Paice, 2019a). There are currently 18.1 million cancer survivors living in the United States, with the expected growth to increase to 22.5 million people by 2032 (American Cancer Society, 2022). Cancer treatment consequences pose a considerable problem for many cancer survivors, defined as those beyond the cancer diagnosis and acute treatment phase. One such side effect is chronic cancer-related pain or pain that persists for ≥ 3 months after the cessation of acute cancer treatment, often caused by cancer treatment, including surgery, radiation, chemotherapy, or other pharmacologic therapies (Paice et al., 2016). The prevalence of chronic pain among cancer survivors is nearly double that of the general US population (Jiang et al., 2019). Chronic cancer-related pain reduces quality of life, lowers treatment adherence to cancer surveillance, and results in higher healthcare utilization (Green et al., 2011). Although there is awareness of the magnitude and ramifications of chronic pain in cancer survivors, what is not known are the unique cancer-specific factors that contribute to the chronic pain experience in survivorship.

In non-cancer populations, chronic pain is influenced by biological, social, and psychological (BPS) factors (Treede, et al., 2015). However, individuals with cancer pain are routinely excluded from chronic pain studies, and multimodal treatment strategies for cancer survivors are lacking (Meghani & Vapiwala, 2018). Due to a lack of alternative treatments, managing chronic cancer-related pain relies on a biomedical model, with opioid management being the cornerstone of treatment (Manchikanti et al., 2018).

As concerns about the risks and lack of efficacy of long-term opioid therapy rise with the opioid overdose crisis, there is a need to understand further the factors that influence cancer survivors' chronic cancer-related pain experience. While psychological approaches such as

cognitive-behavioral therapy and pain self-management have shown promising results in the general population, such interventions have not had widespread implementation in cancer survivors (Darnall, 2019). It is also unclear if psychosocial treatments for chronic pain need to be adapted to cancer survivors who may have a unique chronic pain experience due to cancer-specific psychosocial factors and high rates of opioid use during active cancer treatment. There is an urgent need to fill the literature gap regarding the pain experience in cancer survivors and identify factors that contribute to long-term opioid use (LTOT). Without a clear understanding of the cancer-specific factors that drive chronic cancer-related pain experience and prolonged opioid use, the ability to develop effective multimodal treatments to reduce pain and improve opioid safety in cancer survivors is limited.

Background and Significance

Key Definitions

Cancer Survivors

For the dissertation, a cancer survivor is defined according to the narrow definition developed by the survivorship task force of the European Organization for Research and Treatment of Cancer. According to this definition, a cancer survivor is an individual diagnosed with cancer who has completed primary treatment (chemoprevention maintenance therapy allowed) and has no evidence of active cancer (Bennett et al., 2019).

Chronic cancer-related pain

Chronic pain is an umbrella term for pain lasting over three months (Treede et al., 2019). In 2020, the International Association for the Study of Pain revised the definition of chronic pain as an "unpleasant sensory and emotional experience associated with or resembling that associated with, actual or potential tissue damage (Raja et al., 2020). Chronic pain in cancer

survivors can arise from cancer and non-cancer pain sources and appears more common in specific cancer subpopulations, particularly those with solid tumors such as breast, lung, and head and neck cancers (Glare et al., 2014; Mory et al., 2010). In many instances, it can be difficult for researchers and even cancer survivors themselves to be able to attribute the etiology of pain. The dissertation defines chronic cancer-related pain as pain lasting > 3 months after curative treatment secondary to cancer diagnosis and treatment (Paice et al., 2017; Treede et al., 2019). Common chronic cancer-related pain syndromes include bony complications of corticosteroids, chemotherapy-induced peripheral neuropathy (CIPN), lymphedema, osteoradionecrosis, phantom pain, post-surgical pain, arthralgias from hormonal treatment, and graft versus host disease (Paice et al., 2016).

Opioid Therapy

Opioids are an important aspect of cancer pain management, including medications such as morphine, oxycodone, buprenorphine, tramadol, and fentanyl products (Opioids and Cancer Pain: Patient Needs and Access Challenges, 2019). This dissertation will capture the use of any opioid after three months of curative cancer treatment. The definition of any opioid use for > 3 months is consistent with the most common definition of long-term opioid therapy (LTOT) in the literature (Karmali et al., 2020).

Theoretical Framework

This dissertation uses a multimethod approach. Studies one and three are guided by the biopsychosocial (BPS) model for chronic pain. Study two is a descriptive phenomenology study thus atheoretical. The BPS, initially adapted by Gatchel and colleagues for chronic pain, is a widely accepted and holistic chronic pain model (Baria et al., 2018; Gatchel et al., 2007; Miaskowski et al., 2019). In the BPS, biological, psychological factors, and social factors

interact to influence an individual's experience of chronic pain (Adler, 2009; Baria et al., 2018; Delgado-Guay et al., 2009; Jaremka et al., 2013; Kroenke et al., 2010; Novy & Aigner, 2014). The BPS model has been adapted to various populations and conditions, including chronic pain in older adults, veterans, and HIV-related chronic pain (Baria et al., 2018; Merlin et al., 2014; Miaskowski et al., 2019). The BPS has been used to guide research on acute cancer pain and pain associated with advanced disease (Adler, 2009; Miaskowski et al., 2019; Novy & Aigner, 2014).

Chronic cancer-related pain is associated with many well-known BPS factors, including sleep, fatigue, comorbidities, age, gender, anxiety, depression, post-traumatic stress disorder, substance use disorder, pain-specific behaviors, socioeconomic status, education, and lack of social support. (Baria et al., 2018; Block, 2001; Darnall et al., 2018; Delgado-Guay et al., 2009; Golan-Vered & Pud, 2013; Hermesdorf et al., 2016; Jaremka et al., 2013; Kroenke et al., 2010; Leach et al., 2015; Miaskowski et al., 2019; Novy & Aigner, 2014; Pachman et al., 2012; Smith et al., 2019) For example, untreated post-traumatic stress disorder was observed to increase the risk for chronic pain development in cancer survivors (Ganju et al., 2019; Henry et al., 2019; Sager et al., 2020). Likewise, the BPS factors of depression, sleep disturbances, and fatigue influence the development of chemotherapy-induced peripheral neuropathy in 40 breast cancer patients treated with paclitaxel (Golan-Vered & Pud, 2013). Examining psychosocial factors associated with chronic-cancer pain in cancer survivors has been limited to assessing the common BPS factors of anxiety, depression, PTSD, pain-specific behaviors, substance use, socioeconomic status, and education. (Block, 2001; Delgado-Guay et al., 2009; Golan-Vered & Pud, 2013; Hermesdorf et al., 2016; Jaremka et al., 2013; Jiang et al., 2019; Kroenke et al., 2010; Leach et al., 2015; Miaskowski et al., 2019; Novy & Aigner, 2014; Pachman et al., 2012; Smith et al., 2019).

The contribution of cancer survivors' unique psychosocial factors, such as fear of recurrence (FOR), cancer distress (CD), and cancer-related trauma, have not been studied in the chronic cancer-related pain experience. These major psychosocial factors are closely associated with psychosocial constructs of anxiety, depression, trauma, and social support but are unique to the cancer survivors' experience. The following section will discuss these unique cancer-specific factors and supporting evidence of the potential to contribute to cancer survivors' chronic cancer-related pain experience.

Psychosocial factors

Psychosocial distress in cancer survivors is associated with adverse health outcomes, increased healthcare utilization, lower cancer treatment adherence, and higher healthcare costs (Porter & Keefe, 2011; Zaza & Baine, 2002). Measurement of cancer-specific psychosocial distress is essential in identifying relevant psychosocial factors that may contribute to the cancer survivors' pain experience and inadequate treatment of chronic cancer-related pain (Zaza & Baine, 2002). Understanding the psychosocial aspects of chronic pain is particularly important since the management of chronic pain and psychosocial distress are treated as distinct entities rather than a complex integrated symptom cluster (Darnall et al., 2018). Moreover, cancer survivors experience unique psychological stressors that can potentially impact their experience of chronic pain, including fear of cancer recurrence, pain catastrophizing, cancer distress, and cancer trauma. However, their contribution to chronic cancer-related pain has not been examined.

Fear of cancer recurrence (FCR) is one of the most commonly reported problems and unaddressed concerns by cancer survivors and their caregivers (Simard et al., 2013). The definition of FCR includes 1) excessive worry, preoccupation, rumination, intrusive thoughts, 2)

maladaptive coping, 3) functional impairment, 4) excessive distress, and 5) difficulty making plans for the future (Lebel et al., 2016). FCR can be a distressing symptom for cancer survivors with chronic pain since worsening pain or new pain can signify cancer recurrence (Paice, 2019c). Moreover, uncontrolled symptoms can be an internal stimulus of a perceived threat that may invoke the emotional reaction of fear and problematic behaviors such as avoidance and anxious preoccupations, which contribute to an increased fear response (Custers et al., 2014).

Although not a cancer-specific factor, pain catastrophizing influences the pain experience. Pain catastrophizing describes a pattern of negative cognitive and emotional responses to pain. It includes rumination, feelings of helplessness, and a focus on "worst-case scenarios" such as "what if the pain gets worse?" (Rosenbaum, 2005). Small studies examining pain catastrophizing have been limited to breast cancer. Pain catastrophizing, somatization, and anxiety were associated with greater post-operative pain (Belfer et al., 2013; Schreiber et al., 2013). In non-cancer pain, individuals who worry more about pain and feel helpless regarding pain management experience more prolonged pain and long-term opioid use (Wertli et al., 2014).

Cancer distress (CD) is defined by the National Comprehensive Cancer Network (2017) as a "multifactorial unpleasant experience of a psychological (cognitive, behavioral, emotional), social, spiritual and/or physical nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment". CD is estimated to occur in 3 out of 4 cancer survivors and is associated with worse QoL and well-being in cancer survivors (Baken & Woolley, 2011). Although distress screening is recommended for all cancer patients, less than one-third of cancer survivors discuss their psychosocial concerns with their providers, and fewer survivors receive treatment for distress (American Cancer Society, 2020).

Cancer survivors have high treatment-related psychological trauma rates that may also play a role in the chronic pain experience (Hefner et al., 2014; Robins et al., 2010). For example, in head and neck cancer, 33.4% of individual's experience subclinical post-traumatic stress, and 11.8% meet the criteria for PTSD (Moschopoulou et al., 2018). PTSD, chronic pain, and opioid use are highly comorbid (Tripp et al., 2019).

The lived experience of Chronic Cancer Pain

There are few studies on the lived experience of cancer survivors with chronic cancer-related pain. Four qualitative studies have examined the chronic pain experience of 52 female breast cancer survivors in European countries (Armoogum et al., 2020). From these studies, six themes are recognized in chronic cancer pain: 1) interwoven relationship between cancer and persistent pain, 2) lack of preparedness and support for persistent pain, 3) physical impact of persistent pain, 4) employing coping strategies, 5) emotional experience of persistent pain, and 6) conceptualization of persistent pain (Björkman et al., 2008; Hellerstedt-Börjesson, et al., 2016; Hovind et al., 2013; Peretti-Watel et al. 2012). The described research provides a foundational knowledge of the complex phenomenon of chronic cancer-related pain in cancer survivors and justification for the qualitative work focused on the daily lived experience in the proposed dissertation. The few qualitative studies that examine the chronic pain experience of cancer survivors have been limited to women with breast cancer and occurred outside of the United States. Additionally, the current evidence base does not reflect modern-day cancer survivorship. Many cancer survivors are living longer, shifting the goal to sparing opioids post-treatment, and novel treatments such as immunotherapy pose new treatment challenges (Kaur et al., 2019; Paice, 2020; Schatz et al., 2020)

Purpose and Specific Aims

The comprehensive nature of this dissertation seeks to answer the overarching question of "What are the unique factors that inform the chronic cancer pain experience in cancer survivors?" To develop a deeper understanding of the unique experience of chronic pain in cancer survivors will have conducted three studies that aim to 1) evaluate evidence of the published and peer-reviewed literature regarding patient and disease-specific factors associated with long-term opioid therapy in cancer survivors, 2) gain a deeper understanding of the daily lived experience of cancer survivors with chronic cancer-related pain, and 3) quantify the contribution of cancer-specific psychosocial factors to the chronic-cancer pain experience in cancer survivors. Table 1 provides an overview of the specific aims and the chapter addressing each aim.

Table 1. Chapters and Aims

Specific Aim	Chapter
Aim 1: To evaluate evidence of the published and peer-reviewed literature regarding patient and disease-specific factors associated with long-term opioid therapy in cancer survivors.	I. Chapter II: Exploring Factors Associated with Long-Term Opioid Therapy in Cancer Survivors: An Integrative Review
Aim 2: To gain a deeper understanding of the daily lived experience of cancer survivors with chronic cancer-related pain	II. Chapter III: “It is so easy for them to dismiss”: A Phenomenology Study of Cancer Survivors with Chronic Cancer-Related Pain

Aim 3: To quantify the contribution of cancer-specific psychosocial factors to the chronic-cancer pain experience in cancer survivors	III. IV: The Contribution of Cancer-Specific Psychological Factors to the Chronic Cancer-Related Pain Experience in Cancer Survivors

Implications for Nursing Practice

The management of pain in cancer survivors is highly complex without universal agreement (Paice, 2016). The key to improving chronic pain management in cancer survivors is to understand the patient and cancer-specific factors that influence the experience of chronic cancer pain and opioid use. The dissertation examines the contribution of cancer-specific psychosocial distress to the experience of chronic pain in cancer survivors. The multimethod approach presented in this dissertation is innovative. It acknowledges cancer survivors' whole experience and the multi-dimensional nature of suffering that accompanies a life-threatening and life-altering experience (Ferrell & Coyle, 2008). The outlined dissertation is fundamentally aligned with the goals of nursing: to improve the health and quality of life of individuals and families by exploring and humanizing the experience of illness (Grace & Zumstein-Shaha, 2019).

Chapter II.

Exploring Factors Associated with Long-Term Opioid Therapy in Cancer Survivors:

An Integrative Review

Authors:

Katie Fitzgerald Jones Boston College MSN, APN

William F. Connell School of Nursing

Mei R. Fu PhD, RN, FAAN

Rutgers University, School of Nursing

Jessica Merlin MD, PhD, MBA

University of Pittsburg School of Medicine

Judith A. Paice Ph.D., RN, ACHPN

Northwestern University; Feinberg School of Medicine

Rachelle Bernacki MD

Dana Faber-Cancer Institute

Christopher Lee Ph.D., RN, FAHA, FAAN, FHFSA

William F. Connell School of Nursing

Lisa Wood Magee PhD, RN, FAAN

William F. Connell School of Nursing

This manuscript represents a significant contribution to the dissertation work. It was published in the *Journal of Pain and Symptom Management* on August 11, 2020. The *Journal of Pain and Symptom Management* is an internationally respected, peer-reviewed journal and serves an interdisciplinary audience of professionals by providing a forum for the publication of the latest clinical research and best practices related to the relief of illness burden among patients afflicted with a serious or life-threatening illness. The *Journal of Pain and Symptom Management* has an impact factor of 3.49. Permission was obtained from the editor to publish the article in the dissertation.

Abstract

Context: The prevalence of chronic pain in cancer survivors is double that of the general US population. Opioids have been the foundation of cancer pain management for decades; however, there is a paucity of literature on long-term opioid therapy (LTOT) in cancer survivors. Understanding factors related to LTOT use in cancer survivors is needed to address chronic pain and balance opioid harms in the expanding population of cancer survivors.

Objectives: To analyze the research of LTOT utilization and factors associated with persistent opioid use in cancer survivors.

Methods: A five-stage integrative review process was adapted from Whittemore and Knafl. Data sources searched included: Web of Science, PubMed, Embase, Cochrane, and Google Scholar. Quantitative research studies from 2010 to the present related to cancer survivors managed on LTOT were included. Editorials, reviews, or abstracts were excluded.

Results: After reviewing 315 articles, 21 articles were included. We found several definitions of LTOT in the reviewed studies, but the duration of opioid use (i.e.,> 3 months after completion of curative treatment) was the most common. The reviewed literature describes a relationship between LTOT and important biopsychosocial factors (cancer type, socioeconomic factors, and comorbidities).

Conclusion: The studies in this review shed light on the factors associated with LTOT in cancer survivors. LTOT was common in specific populations of cancer survivors and those with a collection of patient-specific characteristics. This review suggests a critical need for specialized research on chronic cancer pain and opioid safety in cancer survivors.

Key Message: This integrative review describes factors related to long-term opioid prescribing in cancer survivors who have completed curative treatment. The findings highlight the role of cancer type, medical comorbidities, opioid characteristics, mental health diagnoses, and socioeconomic factors associated with the transition to long-term opioid therapy. The results indicate that LTOT is more common in cancer survivors related to specific biopsychosocial characteristics.

Key words: opioids, cancer survivors, long-term opioid therapy, persistent opioid use, chronic cancer pain

Advancements in the field of oncology have led to longer life expectancies for some patients with cancer and greater attention to factors that impact health-related quality of life (QoL), including pain (Chandrasekar et al., 2016). The most common complications of cancer treatment include pain, fatigue, and psychological distress (Miller et al., 2019). Chronic pain is a serious issue for up to 40 percent of cancer survivors, i.e., patients who have survived beyond the acute diagnosis and active cancer treatment phase (Bao et al., 2018; Green et al., 2011). Cancer survivors who experience chronic pain related to cancer or oncologic treatment have poorer QoL, higher health care utilization and cost, and lower preventative treatment adherence (Paice et al., 2016). Chronic pain is defined as pain lasting > 3 months, and in the non-cancer population, it is recognized as a chronic disease that is heavily influenced by biological, social, and psychological factors (Treede et al., 2015). The prevalence of high-impact pain (pain associated with major activity restrictions) in cancer survivors is nearly double that of chronic pain in the general US population (Jiang et al., 2019).

Opioids have been the foundation of cancer pain management for decades; however, the literature on long-term opioid therapy (LTOT) in cancer survivors is scarce and existing studies have focused on individuals with acute cancer-related pain or pain at the end of life (Paice et al., 2016; Schenker et al., 2018). Cancer survivors have higher opioid utilization than the mean national prevalence rate of LTOT of 5.4% in the United States (Mojtabai, 2018). Pain in cancer survivors is sometimes grouped with other forms of chronic pain, where opioid use is controversial (Goodlev et al., 2019). In chronic non-cancer pain, there is a preponderance of literature on the harms of LTOT, including the inability to return to work, increased rates of depression, motor vehicle accidents, falls, opioid use disorders (OUD), and unintentional overdose (Chou et al., 2015). Relevant literature on cancer survivors has provided limited

evidence to support the safety and efficacy of LTOT but identifies several adverse effects, including sexual dysfunction, immune system effects, fatigue, and osteoporosis (Paice et al., 2016). The management of pain in cancer survivors is highly complex without universal agreement; that is made more challenging to navigate by nebulous policies, conflicting guidelines, and regulations that often do not include cancer-specific recommendations (Meghani & Vapiwala, 2018). In cancer survivors, it remains unclear whether chronic cancer pain should be treated like other forms of chronic pain, where opioids are considered high risk and rarely recommended for long-term pain management. The key to improving chronic pain management in cancer survivors and opioid safety is to understand patient and disease-specific factors associated with LTOT among cancer survivors (Merlin et al., 2018; Paice, 2020). The purpose of this integrative review was to evaluate evidence of the published and peer-reviewed literature regarding patient and disease-specific factors associated with LTOT in cancer survivors, specifically related to pain etiology, cancer type and treatment, socioeconomic factors, opioid characteristics, and individual patient factors.

Method

Preparation for the search

This integrative review was conducted using the methodology proposed by Whittemore and Knafl, consisting of five stages: problem identification, literature search, data evaluation, data analysis, and presentation of the findings (Whittemore & Knafl, 2005). The initial phase consisted of a thorough literature search and review to generate key search terms, define LTOT and cancer survivors, and examine guidelines specifying appropriate opioid use after curative cancer treatment. Subsequently, additional search terms were identified using the MeSH

(Medical Subject Heading) database. Multiple consultations were held with the health librarian to ensure the reliability and appropriateness of key search terms (Fu et al., 2013).

The key terms utilized for this review included: opioid, opioid analgesic, narcotic, cancer, neoplasm, and survivor. An overview of keywords is located in Table 1. Various combinations of the key terms were used to search the following databases: Web of Science, PubMed, Embase, CINAHL and the Cochrane Library. Google Scholar was also used to assist in narrowing key terms. An ancestry search with the seminal article, *New Persistent Opioid Use Among Patients with Cancer After Curative- Intent Surgery* published in 2017, was also performed (Lee et al., 2017). The time frame of 2010 to 2020 was specified to reflect the rapid growth of the cancer survivor population, emerging evidence of the dangers of long-term opioid use, and the current opioid crisis. A histogram on PubMed confirmed the appropriateness of this time frame, with peak timing of articles being published from 2015 to the present.

Before the review, key concepts of cancer survivors and long-term opioid therapy were explicated. Cancer survivors can have a variety of definitions; however, for this review, cancer survivor was defined as an individual who is at least 3-months beyond the acute diagnosis and active cancer treatment phase, including those on maintenance treatment or prophylactic treatment, such as hormone therapy. This definition of a cancer survivor is in concordance with the American Society of Clinical Oncology (ASCO) survivorship resources (American Cancer Society, 2020; Glare et al., 2014; Paice et al., 2016). Long-term opioid therapy (LTOT) was defined as any opioid use for > 3-months post curative cancer treatment and is the most common definition of LTOT used in the literature (Karmali et al., 2020). Several months after completion of curative treatment is discussed in ASCO Guidelines for Management of Chronic Pain in Survivors of Adult Cancers as a time when opioid use should be carefully considered (Paice et

al., 2016). It should be noted that many articles in the oncology literature use the term persistent opioid use, which is interchangeable with the definition of LTOT (i.e., opioids use for > 3 months).

Study Selection: Inclusion and Exclusion Criteria

Articles identified from the search were uploaded into Covidence, a systematic review production tool, to facilitate the screening of inclusion or exclusion based on the following criteria (Oliva et al., 2020). Inclusion criteria included: (1) quantitative research related to cancer survivors with LTOT (2) English language (3) published in peer-reviewed journals in the last ten years, and (4) examined opioid use after curative cancer treatment. Articles were excluded if they were: (1) editorials, reviews, or opinion pieces (2) published conference abstracts (3) focused on non-opioid pain management in cancer survivors (4) focused exclusively on substance use disorders in cancer (5) focused on the use of opioids for acute cancer pain and (6) focused on opioid side-effects. Screening to determine if articles were within the scope of this review was undertaken independently by two authors (KFJ and LJW). Discrepancies were resolved through discussion and review of the full text of the article.

Data Extraction and quality assessment

In total, 315 articles were retrieved by applying the key terms to the five databases, and through ancestry search, after removal of 104 duplicates, 205 remained. Inclusion and exclusion criteria were applied, and 187 original peer-reviewed research articles were deemed relevant. Upon full-text review of the 21 articles, all met inclusion criteria. Figure 1 outlines the search results and final study selection using the algorithm, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

The 21 retained articles were appraised for quality using a validated assessment tool to quantify the rigor of the studies (Fu et al., 2013; Tilley et al., 2020; Whittemore & Knafl, 2005). The adapted tool uses a 14 item index for quantitative studies. Each article was assessed and scored, with one point assigned for each criterion. Score discrepancies were resolved by three of the authors (KFJ, LJW, MRF). All criteria were equally weighted, and higher scores indicated better quality studies, with a total potential affirmative score of 14. For this review, studies that received an affirmative score ≥ 10 were considered of adequate quality. This tool has been adapted for other systematic and integrative reviews (Finlayson et al., 2015; Fu et al., 2013; Tilley et al., 2020). All 21 studies were included in this review upon full-text review and after quality appraisal. For each study, we extracted the definition and measurement of LTOT or persistent opioid use, the prevalence and duration of LTOT, and predictive or associated factors of LTOT.

Data Analysis

As outlined by Whittemore and Knafl, data analysis involved an iterative process of constant comparison of the data in the reviewed studies. Data reduction was achieved by extracting relevant data and organizing by quality appraisal and creating a summary table, included in Table 2. Detailed critical appraisal of each article was performed using the Critical Appraisal Skill Programme Method (CASP), and studies were organized by study aim, design, definition, and operationalization of LTOT, rates of LTOT, factors associated with LTOT, other pertinent findings, and quality appraisal. Discussion with expert consultants ensured the identification of salient themes. The heterogeneity of definitions and operationalization of LTOT, various research designs, and diverse patient populations prevented a formal meta-analysis for this review.

Results

Quality of Included Studies

The overall quality of the 21 quantitative studies was adequate (mean= 10.7 ±1.38, range 8-14). Most studies provided Level III evidence as retrospective cohort comparative study designs using large data sets. There was only one appraisal rating of 14 (highest score) since it was the only study with a prospective design (Henry et al., 2019). Table 3 outlines the quality of assessments of the 21 quantitative studies. Data display and analysis was organized into categories of 1) cancer type (underlying diagnosis), 2) cancer treatment, 3) pain etiology, 4) socioeconomic factors, 4) patient-specific characteristics, and 5) opioid characteristics. Many of these factors have been associated with LTOT in chronic non-malignant pain (Hooten et al., 2017). A limitation of the studies reviewed is the various definitions and operationalizing of LTOT. For example, some authors defined LTOT as continuous opioid use demonstrated by an opioid prescription every 6 months, 3-months after cancer treatment. (Barbera et al., 2019) Other studies measured LTOT by the average number of days of opioid prescriptions per patient within a specified time; typically, 3-months after cancer treatment (Cass et al., 2018; Fredheim et al., 2019;. Shah et al., 2019; Vitzthum et al., 2019). Several studies distinguish between incidental, regular, and continuous opioid use (Chen et al., 2019; McDermott et al., 2019; Nelson et al., 2020). The majority of studies defined LTOT/ persistent opioid use as > 1 opioid prescription 3-6 months after curative intention treatment and chronic opioid use as any opioid consumption six months to one-year after treatment cessation (Cata et al., 2019; Desai et al., 2019; Henry et al., 2019; Kwon et al., 2013; Lee et al., 2017; McDermott et al., 2019; Roberts et al., 2020; Saraswathula et al., 2018; Shah et al., 2019; Ward et al., 2019).

Sample Characteristics

A summary of the 21 reviewed studies published from 2013-2020 is included in Table 2. Twelve studies used national databases including insurance claims, Veterans data set, Surveillance Epidemiologic End Result Medicare Data (SEER, n=5), or other government administrative data (Norway and Canada) (Barbera et al., 2019; Desai et al., 2019; Fredheim et al., 2019; Lee et al., 2017; McDermott et al., 2019; Murphy et al., 2018; Nelson et al., 2020; Roberts et al., 2020; Saraswathula et al., 2018; R. Shah et al., 2019; Sutradhar et al., 2017; Vitzthum et al., 2019). Samples sizes ranged from 976 to 106,732 patients. The remaining studies (n=5) were retrospective single-institution medical record reviews (Cass et al., 2018; Cata et al., 2019; Kwon et al., 2013; Ward et al., 2019; Yau et al., 2018) except one of two different Kaiser institutions (Chen et al., 2019) and another examining a Minnesota Rochester county database (Shah et al., 2018). These studies had smaller sample sizes ranging from 104-509 individuals. A prospective longitudinal design was used by Henry et al. (2019); all other designs were retrospective designs.

The time frame for the data collection in the reviewed studies was 1998-2016, with only one study using data after 2016 (Cata et al., 2019). A downward trend in opioid prescribing was reflected in three reviewed studies where opioid use differed in cohorts based on the time of cancer diagnosis. Shah et al. noted that a cancer diagnosis between 2004-2008 was a strong predictor of LTOT in opioid-naïve patients (Shah et al., 2019). Chen et al. described an increase in opioid use between 1994-2014 (Chen et al., 2019), and Cata et al. described a statistically significant reduction in oral morphine equivalence between 2015-2017 (Cata et al., 2019).

A wide range of ages was represented in the reviewed literature spanning 18-107 years old, although several studies limited the examination of LTOT in individuals > 65 years old (n = 10). Greater than 65 years old correlates with the median age of cancer diagnosis of 66 years

(National Cancer Institute, 2015); however, several reported that younger patients were more likely to be prescribed LTOT (Chen et al., 2019; Vitzthum et al., 2019; Ward et al., 2019). Sex as a biologic factor was not significantly associated with LTOT in the majority of studies (Barbera et al., 2019; Cass et al., 2018; Cata et al., 2019; Chen et al., 2019; Fredheim et al., 2019; Henry et al., 2019; Kwon et al., 2013; Lee et al., 2017; Murphy et al., 2018; Nelson et al., 2020; Salz et al., 2019; Saraswathula et al., 2018; Sutradhar et al., 2017), five studies were unable to comment on the role of sex in LTOT given predominate gender make up their cancer population (such as veteran population or breast and cervical cancers) (Desai et al., 2019; Roberts et al., 2020; Vitzthum et al., 2019; Ward et al., 2019; Yau et al., 2018), and only one study reported female gender as more likely to be associated with LTOT (OR 1.4, 95% CI 1.31-1.50, $p < 0.05$) (Shah et al., 2019).

Studies enrolled a diverse race demographic; however, many studies had more White participants than other race categories with the exception of Cass et al. (2018) whose population was nearly 80% African Americans. Two studies commented that being White was more predictive of LTOT whereas Black and Hispanic participants were less likely to be prescribed LTOT (Murphy et al., 2018; Nelson et al., 2020; Roberts et al., 2020; Shah et al., 2019; Vitzthum et al., 2019).

Prevalence and predictors of LTOT

A broad range of prevalence rates of LTOT was reported in cancer survivors ranging from 5-45% (Cass et al., 2018; Cata et al., 2019; Chen et al., 2019; Desai et al., 2019; Fredheim et al., 2019; Henry et al., 2019; Kwon et al., 2013; Lee et al., 2017; McDermott et al., 2019; Roberts et al., 2020; Saraswathula et al., 2018;Shah et al., 2019; Vitzthum et al., 2019; Ward et al., 2019; Yau et al., 2018). LTOT was influenced by several important biopsychosocial factors, including

cancer type, cancer treatment, pain etiology, socioeconomic status, opioid characteristics, and patient-specific characteristics. Table 4. provides an overview of the cancer survivor population examined and the factors associated with LTOT reported in each study.

Primary Cancer Type

Various cancer types were evaluated for LTOT in the reviewed articles, with the most common being head and neck cancer (n=6) (Cata et al., 2019; Henry et al., 2019; Kwon et al., 2013; McDermott et al., 2019; Saraswathula et al., 2018; Yau et al., 2018), followed by breast cancer (n=3) (Desai et al., 2019; Roberts et al., 2020; Yau et al., 2018), colon cancer (n=2) (Chen et al., 2019; A. Shah et al., 2018), lung cancer (n=1) (Nelson et al., 2020) and cervical cancer (n=1) (Ward et al., 2019). Other studies examined a mix of solid tumor types (Barbera et al., 2019; Lee et al., 2017), and no studies exclusively examined hematologic malignancies. The remaining five studies did not classify results by cancer type and compared cancer survivors to individuals without cancer (Cass et al., 2018; Fredheim et al., 2019; Murphy et al., 2018;Shah et al., 2019; Vitzthum et al., 2019).

Individuals who received curative head and neck cancer treatment were the most widely examined cancer for LTOT and had consistently had high rates of LTOT across studies. The prevalence of LTOT in head and neck cancer was 15.4% to 35% (Cass et al., 2018; Cata et al., 2019; Henry et al., 2019; Kwon et al., 2013; McDermott et al., 2019; Saraswathula et al., 2018). One study that examined LTOT beyond 3 months noted a decrease in LTOT over time, with rates dropping to 15.4% at 3 months and 7% after 6 months, suggesting that the trajectory of pain improves over time (McDermott et al., 2019). Tobacco use, opioid use before surgery or radiation treatment, medical comorbidities, anxiety disorder diagnosis, and positive screening for

alcohol use disorder were reported risk factors for LTOT in head and neck cancer subjects (Cata et al., 2019; Henry et al., 2019; Kwon et al., 2013; McDermott et al., 2019; Saraswathula et al., 2018). Rates of LTOT in colon cancer and breast cancer patients were 5-7% (Lu Chen et al., 2019) and 2-4%, respectively (Roberts et al., 2020).

Type of Cancer Treatment

Cancer treatment factors associated LTOT were examined in several studies, including curative surgery, radiation therapy, hormonal treatment, and adjuvant chemotherapy. There were equivocal findings on the influence of specific cancer treatments on LTOT. For example, adjuvant chemotherapy was associated with LTOT in six studies (Cata et al., 2019; Chen et al., 2019; Lee et al., 2017; McDermott et al., 2019; Nelson et al., 2020; Roberts et al., 2020) but not associated with LTOT in two (Barbera et al., 2019; Saraswathula et al., 2018). Four studies reported no change in LTOT across different treatment regimens (Barbera et al., 2019; Henry et al., 2019; Kwon et al., 2013; Vitzthum et al., 2019). Roberts et al. reported that LTOT was 35% lower in breast cancer patients receiving hormone therapy than chemotherapy (RR 0.65, 95% CI 0.44-0.97, P=0.03) (Roberts et al., 2020).

Surgery as a curative cancer treatment had high rates of opioid prescribing 3-6 months after procedures with studies focusing on breast, colon, lung, and head and neck surgery, and Lee et al. examined various curative cancer surgeries. LTOT occurred in 10% to 45% of patients who completed curative surgery, with one study concluding that LTOT is an iatrogenic consequence of cancer care (Cata et al., 2019; Lee et al., 2017; Nelson et al., 2020; Saraswathula et al., 2018; Yau et al., 2018). Less invasive surgery was associated with decreased incidence of LTOT in lung cancer patients (Nelson et al., 2020), but among breast cancer patients, mastectomy compared to lumpectomy did not appear to reduce the risk of LTOT (Roberts et al., 2020; Yau et

al., 2018). Breast reconstruction following mastectomy was associated with LTOT in one study (Yau et al., 2018).

Pain Etiology

Only four studies reported pain etiology as a factor in opioid prescribing, including tongue pain related to head and neck cancer (Cass et al., 2018; Henry et al., 2019), pre-existing non-malignant chronic pain (Cass et al., 2018), pre-existing cancer pain before surgery (Cata et al., 2019), and chemotherapy-induced peripheral neuropathy (CIPN) (Shah et al., 2018). Shah et al. (2018) specifically examined opioid use associated with CIPN, but several other reviews speculated that LTOT was for neuropathic pain such as post-thoracotomy pain and post-mastectomy pain (Henry et al., 2019; Lee et al., 2017; Nelson et al., 2020; Roberts et al., 2020; Shah et al., 2018). Cass et al. reported in 53% of the cancer survivor study sample indicated pain before cancer treatment as the indication for LTOT (Cass et al., 2018). Henry et al (2019). reported opioid prescriptions did not differ based on pain type (general pain, mouth/throat pain, and/or neuropathic pain). In the remaining seventeen studies, there was a paucity of information in the available literature reviewed on specific indications of opioid prescribing, and no studies comment on pain severity or pain interference in individuals on LTOT.

Socioeconomic Factors

Nearly half of the studies reported low socioeconomic factors were associated with LTOT in cancer survivors. Low socioeconomic factors included lower income (Roberts et al., 2020; Sutradhar et al., 2017; Vitzthum et al., 2019), unemployment at the time of cancer diagnosis (Vitzthum et al., 2019), and tobacco consumption (Cass et al., 2018; Desai et al., 2019; Vitzthum et al., 2019) living in a zip code where residents have lower education or an urban area (Barbera

et al., 2019; Lee et al., 2017; Nelson et al., 2020), and a diagnosis of disability for Medicare entitlement (Shah et al., 2019).

Patterns of Opioid Use

Examination of opioid dose during cancer care and in survivorship was reviewed in several of the studies but the findings were inconsistent. For example, several studies reported the majority of LTOT in cancer survivors is a low dose (< 20 mg of oral morphine equivalence) (Chen et al., 2019; Henry et al., 2019; Lee et al., 2017). However, Fredheim and Salz noted that greater than three years after cancer treatment, opioid doses were more likely to be higher (> 90 mg of oral morphine equivalence) in long-term cancer survivors than in non-cancer controls (Fredheim et al., 2019; Salz et al., 2019). The influence of opioid doses during treatment was only examined closely in one study reporting the peak mean morphine equivalence dose during treatment was not associated with LTOT six months after treatment (Kwon et al., 2013). For surgical patients, Cata et al. reported the median morphine equivalence during the hospitalization for curative cancer surgery was significantly higher in those with persistent opioid use opioid one year after surgery (p=.035) however, opioid dose prior to surgery was not associated with LTOT 6 months after surgery (Cata et al., 2019). Henry et al. reported that anxiety disorders (p=.04) upon cancer diagnosis contributed to cumulative mean morphine equivalence dose in the first year after cancer treatment (Henry et al., 2019). Ward et al. reported 20% of cervical cancer survivors received more than one type of opioid prescription six months after treatment (Ward et al., 2019). Two studies reported the rare use of long-acting opioids in cancer survivors (Cass et al., 2018; Yau et al., 2018).

The use of other pain-modifying treatments and high-risk polypharmacy was associated with LTOT in cancer survivors in many studies (Cass et al., 2018; Fredheim et al., 2019; Murphy

et al., 2018; Shah et al., 2018; Yau et al., 2018). Three studies measured the co-prescribing of benzodiazepines and opioids in cancer survivors, with rates of persistent use of both agents ranging from 10-33% (Fredheim et al., 2019; Murphy et al., 2018; Yau et al., 2018). The use of other pain-modifying medications was examined, Shah et al. (2018) reported participants with chemotherapy peripheral neuropathy were more likely to be prescribed opioids and serotonin/norepinephrine reuptake inhibitors (OR 2.87, 95% CI 1.45-5.66) (Shah et al., 2018) and Cass et al. reporting 33% of patients on LTOT were on other pain modifying medication (Cass et al., 2018). Murphy et al. reported significantly more polypharmacy in cancer survivors compared to non-cancer controls, with a large difference observed in central nervous system medications, including anxiolytics, opioid and non-opioid analgesics, antidepressants, and muscle relaxants (Murphy et al., 2018). The use of non-prescribed or active illicit opioid use was not examined as a factors in LTOT prescribing in any of the studies.

Three studies reported opioids prescriptions after cancer treatment were more often provided by non-cancer providers, including ear, nose, and throat specialists, emergency room physicians, family medicine, and primary care providers (Barbera et al., 2019; Cass et al., 2018; Henry et al., 2019). For example, Henry et al. (a United States study) reported of the 931 opioid prescriptions prescribed 12 months after head and neck cancer treatment 18 different prescriber specialties were represented in opioid prescriptions (Henry et al., 2019). Barbera et al. (2019) ’s Canadian study examined persistent opioid use > 5 years after cancer diagnosis and found more 80% of prescriptions were written by family physicians.

Individual Patient Factors

One study found that a history of cancer, regardless of type or time since diagnosis, resulted in higher rates of opioid prescribing than the general population without a cancer history

even 10 years after diagnosis and curative treatment (Fredheim et al., 2019). Salz et al. reported higher rates of opioid use in cancer survivors but concluded that rates of LTOT were blunted in the years following cancer-directed therapy and begin to approximate rates among non-cancer controls by six years after their diagnosis (Salz et al., 2019).

Opioid use prior to curative cancer treatment was noted in ten studies as a risk factor for LTOT (Barbera et al., 2019; Cata et al., 2019; Chen et al., 2019; Fredheim et al., 2019; Lee et al., 2017; McDermott et al., 2019; Nelson et al., 2020; Saraswathula et al., 2018; Vitzthum et al., 2019; Ward et al., 2019). Barbara et al. (2019) found that relative rates for opioid use were 8.5 times higher in patients with opioid use before cancer treatment. Furthermore, Cass et al. found that 53% of cancer survivors on LTOT had been diagnosed with chronic pain before cancer diagnosis and treatment (Cass et al., 2018). Several studies examined the impact of opioid use before cancer diagnosis by delineating opioid naïve patients from those with prior use (Barbera et al., 2019; Chen et al., 2019; Lee et al., 2017; Nelson et al., 2020). Across these studies, it was unclear if prior opioid use preceded cancer diagnosis or whether prior opioid use was in the context of ongoing multimodal treatment for curative cancer. For example, Lee et al. (2017) examined LTOT after curative surgery and found that opioid prescriptions were attributed to cancer surgery if they occurred 30 days before surgery and 14 days after discharge. Patients were defined as opioid naïve if they did not fill an opioid prescription a year before surgery.

Eleven studies reported an association of mental health diagnoses with LTOT (Barbera et al., 2019; Cass et al., 2018; Desai et al., 2019; Fredheim et al., 2019; Henry et al., 2019; Murphy et al., 2018; Saraswathula et al., 2018; Shah et al., 2019; Sutradhar et al., 2017; Vitzthum et al., 2019; Ward et al., 2019). Henry et al. noted that a diagnosis of anxiety was associated with more opioid prescriptions and higher opioid requirements in head and neck cancer patients ($p < 0.00$)

(Henry et al., 2019). Desai et al. noted that LTOT was 33% higher in breast cancer survivors with mental health comorbidities than those without (OR 1.33 CI 1.06-1.68) (Desai et al., 2019). Mental health comorbidities were also associated with higher LTOT use and lower survival in older adults with breast cancer survivors; however, opioid use alone did not account for this difference (Desai et al., 2019). Desai et. examined the role of mental health diagnosis on LTOT in breast cancer patients and noted relative rates of LTOT of 45% in study participants 3-months post-treatment (Desai et al., 2019). This study had a smaller sample (n=137) and younger sample age (mean of 53 years), which may account for variability from Roberts et al., who exclusively examined older adults and reported LTOT rates of 2-4% (Roberts et al., 2020; Yau et al., 2018).

The presence of non-cancer medical comorbidities also was noted to increase rates of LTOT in half of the studies (Barbera et al., 2019; Cass et al., 2018; Chen et al., 2019; Fredheim et al., 2019; Henry et al., 2019; Murphy et al., 2018; Nelson et al., 2020; Roberts et al., 2020; Saraswathula et al., 2018; Shah et al., 2019; Vitzthum et al., 2019). This was most often reported by the Charlson Comorbidity Index, and diabetes was specifically named as a factor in one study (Barbera et al., 2019). Moreover, LTOT was noted to be more common in patients with a history of substance use disorder in seven studies (Cass et al., 2018; Henry et al., 2019; Kwon et al., 2013; McDermott et al., 2019; Shah et al., 2019; Vitzthum et al., 2019; Ward et al., 2019).

Discussion

This review sought to examine the factors associated with LTOT in cancer survivors. The literature sheds light on the biopsychosocial factors associated with the transition to long-term opioid therapy, including the role of cancer type, medical comorbidities, opioid characteristics, mental health diagnoses, and socioeconomic factors. The average prevalence rate of LTOT was 24% (range of 2-45%) (Cass et al., 2018; Cata et al., 2019; Chen et al., 2019; Desai et al., 2019;

Fredheim et al., 2019; Henry et al., 2019; Kwon et al., 2013; Lee et al., 2017; McDermott et al., 2019; Roberts et al., 2020; Saraswathula et al., 2018; Shah et al., 2019; Vitzthum et al., 2019; Ward et al., 2019; Yau et al., 2018), which closely correlated with the reported 20-40% prevalence rate of chronic pain in cancer survivors (Jiang et al., 2019; Paice, 2019a; Van den Beuken et al., 2016). Notably, the average reported prevalence of LTOT in cancer survivors is five times the rate of the mean national prevalence rate of LTOT in the United States (Mojtabai, 2018). This would suggest that opioid use remains the mainstay of chronic cancer pain treatment in cancer survivors.

The literature highlights certain cancer types as high risk for LTOT after curative treatment. Head and neck cancer was the most studied primary cancer with consistently high rates of LTOT. Opioid use in this population is, in part, due to the high rates of chronic pain and opioid exposure in head and neck cancer treatment (Barbera et al., 2019). Among head and neck cancer survivors, 45.1% report chronic pain, and 11.2% report severe pain persisting > 5 years after diagnosis, associated with major depression and low quality of life (Cramer et al., 2018). Early findings suggest other high-risk cancers for LTOT, including lung and cervical cancer, while colon and breast cancer appeared to have lower rates of LTOT (Chen et al., 2019; Nelson et al., 2020; Roberts et al., 2020; Salz et al., 2019; Ward et al., 2019). Specific cancer types with greater rates of LTOT may be important targets for integrating multimodal chronic cancer pain treatments and dedicated studies aimed at understanding the efficacy and safety of opioids on chronic cancer-related pain.

Post-surgical procedural opioid use accounted for higher rates of LTOT of 10% to 45% (Cata et al., 2019; Lee et al., 2017; Nelson et al., 2020; Yau et al., 2018). These rates for LTOT are higher in cancer survivors compared to the 6-8% reported rates in the literature for non-

cancer surgeries (Brummett et al., 2017; Clarke et al., 2014; Soneji et al., 2016). Post-operative pain is more common in cancer survivors (Glare et al., 2014). It has been hypothesized that the aggressive nature of curative cancer surgeries contributes to chronic pain and LTOT (Nelson et al., 2020). The findings of this study were equivocal in determining the relationship between surgery, adjuvant chemotherapy, and radiation on LTOT, although it appears that multimodal treatment does correlate to higher rates of LTOT (Barbera et al., 2019; Cata et al., 2019; Chen et al., 2019; Henry et al., 2019; Kwon et al., 2013; Lee et al., 2017; McDermott et al., 2019; Nelson et al., 2020; Roberts et al., 2020; Saraswathula et al., 2018; Vitzthum et al., 2019). The role of high opioid doses during the intraoperative and postoperative opioids in curative cancer surgeries was highlighted as being associated with greater LTOT; this is consistent with non-cancer surgery studies that also demonstrated that high intraoperative and post-operative can have downstream effects in long-term opioid prescribing (Bugada et al., 2021; Cata et al., 2019). In the current surgery literature, pre-operative and intraoperative techniques to improve post-operative pain, decrease LTOT, and improve opioid safety in cancer survivors is a promising area of novel research (Hah et al., 2018; Martin et al., 2018; Rice et al., 2015).

Nelson et al. and Henry noted that uncoordinated prescribing in cancer survivors (Lee et al., 2017), made more changing by difficult to navigate opioid policies, could be a contributing factor of LTOT post-surgery (Henry et al., 2019; Meghani & Vapiwala, 2018). This may be particularly problematic in surgical oncology, where regular follow-up for chronic pain is not the typical scope of the surgical team. Indeed, in the reviewed literature, opioids were frequently prescribed by specialists and primary care practices (Barbera et al., 2019; Cass et al., 2018). Understanding opioid prescriber environmental and system factors that promote LTOT is needed, as the responsibility for the care of cancer survivors is often shared by oncologists,

subspecialists, palliative care, and primary care (Potosky et al., 2011). The need to coordinate chronic pain management across the healthcare system should be a priority for the rapidly expanding population of cancer survivors (Merlin et al., 2019).

The relationship between LTOT and mental health diagnoses was consistently described in the literature (Barbera et al., 2019; Cass et al., 2018; Desai et al., 2019; Fredheim et al., 2019; Henry et al., 2019; Murphy et al., 2018; Saraswathula et al., 2018; Shah et al., 2019; Sutradhar et al., 2017; Vitzthum et al., 2019; Ward et al., 2019). The role of untreated mental health diagnoses in driving LTOT has been well described in the nonmalignant pain and substance use disorder literature (Klimas et al., 2019; Wilens et al., 2005; Wilsey et al., 2008). High rates of mental health diagnosis in cancer, along with opioid exposure at times of intense uncertainty and stress, may contribute to LTOT (Block, 2001; Kadan-Lottick et al., 2005). The overlap of chronic pain, LTOT, and mood disorders is worrisome for cancer survivors who regularly report high levels of psychological distress (Moschopoulou et al., 2018; Zabora et al., 2001). A new diagnosis of a psychiatric disorder is common in cancer care, particularly in challenging to tolerate treatment regimens such as head and neck cancer and stem cell transplant that carry higher rates of treatment-related psychological trauma (Hefner et al., 2014; Robins et al., 2010). Understanding the psychosocial factors of chronic cancer pain is particularly important since managing chronic pain, and psychosocial distress is often treated as distinct entities rather than a complex integrated symptom cluster (Darnall et al., 2018). For example, the Pain Psychology Task Force of the American Academy of Pain Medicine published the results of a national survey to identify the current practice of mental health clinicians (psychiatrists, therapists, psychologists) treatment of chronic pain; almost 90% of mental health clinicians reported a lack of education in psychological treatments for chronic pain (Darnall et al., 2016). There is a vital need for cancer

survivors to understand the psychosocial factors that modulate chronic pain and long-term opioid use, such as fear of cancer recurrence, trauma, cancer distress, worsening mood disorder, and social isolation. This knowledge would help guide interdisciplinary multimodal pain interventions needing to address the unique total pain that cancer survivors experience, address undertreated psychological factors that may contribute to LTOT, and promote opioid-related harms.

In several studies, the role of race was discussed as factor related to LTOT, with two studies commenting the White race was associated with higher rates of LTOT (Chen et al., 2019; Murphy et al., 2018; Roberts et al., 2020; Shah et al., 2019; Vitzthum et al., 2019). The role of race in LTOT is likely reflective of the racial disparities that exist in the United States in pain treatment. Racial minority groups, specifically African Americans, are less likely to receive prescription opioids for pain than White patients across types of pain and treatment settings (Alexander et al., 2018; Chen et al., 2005). The consequences of racial disparities include the under-treatment of pain, access to treatment for opioid use disorder, and the selection of safe cancer pain treatments in minority groups compared to Whites (Lagisetty et al., 2019; Meghani, et al., 2012; Meghani et al., 2014; Meghani & Chittams, 2015). Furthermore, race and SES overlap significantly in the U.S. Thus, the findings of the independent effect of race on pain outcomes must be interpreted carefully, especially when the racial effect becomes insignificant in a model adjusting for race (as noted in the Roberts et al. study in this review) (Meghani & Chittams, 2015). Race in pain research should be considered in the context of a sociopolitical framework and not a biologic construct (Hoffman et al, 2016; Meghani et al., 2014). Cancer pain research needs to acknowledge if there is an overlap in significant findings then SES effects are indeed race effects and demand examination of the role of structural racism and implicit basis as

driver of race-related health disparities in the United States (Boyd et al., 2020; Meghani & Chittams, 2015). It remains imperative to improve access to adequate pain management during and after cancer treatment in racially diverse groups (Chen et al., 2019; Hoffman et al., 2016; Meghani & Chittams, 2015; Meghani et al., 2014; Murphy et al., 2018; Shah et al., 2019).

Likewise, this review confirmed that socioeconomic factors were predictive of greater LTOT, including low income, unemployment, tobacco use, and zip codes associated with lower educational achievement (Barbera et al., 2019; Cass et al., 2018; Desai et al., 2019; Lee et al., 2017; Nelson et al., 2020; Roberts et al., 2020; Shah et al., 2019; Sutradhar et al., 2017; Vitzthum et al., 2019). Social determinants of health have been consistently associated with a higher incidence of chronic pain (Jiang et al., 2019). Moreover, the lack of access to non-pharmacologic pain management strategies among lower socioeconomic classes and minority groups is a serious issue compromising chronic cancer pain management. For example, lack of access to acupuncture, a recommended treatment for chronic cancer pain, has been noted in racially diverse and low-income groups related to financial and insurance utilization barriers (Kligler et al., 2015; Liou et al., 2019; Paice et al., 2016). Likewise, higher socioeconomic status (SES) is associated with greater use of practitioner-assisted complementary and alternative medicine approaches (CAM), while those of lower SES have greater use of free therapies (Ludwick et al., 2020). The evidence in this review suggests that health disparities play a role in increasing rates of LTOT in cancer survivors. The same disparities of lower education, income, and unemployment are of great concern since they are also associated with greater risks of opioid-related harms (Altekruse et al., 2020). More work needs to be done to ensure adequate and consistent access to multimodal pain management for all cancer survivors.

Nearly 70% of cancer survivors have other chronic health conditions (Leach et al., 2015). This review revealed that comorbidities, most commonly measured by the Charlson Comorbidity Index, were a significant contributing factor for LTOT. Comorbidities contribute to the development of chronic pain. For example, diabetes, nutritional deficiencies, or HIV infection may enhance the risk of cancer pain syndromes such as chemotherapy-induced peripheral neuropathy (Paice, 2011). The number of comorbidities and, by extension, prognosis has been reported to influence opioid prescribing decisions in patients with serious illness (Merlin et al., 2019). The association between comorbidities and LTOT is troublesome as high rates of opioid-related harms and accidental opioid overdose have been reported in liver disease, pulmonary disease, and obesity (Dowell et al., 2016; Zedler et al., 2015). Future evidence-based opioid guidelines are needed to help guide LTOT decisions in cancer survivors with complex health conditions to minimize opioid-related harms while addressing chronic pain needs.

This review revealed that prior opioid use was a consistent predictor of LTOT in cancer survivors (Barbera et al., 2019; Cass et al., 2018; Lee et al., 2017). The trend of one opioid prescription yielding to another is noted in chronic non-malignant pain literature, where each day after the first three days of an opioid prescription, the risk of long-term opioid use increases. In individuals that refill one opioid prescription, nearly 20% of those patients remained on those opioids for > 1 year, and 60% of patients prescribed opioids for 90 days remain on them for > 2 years (Center for Disease Control, 2017). In cancer survivors, the role of prior or prolonged opioid use may reflect the challenges of opioid deprescribing (Carmona-Bayonas et al., 2017; Cheng et al., 2019). Opioid deprescribing has proven to be challenging, and low rates of success are noted in common co-occurring diagnoses in cancer survivors of anxiety and depression (Block, 2001; Delgado-Guay et al., 2009; Kadan-Lottick et al., 2005; Weimer et al., 2016). For

cancer survivors, opioid exposure is common and opioid transition may be difficult, especially in the face of persistent pain and psychological distress. For example, in head and neck cancer, up to 80% of patients receive an opioid prescription during treatment (Ganju et al., 2019; Henry et al., 2019). Likewise, in head and neck cancer, 33.4% of individual's experience subclinical post-traumatic stress, and 11.8% meet the criteria for PTSD after treatment, with fear of cancer recurrence being a major driver of psychological distress (Moschopoulou et al., 2018). It is commonly understood that psychological distress, PTSD, and opioid use are highly comorbid (Tripp et al., 2019; Wilsey et al., 2008). Minimizing LTOT may pose challenges in those with pre-existing opioid use or cancers with higher rates of opioid exposure coupled with psychological distress. Additionally, opioid deprescribing is especially challenging in survivorship care, where the routine assessment of adequate pain control is necessary since new-onset pain or worsening pain can be a sign of recurrence (Paice et al., 2016).

This review highlighted shared risks associated with LTOT and opioid related harms. For example, the common practice of co-prescribing of opioids, benzodiazepines, and other pain-modifying medication was noted in several studies (Cass et al., 2018; Fredheim et al., 2019; Murphy et al., 2018; Yau et al., 2018). These results are worrisome as benzodiazepines and gabapentenoids have been shown to increase the risk for opioid-related mortality (Cass et al., 2018; Gomes et al., 2017; Paice et al., 2016; Peck, Harman, & Anghelescu, 2018). High-dose opioid prescriptions (> 90 mg of oral morphine equivalence) were reported as more common in long-term cancer survivors than in non-cancer controls (Fredheim et al., 2019; Salz et al., 2019). A history of substance use disorder or high risk for opioid misuse was noted in greater than half the studies (Cass et al., 2018; Henry et al., 2019; Kwon et al., 2013; McDermott et al., 2019; Shah et al., 2019; Vitzthum et al., 2019; Ward et al., 2019). SES factors such as poverty and less

than a high school education are shared risks of opioid mortality and LTOT in cancer survivors (Altekruse et al., 2020). Targeted interventions for vulnerable groups, high opioid dose recipients, and those on multiple medications are needed to minimize opioid-related harms. In chronic non-malignant pain, buprenorphine has received increased attention for a broad range of related indications, including opioid misuse, subclinical opioid use disorder, opioid tapers to minimize abstinence syndromes, and complex persistent dependence (Daitch et al., 2014; Jones, 2019; Webster et al., 2020). Buprenorphine has the potential to manage chronic cancer-related pain, given its favorable side effect and safety profile (Schmidt-Hansen et al., 2015; Webster et al., 2020). Currently, only 13% of palliative care clinicians across the country hold a waiver for buprenorphine, and thus there is a significant need to improve access to buprenorphine for chronic pain and high-risk opioid prescribing (Merlin et al., 2019). Moreover, a shift of decreasing in opioid prescribing may be warranted given mounting literature of opioid-related harms; however, there have been few proposed alternative treatments that address chronic pain and are readily available for all cancer survivors (Meghani & Vapiwala, 2018). As the oncology culture attempts to minimize LTOT, there needs to be equal attention to addressing chronic pain in cancer survivors using non-opioid approaches and access to safer opioid options (i.e. buprenorphine) in individuals with complex persistent dependence, opioid misuse, and opioid use disorders. Furthermore, opioid policies may be important to improve opioid safety in cancer survivors, but careful attention to the lessons learned from the implementation of the 2016 Center for Disease Control Prevention Guidelines for Chronic Pain is critical (Center for Disease Control Guideline for Prescribing Opioids for Chronic Pain, 2019). Opioid prescribing trends since the implementation of the 2016 CDC guidelines are not reflected in the majority of the studies in this review (most retrospective data is before 2016) but have resulted in a substantial

reduction in opioid prescribing. Unfortunately, inappropriate application of these guidelines has resulted in forced opioid tapers, mandated opioid dose reductions, clinicians being unwilling to accept patients on chronic opioids, and harmful institution and insurance policies that have given rise to in increased rates of suicide, opioid overdose deaths, and psychiatric destabilization in chronic pain patients (Darnall et al., 2018; Fishbain & Pulikal, 2018; James et al., 2019). Opioid policies play an important role in addressing the opioid overdose public health crisis (Dowell et al., 2016) however more research is needed to understanding the complex and unique phenomenon of chronic pain in cancer survivors to better inform patient-centered opioid policies for cancer survivors.

Limitations of the current literature

The current literature examining LTOT in cancer patients has several limitations that should be addressed. The majority of studies used retrospective designs and large data sets that may have lacked the level of granularity necessary to gain insights into LTOT in cancer. In addition, one-third of the articles used the same Medicare data set, which limits the examination of LTOT to > 65 years old. A large limitation of the literature a lack of a description of the type of the pain for which opioids were prescribed. Thus the available research is limited in commenting on the appropriateness of opioid prescribing. The majority of studies looked at opioid use during peak prescribing times, with only one study collecting data after the CDC guidelines in 2016. Notably, from 2006 to 2017, there has been a 19% reduction in annual opioid prescriptions; therefore, the current literature may not reflect current opioid prescribing practices (Center for Disease Control National Opioid Prescribing Trends, 2019). Additionally, most reviewed studies examined opioid use by prescriptions written or self-report and did not directly measure opioid consumption.

Limitations of the review

This review has several limitations that should be addressed. By seeking a broader understanding of LTOT in cancer survivors, this review included literature that often used different definitions of this phenomenon, which in turn may overstate the prevalence of LTOT. This review was also limited to cancer survivors who were > 3-months from curative treatment based on existing definitions in the literature. However, this time distinction may not reflect the trajectory of cancer pain, where similar pain levels have been reported in survivors compared to those in active treatment (Shi et al., 2011).

Conclusion

This review provides evidence that LTOT in cancer survivors is influenced by several important biopsychosocial factors such as cancer type, cancer treatment, medical comorbidities, opioid characteristics, mental health diagnoses, and socioeconomic factors. A major limitation of current knowledge is a lack of research investigating the correlation of LTOT to pain severity and pain interference; therefore, the appropriateness of LTOT in cancer survivors continues to be an unanswered research question. Moreover, using LTOT in cancer survivors remains a clinical challenge given the high prevalence of chronic cancer-related pain, the need for opioids during active treatment, shared care of cancer survivors, and the lack of evidence-based multimodal cancer-specific pain interventions. Minimizing the use of LTOT and optimizing effective pain management strategies in cancer survivors requires innovation. Successful strategies in non-cancer pain, such as the conservative management of initial prescriptions, are not feasible for cancer patients and may lead to opioid access barriers and undertreated pain (Deyo et al., 2017). Opioids and symptom management play an integral role in the active treatment of cancer and are essential to treatment retention and favorable outcomes in curative disease (Zenda et al., 2011).

Given the inability to limit opioid exposure in cancer treatment, there needs to be increased attention to interventions aimed at minimizing the negative consequences of LTOT, addressing unmet chronic cancer-related pain needs, and the developing best practices to support opioid treatment decisions (Goodlev et al., 2019; Paice, 2020). Minimizing opioid prescribing for cancer survivors is an important consideration for some survivors; however, there is a simultaneous need to provide an alternative evidence-based framework to address the chronic pain experienced by cancer survivors.

Appendix A.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart

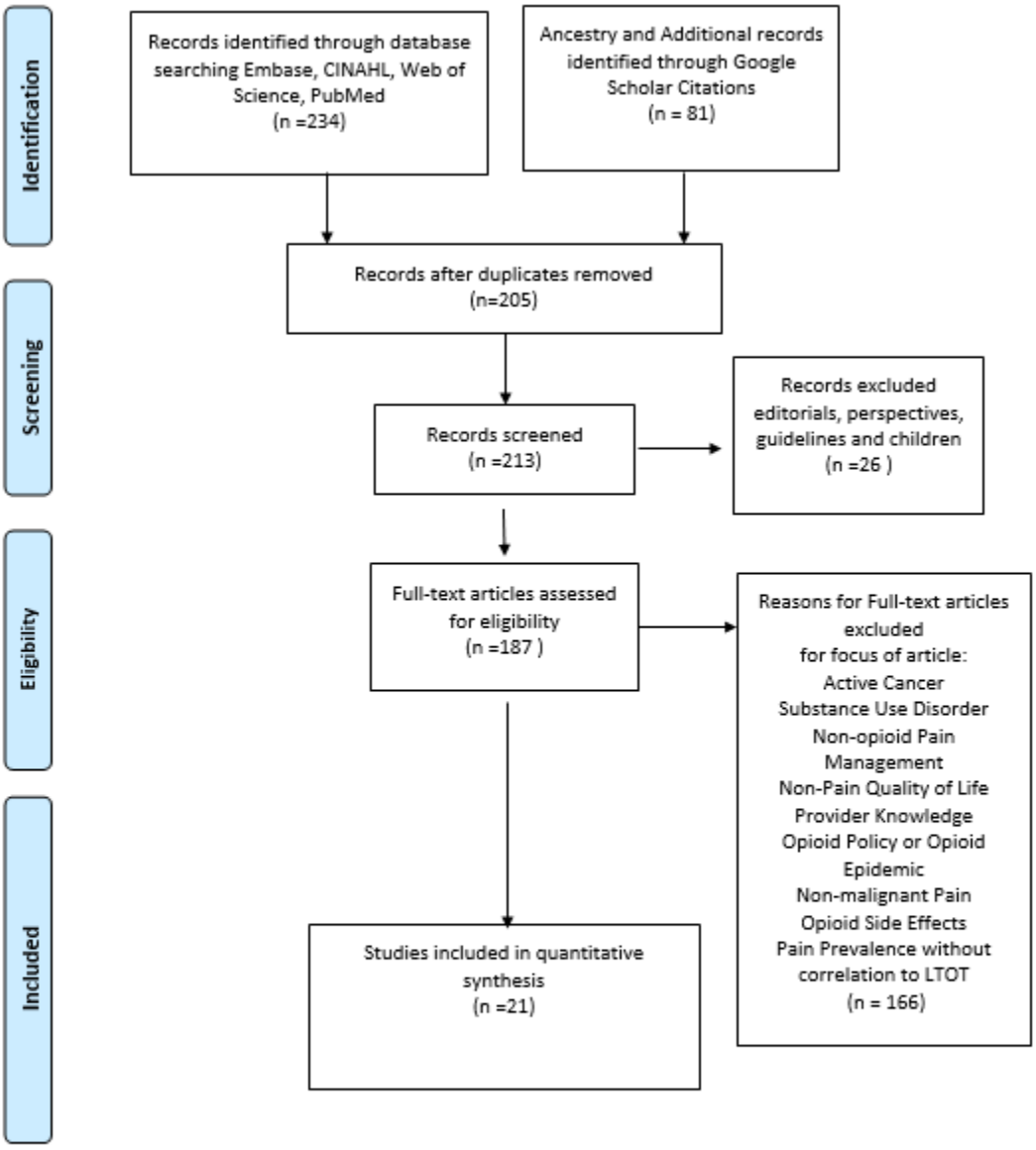


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart illustrating the search strategy

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Table 1. Search Terms

Search term associated with Cancer Survivor	"Cancer" "Cancer" AND "Survivor" "Malignant Neoplasm" "Cancer Survivor"
Search term associated with Opioids	"Opioid" "Narcotics" "Analgesics" "Opiate"
Search term associated with opioid duration	"Long term" "Long-term" OR "persistent use"

Table 2. Summary of Study Finding

Study	Aim & Design	Sample	Definition & Operationalization of LTOT	Rates of LTOT	Factor Associated with LTOT	Other notable findings	QS
Barbera et al., 2019	Aim: Evaluate Factors/ relative rates associated with opioids 5 years of survival from cancer diagnosis Design: Retrospective cohort study using administrative data of government insurance in Canada	Any Solid or Liquid tumor diagnosis (no evidence of disease) N= 7,431	Measured rate of opioid prescriptions, where the numerator was the number of prescriptions from 5 years after diagnosis to the last follow-up and the dominator was the duration of follow-up time. Continuous use was defined as at least one prescription every 5 months since diagnosis	Relative rate for opioid use was 8.5 (in patients with opioid use prior to diagnosis) Relative rates of those with continuous opioid use was 77 times that of individuals with no opioid use.	Continuous opioid use from diagnosis to 5-year anniversary LTOT (RR 46.1; 95% CI 34.8-61.2) Opioid use before diagnosis (RR 1.8; 95% CI 1.4-2.2) A history of diabetes (RR 1.3; 95% CI 1.15-1.54) and depression (RR 1.8; 95% 1.4-2.3) were also associated with higher risk.	80% of opioid prescriptions were written by family practitioners. No association with treatment of surgery or chemotherapy	12
Cass et al., 2018	Aim: Examine patterns of use and factors predicting prolonged prescription opioid medication following treatment with curative intent Design: Single Center retrospective cohort study from the	Cancer patients (all types) following treatment with curative intent N=199 patients	Prescribed an opioid prescription following completion of curative treatment.	38% continued to receive opioids beyond the acute diagnosis and treatment phase.	Chemotherapy was a significant predictor of opioid use (OR 7.3; 95% CI 2.1-25.2; p=0.002) Use of other Pain modifying Medication was a predictor of LTOT (OR 4.61;95% CI 2.3-9.4; p< 0.000)	Pain preceding cancer diagnosis was the most common reason for opioid medication in 53.3% of those on LTOT 29% of persistent users had a history of Substance Use Disorder & 54% were at moderate risk for opioid misuse or use disorder based on Opioid Misuse and Abuse Screening Tool	11

	electronic medical record					Average number of prescriptions was 4.8 over an average of 9 months (range 1-31)	
Cata et al., 2019	Aim: Examine persistent opioid use after oral cancer surgery. Design: Retrospective Cohort Study in a single institution	Oral Tongue Squamous Cell Carcinoma status post-curative-intent cancer surgery N=362	Any active opioid consumption by the patient during follow-up clinic visits between 90-180 days after surgery. Chronic use was defined as any opioid consumption reported by the patient 181-365 days after surgery.	31% had continued opioid use 6 months after surgery 15% were on LTOT at 1 year	Pre-op opioid use ($p<0.001$) Tobacco use ($p=0.040$) Pre-existing tongue pain ($p < 0.001$) Adjuvant chemotherapy ($p < 0.001$) and neck dissection ($p=0.046$)	Statistically significant reduction in OME was noted between 2015-2017	11
Chen et al., 2019	Aim: Describe patterns of opioid use in colon cancer survivors Design: Cohort study in two institutions. Measured quarterly opioid use from 1 year before diagnosis through 5	Colon Cancer Survivors N=2039	Measured opioid prescriptions within fixed 91-day quarters. Quarter 0 was the day of diagnosis through the 90^{th} day after the diagnosis. Distinguished between incidental use (no prior	LTOT increased from 3-5% pre-diagnosis to 5-7% > 1 year after treatment	Age < 50 years old ($p <0.050$) Prior smoking history ($p<0.050$) Higher stage cancer (I-III) ($p <0.050$)	Opioid use increased following colon cancer diagnosis, but doses were low (< 20 OME)	12

	years after diagnosis		prescription in 2 prior quarters) versus continuous use (prescription fill within 2 days of run-out date)				
Desai et al., 2009	Aim: Examine whether there is an association between mental health comorbidities with opioid use in elderly breast cancer survivors Design: Retrospective cohort study SEER Medicare data base with sample matching of breast cancer patients with and without mental health comorbidities	Breast cancer patients on adjuvant endocrine therapy N= 10,452	Use of any opioid during the two years after initiation of adjuvant endocrine therapy	Women with breast cancer with mental health comorbidities were 33% more likely to use opioids (OR, 1.3, 95% CI 1.1-1.7)	Adjusted probability of opioid use with mental health comorbidities 72.5% vs 66.9% without mental health diagnosis p=.010	Mental health comorbidities had a higher rate of opioid use and a lower survival (HR 1.5; 95% CI, 1.0-2.2 p<0.050) Opioid use alone was not a statistically significant factors of increased mortality	11
Fredheim et al., 2019	Aim: Compare the use of non-opioids, opioids, and benzodiazepines of long term survivors 10 years after cancer diagnosis Design: Cross-sectional study of analgesic and benzodiazepine	Long term cancer survivors examined 10 years after diagnosis N=21,426	Greater than 365 defined daily doses during 365 days and to receive prescriptions in all quarters of the year (corresponds to using opioids daily but not necessarily around the clock).	Opioid prescriptions and co-prescribing with benzodiazepines were seen in 22% of survivors, 10 years after diagnosis.	Opioid and benzodiazepine use was highest in lung cancer and upper GI tract than in the general population.	Cancer survivors were at higher rates of high dose opioid use 6.5 vs 4.8/1000 Less than 10% of those on LTOT received only long-acting formulations.	8

	use in long term using Cancer registry of Norway and the Norwegian prescription database						
Henry et al., 2019	Aim: Determine the extent of opioid prescription after head and neck cancer treatment and the role of past or current psychiatric diagnosis Design: Prospective longitudinal study	Head and neck cancer patients N=223	Opioid prescription including dose throughout the first year after head and neck cancer diagnosis.	31.4% remained on opioids > 1 year post-treatment	Anxiety disorder diagnosis associated with increased OME dose (p=0.000)	Opioid prescribing did not differ based on type of pain (i.e. general pain, mouth pain, and/or neuropathic pain). Most prescriptions written by ENT, gastroenterologist, and ER physicians.	14
Kwon et al., 2013	Aim: Describe factors associated with opioid "stoppers and "non-stopper" Design: Retrospective medical record study of patients who continued vs stopped opioids 3 months after treatment and repeated assessment 6 months' post-treatment to identify risks of "non-stoppers"	Squamous cell advanced head and neck cancer status post radiation with or without chemotherapy N=70	Any opioid prescription beyond 3 months after completion of radiation.	63% were prescribed LTOT at 3 months 33% continued opioids for > 6 months' post chemoradiation	Positive Alcohol Use Disorder Screen (OR 5.2, p=.005)	Peak dose of morphine equivalence was not associated with LTOT	11

Lee et al., 2017	Aim: Examine new persistent opioid use and daily opioid dose after curative solid tumor cancer surgery Design: Retrospective cohort study using US National insurance claim data to identify risk factors for LTOT	Curative surgery for melanoma, breast, colorectal, lung, esophageal, and GI cancers N=68,463	Additional opioid prescription between 90-180 days after surgery Any opioid prescription 30 days prior up to 90 days after was attributed to surgery.	10.4% (95% CI, 9.4-10.1%) of opioid naïve patients continued on opioids at 1 year The co-variate adjusted risk for new LTOT in patients receiving adjuvant chemotherapy was 15-21% compared to 7-11% for those with no chemotherapy.	Breast, colorectal, lung, and melanoma were more likely to remain on opioids Adjuvant chemotherapy (p=.002)	Opioid dose was not influenced by procedure type LTOT average doses equivalent was 15 mg OME	10
McDermott et al., 2019	Aim: Determine the risk of acute and chronic opioid use with squamous cell cancer of the oral cavity and oropharynx. Design: Retrospective Population-based study using SEER Medicare data base	Head and neck cancer patients with localized curable disease N=976	Any opioid use 3 months and 6 months after treatment. Opioid use was considered continuous if the time between the last day of one opioid prescription and the first day of the next opioid prescription was less than 30 days.	15.4% had continued opioid use at 3 months 7% had continued use at 6 months	Radiation alone as a treatment type were less likely to continue opioids (OR 0.4; 95% CI 0.2-0.7, p< .001) Not married (OR 2.2; 95% CI 1.2-4.1, p=.011) Opioid prescription prior to treatment. (OR 3.6; 95% CI 2.0-6.5, p <.001) Tobacco Use (OR 3.8, 95% CI 1.4-10.2, p=.007)	83% received an opioid prescription during their treatment Oxycodone prescribed as the first opioid was the least likely to lead to ongoing use at 3 and 6 months (OR 0.3; 95% CI 0.1-0.7, p=.004)	10

Murphy et al., 2018	Aim: Examine patterns of prescription medication use and polypharmacy Design: Population Match Study using Medical Expenditure Panel Survey	Cancer survivors, all types, at least 1 year after diagnosis N=5216 matched cancer survivors with non-cancer controls N=19,588	Opioid prescription at two time points. Newly diagnosis cancer survivor (< 1 year from survey) and previously diagnosed cancer survivors (> 1 year from the survey) compared to non-cancer controls.	10% of survivors were prescribed opioids and/or benzodiazepines compared to 5% of controls. Opioid use was 28.6% (95% CI, 26.5%-30.6%) among cancer survivors > 1 year after diagnosis.	A higher percentage of cancer survivors were prescribed 5 or more unique medication classes (64%; 95% CI 62.3%-65.8%)	Cancer survivors had more than double the prescription expenditure compared to controls, findings persistent across age and comorbidity categories	9
Nelson et al., 2020	Aim: Determine the incidence of persistent opioid use post-surgery Design: Retrospective design using Use of SEER	Non-small cell lung cancer patient who were status post-surgical resection N=6948	Opioid prescription > 90 days after lung surgery. Examine pre-operative opioid use.	31% with post-operative LTOT, including 17% of opioid naïve patients (no opioid use prior to surgery)	Adjuvant radiation (OR 1.36, 95% CI 1.06-1.74), chemotherapy (OR 1.87, 95% CI 1.49-2.33) 66-70 years' old (OR 1.55, 95% CI 1.16-2.06) Higher Charlson comorbidity index, score 1 (OR 1.35 CI 1.10-1.64), score 2 (OR 1.27, 95% CI 1.0-1.6) Zip codes with lower education (OR 1.86, 95% CI 1.32-2.61)	Less invasive surgery had decreased likelihood of POU (OR 0.75, 95% CI 0.62-0.92)	10

Roberts et al., 2020	Aim: Determine extent, historical trends, and predictors of new onset opioid use Design: Overall and Quartile adjusted probabilities of new-onset persistent opioid use using SEER data	Older Adult Women (66-90 years old) after active breast cancer treatment Stage 0-III breast cancer N=24,631 Study excluded individuals with prior opioid use 3 month leading up to cancer diagnosis.	Greater or equal 90 day opioid supply during the 12 month follow up period after breast cancer treatment	2-4% had a new LTOT Alterative definition of POU was used as any opioid fill 90-180 days after treatment with rates of LTOT of 11.4-14.7%	Chemotherapy use (4.9-2.4%; P < 0.01) Risk for LTOT was 35% lower for those with hormone therapy treatment (RR, 0.65; 95% CI 0.44-0.97; P=0.03) Lower SES (RR 0.5; 95% CI 1.01-2.28; P=.04)	66% of subjects received opioids during cancer treatment Probability of LTOT was stable in this cohort since 2008	10
Salz et al., 2019	Aim: Examine trends of opioid use over time in cancer survivors compared to non-cancer control Design: Retrospective cohort study using SEER Medicare linked cancer registry claims	N= 46,789 survivors and 138,136 noncancer control	Chronic use was defined as 90 consecutive days of opioid use allowing for up to a 7 day gap between consecutive refills.	Chronic use among colorectal and lung cancer survivors exceeded chronic use among controls Colorectal cancer (OR 1.34; 95% CI 1.22-1.47) Lung cancer (OR 2.55; 95% CI 2.34-2.77) Chronic opioid use was less in breast cancer survivors than non-cancer controls.	Cancer survivors were more likely to have high dose opioids (> 90 OME equivalence day) than none cancer controls (OR 3.65-5.54, p < .05)	Differences in chronic use between survivors and controls declined each year after index date, 6 years after diagnosis survivors were no were likely to be chronic opioid users.	9

Saraswathula et al., 2019	Aim: Describe prevalence of persistent opioid use and risk factors Design: Retrospective cohort study using SEER Medicare linked cancer registry claims	N=866 Older (> 65 yo) head and neck cancer patients who underwent primary resection	New opioid prescription 90-180 post operatively	33.3% of all patients (including those with previous opioid use and opioid naïve patients). Persistent use noted in 48.3% of patients on opioids before surgery Persistent use was noted in 18.5% that were opioid naïve prior to surgery	Postoperative radiation (OR 1.99; 95% CI 1.33-2.98) Higher Charlson comorbidity index (OR 1.20; 95% CI 1.03-1.41, p <.001) Pre-operative opioid use (OR 3.96; 95% CI 2.80-5.59)	Postoperative chemotherapy was not associated with LTOT.	10
AShaul et al., 2018	Aim: Assess disease burden of chemotherapy induced peripheral neuropathy (CIPN) Design: Retrospective cohort study using Rochester Epidemiology database and electronic medical record	Residents of Olmstead County Minnesota receiving neurotoxic chemotherapy N=509 with 268 (52.7%) diagnosed with Chemotherapy induced peripheral neuropathy (CIPN)	Any opioid use during study period	CIPN group with 33.1% with POU (CIPN negative group with 20% POU)	Those with CIPN surviving > 5 years were more twice as likely to be prescribed opioids five years after treatment (OR 2.0, 95% CI 1.06-3.69)	Those with a diagnosis of CIPN were more likely to use opioids than those without a diagnosis. Subjects with CIPN were more likely to use other pain modifying treatments such as serotonin/norepinephrine reuptake inhibitors (OR 2.87; 95% CI 1.16-2.90)	9
R Shaul et al., 2019	Aim: Examine rates and predictors of long term opioids in	Older adults (66-107 years' old) Cancer survivors of Solid tumors	Having at least a 90 day supply of opioids in the year following cancer treatment	LTOT in all survivors 5-18 years since cancer diagnosis was 12-13.3% and	LTOT was 45.8% with chronic pain diagnosis	The most prevalent pain diagnoses were joint pain/ arthritis (32.7%), abdominal or chest pain	10

	older cancer survivors <u>Design:</u> Retrospective cohort study using Medicare Enrollment and opioid prescription claims	(breast, prostate, GI, lung, and other) N=63,815 cancer survivors		increased from 1.4 to 7.1% for opioid naïve survivors.	Being diagnosed with cancer in 2004-2008 was a strong predictor of LTOT for opioid naive patients (OR=1.78, 95% CI 1.64-1.94) • History of drug abuse (OR=2.51, 95% CI 1.96-3.22) • Female sex (OR 1.4, 95% CI 1.31-1.50) • History of depression (OR 1.32, 95% CI 1.23-1.36) • 1 or more Comorbidities (OR 1.29, 95% CI 1.23-1.36) • Diagnosis of disability for Medicare entitlement (OR 1.78, 95% CI 1.66-1.91)	(16.3%), and back pain (15.9%).	
Sutradhar et al., 2017	<u>Aim:</u> Examine the association between survivorship and rate of opioid prescriptions. <u>Design:</u>	Various cancer types with matched controls N=17,202 Cancer survivors=8601 Matches Controls=8601	Rate of opioid prescription as measured by any prescribed and filled opioid prescription	Opioid prescribing was 1.22 times higher among cancer survivors than matched controls even 10 years after cancer diagnosis (RR 1.2,	Lower income (p< 0.01) Lower age (< 61 years old (RR .97, p<.0001)	Opioid prescribing was not associated with gender.	10

	Retrospective population wide matched cohort study			95% CI 1.09-1.42, p<.001)	Rural neighborhoods (RR 1.22, p.008) More comorbidities had significantly higher prescribing rates even 10 years after cancer diagnosis (RR1.93, p <.0001)		
Vitzhum et al., 2019	<u>Aim:</u> Identify clinical risk factors and create a risk score to help identify patients at risk for persistent opioid use and abuse <u>Design:</u> Retrospective cohort study	Veterans solid tumor cancer survivors N=106,732	120 days or greater or greater supply or 10 or more prescriptions from 1-2 years after start of curative treatment.	8.3% all cancer survivors (95% CI 8.1-8.4%) LTOT varied by type of cancer: Prostate cancer lowest rate of 5.3% (95% CI 5.1-5.5) Highest liver cancer 19.8% (95% CI 17.2-22.5%)	White Race Unemployment at the time of cancer diagnosis Lower income Comorbidities Current or prior tobacco use (p values not reported)	Stage, local treatment, and chemotherapy use were not associated with persistent opioid use with the exception of higher stage colon, breast, and head and neck cancer Rate of opioid abuse and dependence was 2.9%. Rate of opioid related hospitalization was 2.1%	12

Ward et al., 2020	Aim: Describe patterns of opioid use in cervical cancer survivors Design: Retrospective cohort study via chart review of a single institution	Cervical cancer patients who completed Radiation N=104 women	Continued opioid prescriptions 6 months after radiation	25% remained on opioids at 6 months after completion of radiation 29% at 3 months after completion of radiation	Younger age < 40 years' old (p <0.05) History of depression, or anxiety (adjusted OR 6.28, 95% CI 1.70-23.30) History of substance abuse (adjusted OR 6.28, 95% CI 1.70-23.30)	Rates of death were higher in persistent opioid users (17 % persistent users vs 4% non-persistent users)	12
Yau et al. , 2018	Aim: Evaluate relative use for opioids and benzodiazepines before, during, and after curative chemotherapy Design: Retrospective study using electronic medical record	Curative breast cancer Treated with 60% (n=90) lumpectomy followed by chemotherapy (n=56) N=137 (one male)	Any opioid prescription 90 days after treatment	LTOT was 45%	Concomitant opioid + benzodiazepine use 16% (p<0.001 compared to baseline use before diagnosis)	Less than 3% use long-acting opioids Opioid and benzodiazepine use increased during and after chemotherapy (p< 0.001)	11

LTOT= Long term opioid therapy, OME= oral morphine equivalence, SEER= Surveillance, Epidemiology, and End Results US Medicare Data, OR= odds ratios, RR= Relative Rates, CI= Confidence Interval, QS= Quality score

Table 3. Results of Quality Assessment Scores

	Full Quantitative Studies n=21
Explicit and soundness of literature review	21
Clear aims and objectives	21
Clear description of setting	11
Clear description of sample	21
Appropriate sampling procedure	21
Clear description of data collection	21
Clear description of data analysis	20
Provision of recruitment data	1
Provision of attrition data	1
Provision of psychometric properties (rigor of measurement of POU)	11
Appropriate statistical analysis	19
Findings reported for each outcome	19
Description of validity/reliability of results	19
Provision of Strengths and limitations of the study	20
Total Average	10.7 (range 8-14 ±1.38)

Table 4. Overview of Factors related to LTOT in Cancer Survivors

	Cancer Type							Cancer Treatment			Socioeconomic Factors					Pain etiology		Patient characteristics					Opioid Prescribing Characteristics			
	Variety of Cancers	Head and Neck	Breast	Colorectal	Lung	Cervical	Prostate	Surgery	Chemotherapy	Radiation treatment	Low Income	Tobacco Use	Unemployment	Urban	Zip code associated with lower education	CIPN	Pre-existing Pain	Age	White race	Comorbid conditions	Mental health diagnosis	Substance Use Disorder	Prior Opioid Use	Polypharmacy	High dose	Prescribed by non-cancer provider
Barbara et al., 2019	X	X	X	X	X		X							+						+	+		+			+
Cass et al., 2018	X		X		X	X	X		+								+			+	+	+		+		+
Cata et al., 2019		X						+	+								+						+			
Chen et al., 2019				X								+						+		+			+			
Desai et al., 2009			X															+			+				+	
Fredheim et al., 2019	X				X															+			+	+	+	
Henry et al., 2019		X															+	-		+	+	+			+	+
Kwon et al., 2013		X										-						-	-			+			-	
Lee et al., 2017	X		X	X	X				+	+								-					+			
McDermott et al., 2019		X						+		-	+	+	+					+				+	+		+	
Murphy et al, 2018	X												+					-		+	+			+		
Nelson et al. 2020					X		+	+	+	+					+			+		+			+			
Roberts et al., 2020			X					+	+		+	+							+	+						
Salz et al., 2019	X		X	X	X													-							+	
Saraswathula et al., 2019		X						+	-	+								-		+	+		+			
A.Shah et al, 2018				X					+							+								+		
R. Shah et al., 2019	X													+						+	+	+				
Sautradhar et al., 2017	X										+			-				+			+					
Vitzhum et. al, 2019	X	X	X	X		X			-	+	+	+	+					+	+	+	+	+	+			
Ward et. al, 2020						X		-	-	-			-					+			+	+	+			
Yau et al. 2018			X			+															+			+		

(+) associated with LTOT (–) measured but not associated with LTOT

Chapter III.

Proposed Title: "It is so easy for them to dismiss."

A Phenomenological Study of Cancer Survivors with Chronic Cancer-Related Pain

Proposed Authors:

Katie Fitzgerald Jones MSN, APN

Boston College, William F. Connell School of Nursing

Mei R. Fu, PhD, RN, FAAN

Rutgers University, School of Nursing–Camden

Lisa Wood Magee PhD, RN, FAAN

Boston College, William F. Connell School of Nursing

Jessica Merlin MD, PhD, MBA

University of Pittsburgh

Devon K. Check, PhD

Duke Cancer Institute

Melissa McTernan PhD

Boston College

Rachelle Bernacki MD

Dana Faber-Cancer Institute

Hailey Waddell Bulls PhD

University of Pittsburgh

This manuscript represents a significant contribution to the Dissertation Work.

The target journal is the *Journal of Palliative Medicine*, an interdisciplinary journal reporting on the clinical, education, legal, and ethical aspects of palliative care for patients with intractable pain, focused on improving quality of life. The Journal of Palliative Medicine has an impact factor 2.947. Submission of the manuscript is planned post-defense.

Cancer-related pain, often caused by cancer treatment, including surgery, radiation, chemotherapy, immunotherapy, and targeted therapies, poses a challenge for many cancer survivors (Paice, 2019b). Chronic cancer-related pain is pain that persists for ≥ 3 months and is an umbrella term for chronic pain secondary to cancer as opposed to chronic pain from non-cancer etiologies (Treede et al., 2019). The prevalence of chronic pain among cancer survivors is nearly double that of the general US population, with estimates of 35-40% or 5.39 million cancer survivors experiencing chronic pain (Jiang et al., 2019; Van den Beuken et al., 2016). Chronic cancer-related pain reduces quality of life and interferes with survivorship care, including adherence to and engagement in surveillance care (Chwistek et al., 2016; J. A. Paice, 2019a).

Examining chronic pain in cancer survivors can be challenging because there are several definitions of a cancer survivor. For this reason, we use the definition set forth by the Survivorship Taskforce of the European Organization for Research and Treatment of Cancer, which defines cancer survivors as people who have completed primary care treatment (except for maintenance therapy) and have no active disease (Bennett et al., 2019). Examining chronic cancer-related pain in cancer survivors, using a narrow definition and focusing on pain attributed to cancer treatment, is especially relevant now that many cancers' detection, treatment, and survival have dramatically improved (Miller et al., 2019).

Clinicians and cancer survivors are often surprised that cancer-related pain persists after curative cancer treatment and may struggle with devising management strategies (Chwistek et al., 2016). Historically, cancer survivors are referred to as being "lost in translation" because there is a lack of awareness and coordinated care of medical, functional, and psychological

consequences of cancer care (The Institute of Medicine, 2005). In many instances, the treatment of pain may follow the same approach as it did during cancer treatment (Nekhlyudov et al., 2018), but it remains unclear whether this is an appropriate approach for cancer survivors with longer prognoses, particularly concerning opioids therapy (Nekhlyudov et al., 2018) Yet, cancer survivors several months or years after curative treatment use opioids at a significantly higher rate than the general population (Barbera et al., 2019; Jones et al., 2021; Salz et al., 2019).

The higher rates of opioid prescribing in cancer survivors likely reflect that cancer-related pain is treated differently than non-cancer pain. For better or worse, cancer-related pain is exempt from guidelines that often favor an opioid-sparing approach, such as the Center for Disease Control Guidelines for Prescribing Opioids for Chronic Pain and state-based laws limiting opioid prescriptions (Bulls et al., 2021; Dowell et al., 2016). The divergent treatment approach leaves cancer survivors in limbo between treatment paradigms. It remains unclear whether cancer-related pain management approaches are entirely different or akin to people with active disease or non-cancer-related pain or whether cancer survivors require a hybrid of both (Meghani & Vapiwala, 2018).

Little is known about the pain experience in cancer survivors. The few available qualitative studies do not reflect the current reality of prolonged survival with newer agents. For example, immunotherapy has revolutionized the treatment of several cancers but can be associated with painful sequelae, such as rheumatologic toxicities (Creţu et al., 2021; Laroche et al., 2017). Nor does existing literature reflect the cancer survivors' perspective on the current tension of opioid use and guidelines prioritizing opioid-sparing approaches (Goodlev et al., 2019). Also, existing studies often focus on a single pain syndrome, such as post-mastectomy

pain or chemotherapy-induced peripheral neuropathy (Armoogum et al., 2020) which fails to capture the collective burden of co-occurring pain syndromes affecting multiple body locations (Bao et al., 2018). To address this evidence gap, the purpose of this study was to gain a deeper understanding of the daily lived experience of cancer survivors with chronic cancer-related pain, independent of cancer type.

Method

Study Design

Husserl's descriptive phenomenology, qualitative method was used for bracketing, gathering, and analyzing data (Husserl, 1931; Porter, 1998).

Sampling and Participants

Consistent with acceptable guidelines for descriptive phenomenology, purposive convenience sampling was used (Porter, 1998), intentionally selecting people with a variety of pain intensities to capture diverse experiences and the universality of living with chronic cancer-related pain. Sampling continued until data saturation was achieved, which in phenomenological studies can range from a minimum sample size of six to fifteen. (Morse & Field, 1996; Sandelowski, 2000)

Potential participants were identified from an adult survivorship program at a high-volume cancer center in the Northeast United States. Recruitment letters were sent to participants following an electronic medical review done by the principal investigator (KFJ) using eligibility criteria. Patients were eligible if they were 1) solid tumor cancer survivor ≥ 18 years old at the time of enrollment and during cancer treatment, 2) free of active disease, 3) self-reported chronic

cancer-related pain that is a result of cancer diagnosis and treatment, 4) ≥ 3-months from last active cancer treatment (chemotherapy, radiation, or surgery), 5) able to provide informed consent and read and comprehend 5th grade English, and 6) participate in an online interview using Zoom. Participants with chronic pain before cancer diagnosis or pain unrelated to cancer were excluded. Potential subjects were provided a telephone number to call or text if they were not interested in participating in the study. For those who did not opt-out, the first author (KFJ) contacted potential participants to assess interest in participation and confirm eligibility. The study was advertised on patient-facing platforms (survivorship website and exam rooms), and participants could be referred directly by clinicians.

Study Procedure and Data Collection

The research team developed and pilot tested an interview guide using a descriptive phenomenological method to answer three overarching research questions: 1) What is the lived experience of chronic cancer-related pain in cancer survivors? 2) How do cancer survivors manage chronic cancer-related pain in their daily lives? 3) How does the experience of chronic cancer-related pain shape cancer survivors' everyday life and pain management choices? The interviews were conducted by (KFJ) after training and with supervision from a qualitative expert (MRF). The interviews lasted approximately sixty minutes from November 2021 to March 2022 over zoom in a single study visit. The interview guide is located in the appendix B. The interviews were recorded and professionally transcribed; participants received a $60 gift card. The Institutional review board approved the study and procedures.

Before the interview, participants completed an informed consent using the browser-based research electronic data capture (REDCap) platform. Following consent, a REDCap secure link was sent to each participant to collect demographic information about age, marital status, gender, education, employment status, residence, and income. Participants self-reported primary cancer type, cancer treatment (i.e, surgery, radiation, chemotherapy, hormone or immunotherapy), length of time since treatment, and details about pain diagnosis, pain medication (including opioid use), supplements, and management strategies.

To better describe the phenotype of our sample in terms of the pain experience, the Brief Pain Inventory (BPI) was collected. The BPI is an 11 item self-administered questionnaire on a 0 (no pain) to 10 (worst pain imaginable) measuring the degree to which pain interferes with general activity, mood, walking ability, normal work, mood, relations with other people, sleep, and enjoyment of life (Atkinson et al., 2010). Additionally, each participant completed the Collaborative Health Outcomes Information Registry (CHOIR) body map, an electronic, visual representation of a body enabling participants to select the areas where they are experiencing pain (Scherrer et al., 2021).

Data Analysis

To ensure the credibility of data analysis, we used a modified iterative seven-step descriptive data analysis method to examine data, compare codes, challenge interpretations, and inductively develop themes (Dory et al., 2017; Fu, 2005; Fu & Rosedale, 2009; Fu et al., 2008). The data analysis steps are outlined in Figure 1.

Rigor and Trustworthiness

Credibility, transferability, dependability, and confirmability were the criteria for assessing trustworthiness (Lincoln & Guba, 1985). The use of reflective journals, field notes, and verbatim transcriptions confirmed credibility, which was further ensured by listening to the recording of each interview while checking against the transcripts to guarantee accuracy. Detailed descriptions from participants supported transferability. The emergence of similar data from different participants in this study demonstrated strong evidence of dependability. Interrater reliability established during data analysis provided evidence for confirmability of the study. Finally, the researchers discussed the analysis and reached a consensus regarding the results.

Results

Thirteen cancer survivors were enrolled and participated in qualitative interviews. The sample size was determined by data saturation by the principal investigator (KFJ) and qualitative expert (MRF). Data saturation occurred at 11 participants, and two additional participants were interviewed to ensure no new information or themes emerged.

Table 1 outlines participant demographics. Participants had a mean age of 58.8 (*SD*= 7.1) years and a variety of primary cancer types and treatments, including breast (n=6), head and neck (n=5), and lung (n= 2); one participant had both lung and breast cancer, sarcoma (n=1). The time since treatment ranged from 6 months to > 10 years, with 53.8% being more than three years post-treatment.

Table 2 summarizes individual participants' clinical characteristics, including prior cancer treatments, pain diagnosis, pain scores, and a body map depicting pain locations. Participants had a variety of co-occurring cancer pain diagnoses (chemotherapy-induced peripheral neuropathy n=5, post-surgical pain n=7, pain related to radiation treatment n=6, bone

pain n=2, lymphedema n=4, and other cancer-related pain diagnoses n=6). All participants had > 3 locations of pain.

Several themes emerged to describe cancer survivors' perceptions of living with and managing chronic cancer-related pain. The three essential themes epitomized the experience of living with chronic cancer-related pain: invisible suffering at the cost of survival, an opioid paradox, and a need to try everything.

Invisible suffering as the cost of survival

Participants described chronic cancer-related pain as an unanticipated tradeoff for being alive; it is a "very complicated thing to be grateful and also to acknowledge that you have this pain and it's frustrating, and it is a result of saving your life" (Participant 6). For some, survival was a second chance at living; citing gratitude helps buffer the hardships of adjusting to chronic cancer-related pain.

Participants expected that they should be grateful and maintain an optimistic attitude in survivorship. When they did not, many were critical of themselves and frustrated by the toll of chronic cancer-related pain. "I'm grateful... I'm blessed that I was able to fight it, and I should be happy… should be dancing on air, but it's just not like that, and pain is one of the things added to the mix" (Participant 4).

Participants reported that chronic cancer-related pain differed from pain in active treatment because it brought a new type of suffering that was invisible to friends, family, and clinicians. Living with chronic cancer-related pain impacted how participants saw themselves, "sometimes you feel a little lesser than everybody else...cause they're not walking around in pain

and I am…No one, no one really understands.... Other people don't know … they don't understand how bad it is and that hurts" (Participant 3).

Participants described an assumption on the part of clinicians, family, and friends that they should be back to their pre-cancer selves but living with pain after cancer prevents them from ever fully returning to the way things were before. ″ The interesting thing about living with chronic pain, especially pain that you have gotten after cancer is that people think, well you're okay now …I think when you have pain after cancer, it's like the body says, Hey PS, we got sick. We pulled you through, but don't forget it" (Participant 8).

Several participants described less clinical attention once there was no identifiable source of pain or when there were no answers. "You go to the doctor's office, and they're like, how bad is the pain? Oh, it's, it's mild, but it's constantly there… it's so easy for them to dismiss something that's consuming of your life" (Participant 1).

An Opioid Paradox

Six of the thirteen participants remained on opioids for their chronic cancer-related pain. The paradox of opioids created a strain on relationships with clinicians, whether a participant was taking opioids or not.

For cancer survivors on opioids, they perceived the clinician's urgency to stop opioids after cessation of cancer treatment because of concerns of long-term risks. This priority was often a mismatch with the goals and values of cancer survivors "that you can't deny the moment in terms of what you need to do. There is quality of life immediately versus risks… So it's like you're balancing these different things in terms of what makes sense now" (Participant 5).

Opioids, for many, were a roadblock to meaningful person-centered communication. "I think the biggest concern of the doctors is my opioids. And I understand that, but I'm tired of being a guinea pig…I feel like I found something that works for me. So why change it? …if it's not broken, don't fix it. I have something to help me manage it now" (Participant 4). For others, remaining on opioids triggered stigma among interdisciplinary team members and within themselves. "I remember I came home crying one day because one of the pharmacists commented out loud about me being on pain meds... And I was ashamed. I was ashamed that I had to rely on [opioid] pain meds" (Participant 10).

Seven participants favored avoiding opioids which generated a clinician's assumption that this meant their pain was minimal and did not warrant treatment. Cancer survivors felt dismissed by clinicians who treated opioids as a proxy for pain severity, "they assume because you're not taking anything that it must not be so bad... But I'm not taking anything because I don't want to live on [opioid medication] and it is bad" (Participant 1).

Even among cancer survivors themselves, opioids represented pain severity. If they chose not to use opioids, they had to "live with it" (Participant 9) or use an alternative word to pain "I always use the word misery. I don't use the word pain. And the reason why is when I think of pain, I think of an opioid" (Participant 3).

A willingness to try anything

Despite having diverse pain experiences, participants believed clinicians "don't have answers. It's all very vague…We're busy researching what keeps people alive. We don't give this enough attention…and maybe it's not a matter of life and death, but if I had the information, it would help me figure out what I need to do and how to cope with it" (Participant 1). Participants

also described it would have been helpful to know chronic cancer-related pain could last the rest of their lives, and they could have developed a self-management plan sooner. "They told me it would be painful for a little while…And when I was into this several years in, I told my oncologist that the pain was still going. She says you might have it permanently. And I said, why didn't you tell me that in the beginning?" (Participant 9).

Participants described that oncology-based clinicians were ill-prepared to manage chronic cancer-related pain and frequently sent participants to other specialists hoping for a solution. "I was almost like racing to see what they could do to make this stop…like everybody keeps wanting to send me different places …it's really, really hard to go to all the appointments to begin with and then to go and feel like you have some hope and then the rug is pulled out and that's happened a couple of times" (Participant 7).

In light of the lack of clinician support, participants reported that managing chronic pain in survivorship required troubleshooting and a willingness to try many approaches, some evidence-based and some not. Many participants reported being surprised there were effective treatments, but cost, insurance, availability, and pilot program duration were common issues. Indeed, often non-pharmacologic treatment was preferred "I've been on all different kinds [of treatment], but I'll tell you the best thing…I would take that [acupuncture] in a heartbeat, over [opioid] pain meds, over anything. It is amazing how that works, but it's so expensive. And your insurance company won't pay for it." (Participant 10).

Additionally, participants reported a combination of treatments was necessary to manage co-occurring cancer-related pain syndromes and pain in multiple body locations. Many felt that chronic-pain management involves "exploring all the avenues…it needs to be a 360 approach

and be open to trying anything. but you have to do a lot of the work on your own" (Participant 8). Participants described the importance of the need for advocacy in developing their treatment plan. "You need to be more assertive and not allow providers to dismiss it. Don't shut up and live with it." (Participant 1). Participants described unnecessary and prolonged pain if they did not speak up and advocate for a treatment plan aligned with their pain and functional impairments. ″I don't think I said very much. I just assumed I had to live with. but later on finding out that there were other options, like a good physical therapist. I could have lived much better sooner." (participant 13).

Discussion

The findings of this study of cancer survivors provide insights into the lived experience of chronic cancer-related pain in cancer survivors. They suggest an opportunity for pain self-management, education, and psychosocial interventions to optimize pain. The study also highlights several areas where cancer care falls short in managing chronic cancer-related pain. Participants described communication challenges with clinicians, particularly surrounding opioids and ignoring the suffering associated with chronic cancer-related pain. Participants also described the importance of developing an individualized multimodal pain treatment using an approach centered on advocacy and trying many recommended and alternative treatments.

Participants desired clinician acknowledgment and advisement concerning chronic cancer-related pain management. Participants at different times wanted clinicians to offer problem-focused strategies (i.e. referral to physical therapy) and emotionally focused strategies (i.e. recognizing pain and avoiding assumptions). Failure to offer emotional support or solutions compounded the suffering of those living with cancer-related pain. This similar finding is

observed in people with non-cancer pain who describe chronic pain as a "hidden" condition (Dassieu et al., 2021). Many of our participants noted putting their life on hold because they did not know how long pain would last and if it would improve. For some participants, focusing too much on identifying a clear trajectory of the pain appeared to stall the development of a comprehensive biopsychosocial treatment plan that could improve function and provide relief earlier in survivorship. In the chronic non-cancer pain literature, when psychosocial factors of chronic pain are ignored, including pain-related suffering, opioid discontinuation can be challenging, and the success of opioids themselves is undermined (Darnall, 2019).

A challenge to integrating treatment for pain into psychosocial oncology interventions is that most physicians, nurse practitioners, and mental health clinicians report having little education or training about chronic pain and express low confidence in treating chronic pain (Darnall et al., 2018; Darnall et al., 2016; Merlin et al., 2012). Many of the participants felt that their cancer team did not have answers to help them manage their pain. Although cancer centers are often comprehensive, our findings mimic others that chronic pain care, especially psychosocial-based treatments, are not well integrated into cancer pain treatment, particularly post-treatment (Azizoddin et al., 2021).

While our study recruited participants from a prominent survivorship program, for many cancer survivors, care is shared among primary care, oncology, survivorship, and palliative care clinicians. In our prior work, we have demonstrated that clinicians feel uncomfortable about who should manage chronic cancer-related pain, and participants in this sample described being sent to a host of specialists, some more helpful than others (Check et al. 2022). The lack of a "medical home" for people with chronic cancer-related pain is problematic. The study findings point to the

importance of a service or discipline that can lead the charge of providing comprehensive, high-quality multimodal pain treatment, including opioid care and pain education. However, operationalizing chronic cancer-related pain care is fraught because people with cancer are seen as a "different population," and clinicians describe insufficient knowledge to manage chronic pain in cancer survivors (Burke et al., 2017; Schenker et al., 2021a). Recent work within the Veterans Health Organization and other prominent pain centers provides a blueprint for interdisciplinary virtual pain cancer for unique populations using telehealth. These interdisciplinary models facilitate collaboration, access, tailoring of non-pharmacologic treatments, and individualized medication management with promising results in patient satisfaction (Edmond et al., 2022; Tauben et al., 2020). Such innovation is sorely needed for cancer survivors, who currently are navigating treatment alone with a piecemeal approach that relies heavily on self-advocacy and resources.

The transition from acute to chronic cancer-related pain was difficult for participants. In some ways, their experience resembles non-cancer pain. For example, many were surprise that pain did not resolve once the cancer was treated. Similar to people living with non-cancer pain, this led some participants to continue searching for answers and rely on effective strategies used during treatment, like opioids (Darnall, 2019). When opioids were not used as treatment strategies, participants noted that clinicians did not have more to offer and relied on the philosophy of 'trying everything'. The current emphasis on opioids in cancer care appears to have negative consequences for our participants, including impaired communication on the risks and benefits and collaboratively working to craft an individual treatment plan. For people who did not use opioids, opioids were often offered, and if they did not wish to use opioids, frequently

their clinicians minimized their pain and did not offer alternative chronic pain treatment modalities.

Our findings underscore a greater need to attend to psychosocial aspects of pain unique to the cancer survivors experience of chronic cancer-related pain. The role of gratitude and positive psychology was an important feature of the experience of living with chronic cancer-related pain. Many of our participants viewed chronic cancer-related pain as a tradeoff to being alive, leveraging optimism to cope with chronic cancer-related pain. In women with breast cancer, a gratitude journal positively impacted daily psychological functioning, perceived support, and adaptive coping strategies (Sztachańska et al., 2019). For other participants, there was a different reaction, e.g., a sense they "should be grateful," creating cognitive dissonance and leading them to push aside recognition that cancer related-pain has immeasurably changed their life. Acceptance and commitment therapy (ACT) can be an alternative psychosocial intervention. ACT can target thinking patterns moving away from reducing negative thoughts and instead toward value-oriented actions and behaviors (Driscoll1 et al., 2021). It has the potential to improve cancer and pain-related distress for people who feel victimized by cancer, but its use has been limited to stress, anxiety, fatigue, and depression (Driscoll et al., 2021; Li et al., 2021). Expanding access and options for psychosocial-based interventions that target disordered thinking and positive psychology can improve chronic cancer-related pain in cancer survivors and perhaps decrease the use of opioids (Darnall et al., 2018).

An unexpected finding of our study was all participants experienced multisite pain. Multisite pain, defined as pain in more than one part of the body, is increasingly accepted as a chronic pain phenotype associated with worse pain severity and function, leading to greater

opioid use. (Coggon et al., 2013). Chronic multisite pain is associated with psychosocial stressors, including adverse life experiences and falls, common conditions in cancer survivors (Generaal et al., 2016; Wechsler & Wood, 2021). Multisite pain is an important area for further research in cancer survivors with cancer-related pain. Better recognition of multisite pain can improve pain self-efficacy and self-management practices (Kawi, Duke, & Maduka, 2020).

Limitations

The goal of qualitative research is not generalizability but a deep understanding of a phenomenon (Morse & Field, 1996; Sandelowski, 2000). Consistent with the objective of the descriptive phenomenological approach, we were able to capture a deeper understanding of the lived experience of chronic cancer-related pain in cancer survivors. Notably, most participants in the study were White, middle-class, female breast cancer survivors. Further examination with a more diverse sample would help ascertain whether there are divergent or consistent findings. The findings of this study were also based on a single cancer center. Cancer survivors receiving care at different cancer centers may have a different perception and management of chronic cancer-related pain influenced by the availability of pain treatments or organizational culture.

Conclusion

Pain management is a consistently reported unmet need in cancer survivors beyond active cancer treatment (Chwistek et al., 2016; Jiang et al., 2019). Our study provides insight on perceptions and management strategies used by a diverse group of cancer survivors with chronic cancer-related pain. The findings describe how a lack of recognition of pain, opioid stigma, and opioid-sparing approaches compromise therapeutic relationships with cancer survivors and their

clinicians. Research, policy, and clinical practice should prioritize access to multimodal pain treatments, improve high-quality communication, and expand clinicians' knowledge and skills to manage chronic pain. Increasing pain education to survivors with chronic cancer-related pain can potentially improve the development of an individualized treatment plan.

Appendix B

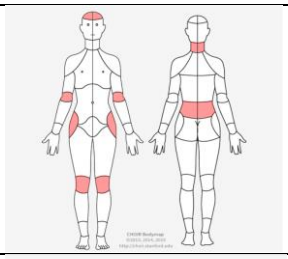
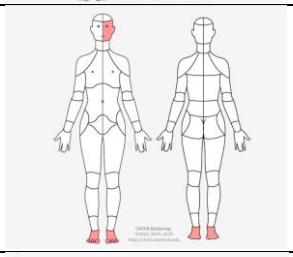
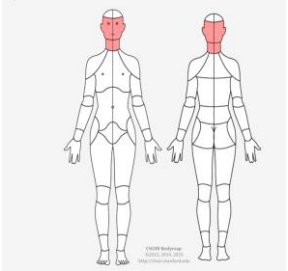
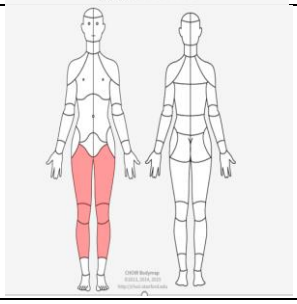
Table 1: Participant Demographics

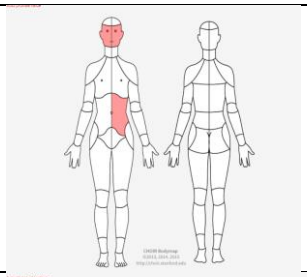
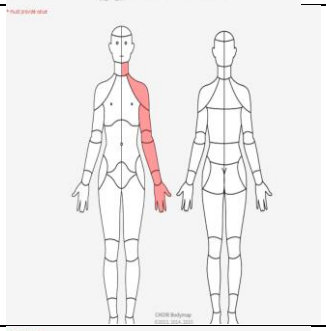
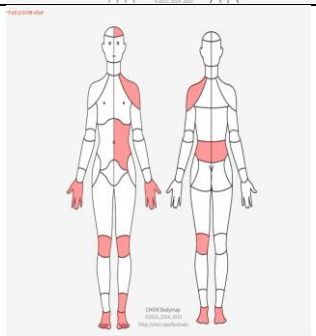
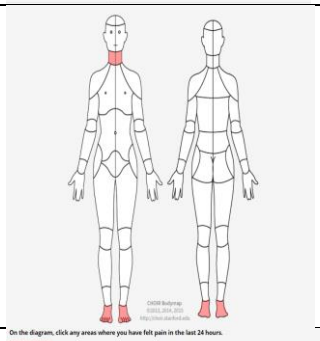
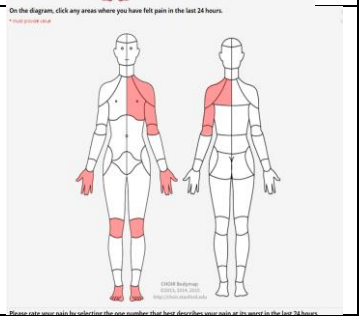
N=13

	N (%)
Age (Mean, SD)	58.8±7.1
Gender Self-report	
Man	2 (15.4%)
Women	11 (84.6%)
Education	
HS or Partial College or Associates Degree	4 (30.7%)
Bachelor's Degree	4(30.7%)
Graduate Degree	5 (38.5%)
Financial Status	
Comfortable	5 (38.5%)
Have enough to make ends meet	7 (53.8%)
Do not have enough	1 (7.7%)
Partnered Status	
Single	1 (7.7%)
Married	8 (61.2%)
Divorced	4 (30
Employment	
Employed	6 (46.1%)
Unemployed	1 (7.7%)
Retired	2 (15.4%)
Sick Leave	3 (23.1%)
Volunteer	1 (7.7%)
Cancer Type	
Breast*	6 (46.1%)
Head and Neck	5 (38.5%)
Lung*	2 (15.4%)
Sarcoma	1 (7.7%)
Time since treatment	
3 months-1 year	3 (23.1%)
Between 1-3 years	3 (23.1%)
Between 3- 6 years	2 (15.4%)
Between 7-10 years	4 (30.7%)
More than 11 years	1 (7.7%)
Pain Interference (Mean, SD)	4.3±1.6
Pain Severity (Mean, SD)	4.4 ±1.6
Number of Sites of Pain (Mean, SD)	11.5 ±6.3 (3-24)

*one participant had a history of breast and lung cancer

Table 2. Individual Participant Characteristics

Participant Number	Age	Gender	Disease Site	Treatment	Time since treatment	Pain at its worse in	Pain Diagnosis	Body Map
1	52	F	breast	Surgery Radiation Hormone treatment	1 year	6	Generalized bone pain from cancer treatment Post-surgical pain	
2	63	M	Head and Neck	Surgery Radiation Chemotherapy	1-3 years	3	CIPN Post-Surgical Generalized bone pain from cancer treatment Pain-related to radiation	
3	58	M	Head and Neck	Surgery Radiation Chemotherapy	3-6 years	6	Post-surgical Pain-related to radiation	
4	60	F	Lung	Chemotherapy Immunotherapy	1 year	7	Bone pain from cancer treatment	

5	73	F	Head and Neck	Surgery Immunotherapy	1 year	4	Post-surgical Generalized bone pain from cancer treatment Lymphedema	
6	61	F	Sarcoma	Surgery Radiation	>11 years	7	Post-surgical Lymphedema	
7	69	F	Breast	Surgery Chemotherapy	7-10 years	8	CIPN Post-Surgical Lymphedema	
8	48	F	Head and Neck	Radiation Chemotherapy Immunotherapy	1-3 years	4	CIPN Pain-related to radiation	
9	63	F	Breast	Surgery Hormonal treatment	7-10 years	5	Post-surgical Generalized pain	

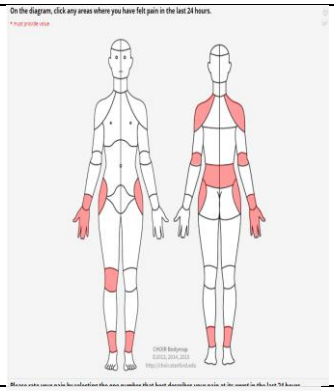
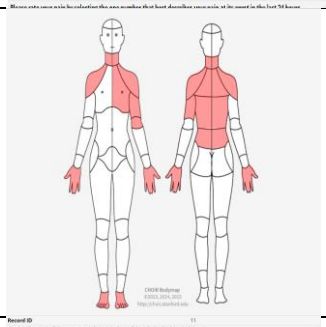
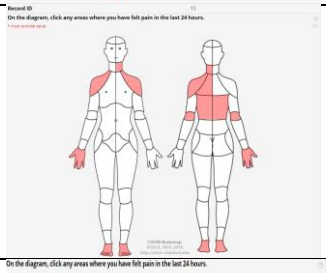
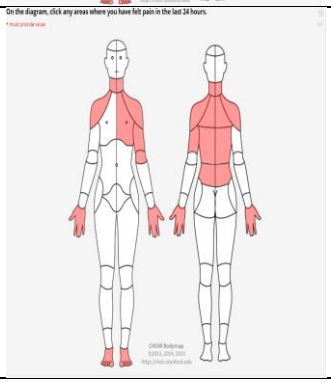
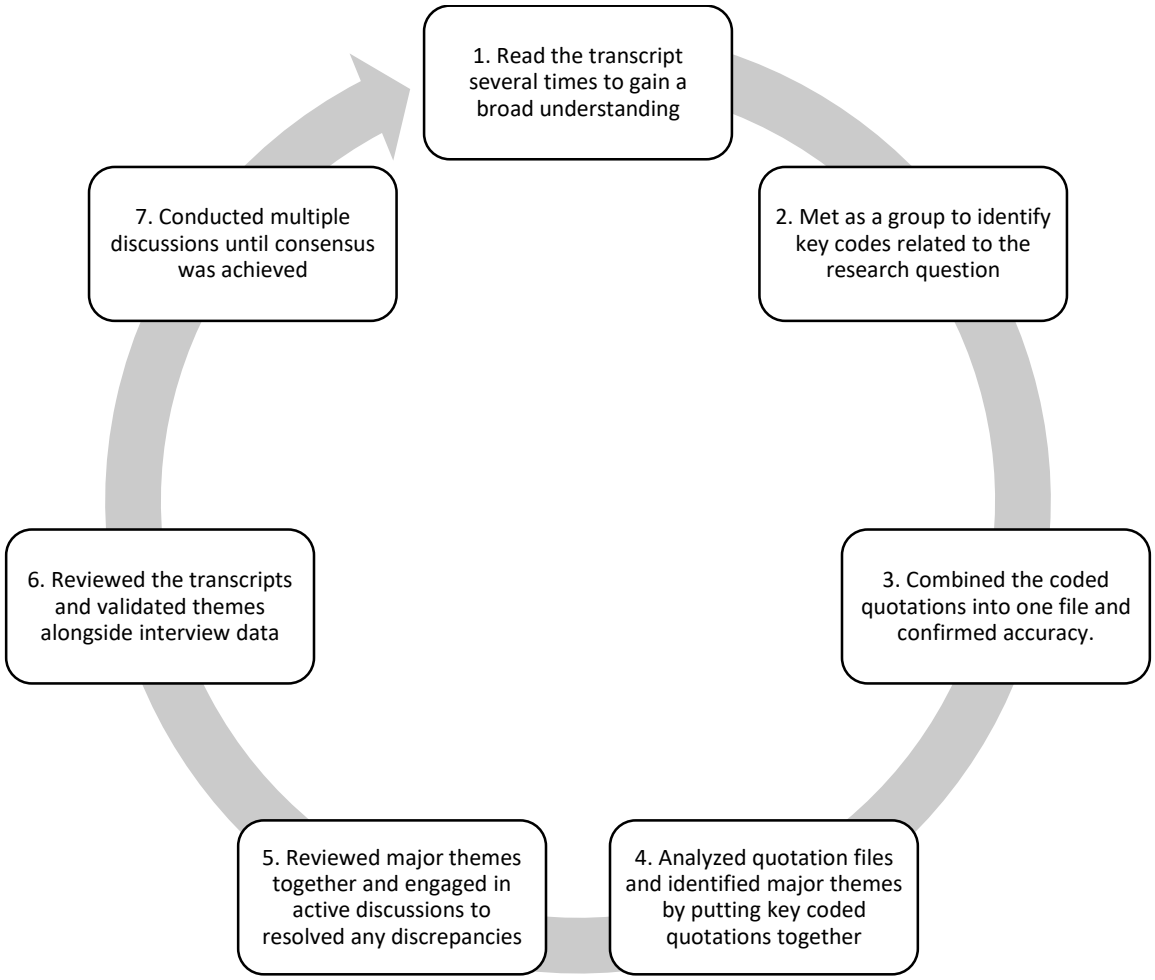
10	51	F	Breast and Lung	Surgery Radiation Hormonal treatment	3-6 years	7	Bone pain from cancer treatments DeQuervain tenosynovitis	
11	55	F	Breast	Surgery Radiation Chemotherapy	7-10 years	7	Surgery Radiation Chemotherapy	
12	58	F	Head and Neck	Surgery Radiation Chemotherapy	7-10 years	6	CIPN Post-surgical Pain related to radiation	
13	55	F	Breast and Lung	Surgery Radiation Chemotherapy	7-10 years	10	CIPN Post-surgery Pain related to radiation Lymphedema	

Figure 1: Seven-Step Method for Data Analysis



Adapted from Fu &Rosedale, 2009

Interview Guide

3 overarching research questions:

1. *What is the lived experience of chronic cancer-related pain in cancer survivors?*
2. *How do cancer survivors manage pain in their daily lives?*
3. *How does the experience of chronic cancer-related pain shape cancer survivors' everyday life and pain management choices?*

1. Please tell me what it was like for you when you were diagnosed with cancer.

   Probes:

   a. When and how were you diagnosed with cancer?

2. Please describe to me your experience of having pain related to cancer and cancer treatment or as we call cancer-related pain.

   Probes:

   a. When did you start to experience pain related to cancer or cancer treatment?
   b. How has your experience of pain changed over time since you completed your cancer treatment?

3. Before your cancer treatment, did anybody tell you about the possibility of having chronic cancer pain?
4. What has it been like for you to experience chronic cancer-related pain.

   Probes:

   a. What is hard for you in your everyday to due to your chronic cancer-related pain and cancer experience?

5. Tell me how your life has changed since you have had chronic cancer-related pain?
   a. How have things changed with regard to your typical day?
   b. How have things changed for you with regard to your family and friends?
   c. How have things changed with regard to your work outside the home (if this applies)?
   d. How have things changed with regard to your favorite leisure activities?
   e. How have things changed with regard to your social activities?
6. As a person who has chronic cancer-related pain, please tell me what do you do to manage your chronic cancer pain?

   Probes for the questions:

   a. What types of things do you do to manage your pain? Medications, coping strategies, non-pharmacologic treatments.
   b. How much do these things help you manage your pain?
   c. I am interested in knowing how you select your pain management choices?
   d. What motivates you to manage your pain?
7. How much do you think about your pain
   a. Please tell me about your thoughts when you experience pain or what you think courses the pain. For example, people worry about pain because they see pain as the sign of cancer recurrence or other reasons.
   b. How do you deal with these feelings?

c. Please describe for me any changes that you have to make for your plans for future because of your experience of chronic cancer pain.

8. What advice would you give to other cancer survivors who experience chronic cancer pain?

Chapter IV

The Contribution of Cancer-Specific Psychosocial Factors to the Chronic Cancer-Related Pain Experience in Cancer Survivors

Proposed authors:

Katie Fitzgerald Jones

Boston College MSN, APN

William F. Connell School of Nursing

Lisa Wood Magee PhD, RN, FAAN

William F. Connell School of Nursing

Mei R. Fu PhD, RN, FAAN

Rutgers University School of Nursing-Camden

Rachelle Bernacki MD

Dana Faber-Cancer Institute

Hailey Bulls, PhD

University of Pittsburgh School of Medicine

Jessica Merlin MD, PhD, MBA

University of Pittsburg School of Medicine

Melissa McTernan PhD

Boston College Academic Research Services

This manuscript represents a significant contribution to the dissertation work. The manuscript will be submitted after the dissertation defense.

The target journal is the *Oncology Nursing Forum*, Impact Factor 1.728. The *Oncology Nurse Forum* is the Oncology Nursing Society's official and internationally respected journal serving oncology nurses. *The Oncology Nurse Forum* publishes peer-reviewed findings from oncology nursing research and the translation of research evidence to practice

Chronic pain is one of the most common long-term effects experienced by the growing population of cancer survivors (Paice, 2019b). Chronic cancer-related pain is defined as pain resulting from cancer or its treatments lasting beyond the expected course of healing or greater than three months after the completion of therapy (Treede et al., 2019). Chronic cancer-related pain syndromes include chemotherapy-induced peripheral neuropathy, bony complications of corticosteroids, lymphedema, post-surgical or radiation pain, and arthralgias from hormonal treatment (Paice et al., 2016). Chronic pain occurs in 20 to 50% of cancer survivors (Gallaway et al., 2020; Van den Beuken et al., 2016). Severe pain interfering with major activities is twice as common in cancer survivors than in the general population (Jiang et al., 2019). Chronic-cancer pain leads to numerous physical, emotional, and financial burdens (Paice, 2020).

Cancer survivors are individuals who have completed primary cancer treatment and have no active disease (Bennett et al., 2019). There is awareness of the magnitude and consequences of chronic cancer-related pain. Yet, the contribute of unique cancer-specific psychosocial factors to the chronic cancer-related pain experience has not been investigated in cancer survivors. Understanding the contributions of psychosocial factors to chronic cancer-related pain is an essential prerequisite to managing the multidimensional experience of chronic pain (Miaskowski et al., 2019). The combination of biopsychosocial factors across physical, psychological, social, emotional, and spiritual domains often results in a "total pain" experience specific to each person, circumstance, and illness (Mehta & Chan, 2008).

Indeed, coping in the aftermath of cancer poses distinctive challenges (Chaturvedi, 2012). Fear of cancer recurrence (FCR) is one of cancer survivors' most commonly reported problems.

FCR may be particularly distressing when living with chronic cancer-related pain since worsening or new pain can signify cancer recurrence (Chwistek et al., 2016). Cancer distress occurs in 3 out of 4 cancer survivors and is associated with impaired coping with cancer-related symptoms (Baker et al., 2016). Cancer-related trauma may also play a role in chronic cancer-related pain. For example, in head and neck cancer survivors, a population with high rates of chronic pain, many report post-traumatic stress, and 11.8% meet the criteria for post-traumatic stress disorder (Moschopoulou et al., 2018). Previous literature has demonstrated that trauma, chronic pain, and opioid use are highly comorbid (Baria et al., 2018). Our recent work demonstrates that opioid use in cancer survivors is much approximately five times higher than in the general population (Jones et al., 2021). Attention to psychosocial factors is an essential area of research because cancer-specific biological factors (disease type, tumor stage, and treatment) often fail to account for differences in pain or opioid use in cancer survivors (Lee et al., 2017; Paice, 2011; Roberts et al., 2020).

Pain catastrophizing and multisite pain can influence chronic pain in the general population but are rarely the focus of an investigation of chronic cancer-related pain in cancer survivors. Pain catastrophizing is characterized as a tendency to ruminate about pain increasing distress, pain severity, and debility (Goodlev et al., 2019; Paice et al., 2016). In people with diverse cancer stages and types, pain catastrophizing was uniquely associated with pain, opioid use, and acute care utilization (Azizoddin et al., 2022). Likewise, multisite pain can influence daily function and social activities. Multisite pain or pain to in more than one anatomical location has a more significant impact than single-site pain (Butera et al., 2019). The role of multisite pain has not been extensively investigated in cancer survivors. One study reported that among breast

cancer survivors living with chronic pain, 47% experienced two types of pain, and 23% had more than three types of pain (Bao et al., 2018). Historically, research on chronic cancer-related pain focuses on a single pain syndrome rather than the collective burden of pain and co-occurrence of chronic cancer-related pain syndromes (Armoogum et al., 2020; Bao et al., 2018; Paice et al., 2017).

This study aimed to assess the association between unique cancer-specific psychosocial factors and pain interference and severity in cancer survivors. Our conceptual model is depicted in Figure 1. We hypothesized that fear of cancer recurrence, cancer distress, and/or cancer-related trauma would significantly contribute to the pain experience in cancer survivors. We recruited cancer subpopulations with high rates of chronic pain, including breast, lung, and head and neck cancer (Berger et al., 2020; Nelson et al., ; Paice, 2019b) and excluded cancer survivors with pre-existing chronic pain or pain unrelated to cancer. The study was guided by the biopsychosocial model (BPS) of pain, a widely accepted model previously used in cancer that recognizes the complex interaction of biologic, psychological, and social factors that modulate a person's experience of pain (Gatchel et al., 2007; Novy & Aigner, 2014).

Method

The data collected during this study was part of a more extensive multimethod study that examined chronic cancer-related pain in cancer survivors. The qualitative results are discussed elsewhere; here, we report on the quantitative cross-sectional data collected between November 2021 and July 2022. Participants were recruited from a high-volume cancer center and adult cancer survivorship program using recruitment letters, clinician referrals, and advertisements on patient-facing platforms. Participants were eligible for inclusion if they were: 1) solid tumor

cancer survivors, 2) ≥ 18 years old with no active disease or signs of recurrence, 3) experience pain related to cancer diagnosis and treatment, 4) ≥ three months from the last active cancer treatment (chemotherapy, radiation, or surgery; hormone therapy for chemoprevention was acceptable), and 5) able to read and comprehend 5th grade English.

Participants received a $20 gift card after completing informed consent and study measure electronically using the browser-based research electronic data capture (Redcap) platform on their devices. Institutional review boards approved the study.

Measures

Demographic and Clinical Data

A standard demographic survey was collected to describe our sample, including age, marital status, gender, education, employment status, residence, and income. Cancer and pain treatment details were collected via self-report, including time since treatment, primary cancer type, treatment types, details about pain diagnosis, pain medication including opioids, supplements, and management strategies.

Pain Interference and Pain Severity

The pain experience was captured using the Brief Pain Inventory pain interference (BPI-PI primary outcome) and pain severity (secondary outcome) scales. The Brief Pain Inventory meets the standards of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) and has been validated measures in cancer survivors (Abahussin et al., 2019; Dworkin et al., 2005; Turk et al., 2003). Pain interference is the average score of 11 items from the Brief Pain Inventory pain interference (BPI-PI) scale. The BPI-PI captures the degree to

which pain interferes with general activity, mood, walking ability, normal work, mood, relations with other people, sleep, and enjoyment of life, where 0 refers to "does not interfere" and 10 indicates "interferes completely (Atkinson et al., 2010). In our sample, BPI-PI demonstrated good internal consistency (α=0.85, ω=0.95). Pain severity was measured using a previously validated single question of the Brief Pain Inventory Severity (BPI-S), asking participants to rate their average pain over the past seven days on 11-point numeric scale ranging from 0 (no pain) to 10 (worst possible pain) (Abahussin et al., 2019).

Fear of Cancer Recurrence

Fear of Cancer Recurrence is the sum of the seven-question scale (FCR7) previously validated in cancer survivors (Simard et al., 2013; Yang et al., 2019). The FCR7 includes seven items, such as, "I am afraid that my cancer will recur" and "I get waves of strong feelings about cancer coming back". Participants rate each concern on a scale of 0 (no at all) to 4 (very seriously). In our sample, FCR demonstrated good internal consistency (α=0.85, ω=0.95).

Cancer Distress

Cancer distress was assessed using the CancerSupportSource (CSS), an evidence-based psychosocial distress screening tool endorsed by the National Comprehensive Network (Buzaglo et al., 2020). Respondents rate their level of concern from 0 (not at all) to 4 (very seriously) for 25 items in five domains: 1) emotional well-being, 2) symptom burden and impact, 3) body image and healthy lifestyle, 4) healthcare team communication, and 5) relationships and intimacy. A sum of the 25 items derives a single cancer distress score. In our sample, CSS demonstrated good internal consistency (α=0.92, ω=0.94).

Cancer Trauma

Cancer Trauma was measured using the Impact of Events Scale-Revised (IES-R), a widely used measure of event-specific distress (Salsman et al., 2015). The IES-R score is the sum of 15 items that assess the frequency of intrusive and avoidant cognitions associated with a specific stressor (Salsman et al., 2015). Subjects respond using a four-point scale, ranging from 0 (not at all) to 4 (often), depending on how often they experienced specific symptoms during the past week. In our sample, IES demonstrated good internal consistency (α=0.93, ω=0.95).

Pain Catastrophizing

Pain catastrophizing was ascertained using the Pain Catastrophizing Scale (PCS), the sum of 13 items indicating the degree they experience thoughts and feelings that occur during pain episodes on a 5-point scale with 0 (not at all) to 4 (all the time). In our sample, the PCS demonstrates good internal consistency (α=0.93, ω=0.95).

Number of Sites of Pain

The Collaborative Health Outcomes Information Registry body map (CHOIR) was used to measure the number of sites of pain by asking participants to indicate the location(s) of pain (Scherrer et al., 2021). There are 74 regions that may be selected, and the total number of sites of pain reflects the sum of the selected region for each participant (Alter et al., 2021) (Scherrer et al., 2021). The CHOIR body map has been used in prior research to describe chronic pain phenotypes and pain impact (Kong et al., 2021; Ziadni et al., 2022).

Data Analysis

All statistical analyses were performed using R version 4.1.2 and RStudio version 2021.09. In the descriptive analysis, means and standard deviations were computed for

continuous variables, and frequencies and percentages were calculated for categorical variables. There was no missing data.

First, bivariate correlations (*r*) were calculated to measure the strength and direction of the linear relationship between all independent variables. The associated effect sizes were measured using Cohen's *d* standard convention for reporting small to medium (*d* = 0.1-0.3), medium to large (*d* = 0.3-0.5), and large to very large (*d* = 0.5-1.0) (J. Cohen, 2013). We also fit simple linear regression models to assess the bivariate relationship for each predictor (cancer-specific psychosocial variables of FCR, CCS, IES), pain catastrophizing (PCS), and the number of sites of pain, where the primary response variable is pain interference (BPI-PI). Finally, to test our research hypotheses that fear of cancer recurrence, cancer distress, and/or cancer trauma would significantly contribute to the pain experience in cancer survivors over and above pain catastrophizing and multisite pain, we fit a series of nested linear regression models. Specifically, for each cancer-specific psychosocial factor, we fit 1) a model with the cancer-specific independent variables, along with pain catastrophizing and the number of sites of pain; and 2) a model with pain catastrophizing and the number of sites of pain that excludes each cancer-specific independent variable one at a time to assess for change in R^2 and allow for likelihood ratio testing (Rights & Sterba, 2020). The likelihood ratio test is, therefore, a test of significance for the contribution of each cancer-specific psychosocial variable on the outcome variable of pain interference. The null hypothesis of the likelihood ratio test is that the cancer-specific psychosocial variable does not account for any additional variance in pain experience over and above pain catastrophizing and the number of pain sites. An identical process for the secondary response variable, pain severity, was used. Model assumptions for all models were checked using

residual diagnostic plots, including q-q plots to assess the assumption of normality and Cooke's distance criteria for outliers (Cook, 1977).

Sample Size and Power Considerations

The study was powered for the ability to detect a significant change in R^2 between nested linear models using conventional effect sizes of Cohen f^2 (1988) of small (0.02), medium (0.15), and large (0.35). We determined that a minimum sample size of 40 was sufficient to detect a medium effect size with a change in degrees of freedom of 1, using standard Cohen f^2 (0.15) with 80% power (α=0.05) with five predictors in the model.

Results

Participants

We recruited 41 cancer survivors who self-reported chronic cancer-related pain. Table 1 shows the study sample's demographics and clinical characteristics of the study sample. Participants were 92.6% female, and the mean age was 59.58 (*SD* = 9.07*)*, and most participants were married or partnered and financially comfortable. Participants had a variety of cancer types- 65.9% were breast cancer survivors, 12.5% were head and neck cancer survivors, 10% were sarcoma survivors, and the remaining were survivors of either lung, gastrointestinal, or gynecological cancers. Over half (58.5%) of the sample was more than six years since cancer diagnosis and treatment, with the majority (78.0%) being more than three years from cancer treatment. Surgery was the most common cancer treatment (95.1%), but all participants were treated with multimodal cancer treatment (i.e. surgery and radiation or surgery and chemotherapy). Ten participants were on maintenance hormonal or immunotherapy during data collection. The cancer-related pain syndromes reported were postoperative pain 48.4%,

lymphedema 39.0%, radiation-induced pain 39.0%, chemotherapy-induced peripheral neuropathy 24.4%, and 63.4% of participants had more than one pain diagnosis. The mean BPI-PI score was 4.69 (*SD* = 2.38), and the mean pain severity was 4.39 (*SD* =1.80) on zero to ten scales. The mean number of pain sites was 9.29 (*SD*=7.72). The mean pain catastrophizing score on a 0 to 52 scale was 12.93 (*SD*=8.94). Table 2 shows descriptive statistics and histograms of all the study variables. The management of pain with pharmacologic treatment was common with 26.8% of the sample using opioids, 12.2% using cannabis, 19.5% using gabapentinoids, and 29.3% using acetaminophen or nonsteroidal anti-inflammatories. Participants used non-pharmacologic strategies such as exercise, mindfulness, massage, and acupuncture; 48.8% did not report using complementary or alternative therapies to manage chronic cancer-related pain.

Correlations and Bivariate Testing

A strong relationship was observed between CSS and PCS (r=0.65), between CSS and IES (r=0.74), and between FCR and CSS (r=0.50). There was a moderate relationship observed between IES and PCS (r=0.50), between the number of sites of pain and PCS (r=0.34), and between the number of sites of pain and CSS (r=0.37). There was a weak relationship between FCR and PCS (r=0.28) and between FCR and the number of pain sites (r=0.23). The correlation coefficients were within the accepted limits of <0.80 to be contained concurrently within the model (Vatcheva, Lee, McCormick, & Rahbar, 2016). Additionally, the variance inflation factor (VIF) for each predictor (and for each model) was < 5, suggesting there was no extreme multicollinearity.

Using simple linear regression, PCS was a significant predictor of variability BPI-PI scores (adjusted R^2 = 0.36, $F(1, 39) = 23.94$, p <0.001). The number of sites of pain was a

significant predictor of variability BPI-PI scores (adjusted R^2 = 0.29, $F(1, 39)$ =18.00, p <0.001). CSS was a significant predictor of variability BPI-PI scores (adjusted R^2 =0.36, F (1, 39) =23.55, p <.0001). FCR did not significant predict variability BPI-PI scores (adjusted R^2 0.05, F (1, 39) =2.93, p=0.095). Finally, cancer trauma was a significant predictor of variability BPI-PI scores (adjusted R^2 0.17, F (1, 39) =9.14, p =0.004).

Likewise, we performed simple linear regression to test the relationship of each independent variable, pain catastrophizing, and the number of sites of pain on pain severity. PCS was a significant predictor of variability pain severity (adjusted R^2 0.14, $F(1, 39)$ =7.40, p =0.010). The number of pain sites was a significant predictor of the variability of pain severity (adjusted R^2 0.25, $F(1, 39)$ =14.52, p<0.001)). CSS was not a significant predictor of variability pain severity (adjusted R^2 0.04, $F(1, 39)$ =2.84, p =0.100). FCR did not significant predict variability pain severity (adjusted R^2 =0.01, $F(1, 39)$ =0.64, p=0.429). IES was not a significant predictor of variability in pain severity (adjusted R^2 0.07, $F(1, 39)$ =3.86, p =0.057).

Linear Regression Models and Likelihood Ratio Tests

Primary Outcome: Pain Interference

In model 1a, BPI-I was regressed on the number of sites of pain and PCS; these predictors explained a significant degree of variance in BPI-PI scores (adjusted R^2 = 0.50, $F(2, 38)$ =20.65, p <0.001). For model 2a, when BPI-PI was regressed on cancer distress additionally to pain catastrophizing and the number of sites of pain, it was a significant predictor of variance in the outcome (adjusted R^2 0.53, $F(3, 37)$ =15.93, p <0.001), but using a likelihood ratio test to compare the nested models we could determine cancer distress did not significantly explain variability in BPI-PI scores over and above the number of pain locations and PCS (p= 0.065,

Cohen's f^2 0.10). For model 3a, BPI-PI was regressed on FCR additionally to pain catastrophizing and the number of sites of pain; it was a significant predictor of variance (adjusted R^2 0.48, $F(3, 37) = 13.50$, $p < 0.001$), but using likelihood ratio testing to compare nested models FCR did not significantly contribute to the variability in BPI-PI over and above the number of pain locations and PCS ($p = 0.721$, Cohen's $f^2 < 0.01$). For model 4a, pain interference was regressed on IES additionally to pain catastrophizing and number of sites of pain, it was a significant predictor of variance in BPI-PI (adjusted R^2 0.498, $F(3, 37) = 14.230$, $p = < 0.001$); but using likelihood ratio to compare nested models it did not significantly predict variability in BPI-PI over and above the number of pain locations and PCS ($p = 0.284$, Cohen's f^2 0.030). Lastly, we regressed all cancer-specific psychosocial factors to assess the combined effect on pain variability, over and above PCR and number of pain sites (model 5a; adjusted R^2 0.505, $F(5, 35) = 9.150$, $p < 0.001$); using likelihood ratio testing of nested models, cancer-specific psychosocial factors did not significantly predict variability in BPI-PI ($p = 0.313$, Cohen's f^2 0.110) over and above PCS and number of sites of pain. Table 3 provides a summary of regression models 1a through 5a.

Secondary Outcome: Pain Severity

Using identical processes as above and depicted in Table 4, we generated model 1b to assess pain severity regressed on the number of sites of pain and PCS determining it was a significant predictor of average pain scores (adjusted R^2 0.20, $F(2, 38) = 6.09$, $p = 0.005$). For model 2b, when pain severity was additionally regressed on cancer distress in addition to variables in model 1b it was a predictor of variance in pain severity (adjusted R^2 0.19, $F(3, 37) = 4.13$, $p = 0.013$), but using a likelihood ratio test to compare the two nested models we could

determine cancer distress did not significantly contribute to variability in pain severity over and above the number of pain locations and PCS (p= 0.52, Cohen's f^2 0.01). We then added FCR to the model 3b with the variables in model 1b it was a significant predictor of variability of pain severity (adjusted R^2 0.18, F (3, 37) =3.99, p =0.015), but using likelihood ratio testing of nested models, we determined that FCR did not significantly predict variability in average pain over and above pain catastrophizing and the number of sites of pain (p= 0.755, Cohen's f^2 <0.01). Then pain severity was regressed IES as model 4b in addition to the variables in model 1b it was a significant predictor of the outcome (adjusted R^2 0.185, F(3, 37) =4.033, p =0.014), likelihood ratio testing indicated that cancer trauma did not significantly predict variability in pain severity (p=0. 666, Cohen's f^2 <0.01) over and above PCS and number of pain sites. Lastly, we regressed all unique cancer factors to assess the combined effect of cancer-specific psychosocial factors on pain severity over and above the variance explained by PCR and the number of pain locations (model 5b; adjusted R^2 0.17, F(5, 35) =2.67, p =0.039). Cancer-specific psychosocial factors did not significantly predict variability in pain severity over and above the number of pain sites and PCS (p= 0.668, Cohen's f^2 =0.04).

Discussion

This study of cancer survivors with diverse cancer-related pain experiences determined the relative contribution of three cancer-specific psychosocial factors to the chronic cancer-related pain experience while accounting for pain catastrophizing and the number of pain sites. Our results indicate that cancer-specific psychosocial factors of fear of cancer recurrence, cancer distress, and cancer trauma explain relatively little variance in pain interference and average pain severity compared to pain catastrophizing and the number of pain sites. The findings should be

interpreted within the context of other literature on chronic cancer-related pain and recognition of the strengths and limitations of the study approach and sample.

Our study adds to the growing body of evidence that pain catastrophizing is among the most important psychosocial factors contributing to the pain experience even among cancer survivors with chronic-cancer related pain (Akbas et al., 2021; Leysen et al., 2021; Wilson et al., 2022). In addition to potentially worsening pain, a lack of attention to pain catastrophizing can contribute to reliance on opioids and other pharmacologic treatments (Azizoddin et al., 2022). Over half of our sample had PCS scores above the therapeutic target of 10, and 56% had scores greater than 13. In other studies, PCS scores greater than 13 to 16 have shown a higher likelihood of an opioid prescription (Sharifzadeh et al., 2017). In our sample, we did not test the relationship of opioid use with psychosocial measures since data collection was self-report rather than an exhaustive measure capturing consistent or prior use. Nevertheless, at the time of data collection, nearly 25% used opioids and/or gabapentoids to manage cancer-related pain, and half of our sample did not use non-pharmacologic treatment. The reliance on opioids and other pharmacologic treatments is similar to the prevalence reported in other studies (Jones et al., 2021). Still, it is worrisome since there is a lack of evidence on the efficacy and safety of adjuvant analgesics and opioids in cancer survivors with chronic-cancer related pain, and unaddressed pain catastrophizing can undermine the effectiveness of pharmacologic management (Rai et al., 2017). Targeting pain catastrophizing can lead to meaningful improvements in pain-related interference and decrease reliance on pharmacologic treatments (Azizoddin et al., 2021; Darnall et al., 2021; Darnall et al., 2019). Moreover, treatment approaches that address pain catastrophizing, such as cognitive behavioral therapy, have less risk of side effects and toxicity-

an important consideration in cancer survivors with a longer prognosis. Innovative work to address pain catastrophizing using a single visit resulted in clinically significant improvements in pain catastrophizing, pain interference, and pain intensity that was not inferior to an eight-week cognitive behavioral therapy session (Darnall et al., 2021).

Lack of attention to pain catastrophizing can also lead to poor self-efficacy to control pain and lead to chronic pain in multiple locations of the body (Kawi et al., 2020). Participants in our study had a large burden of pain sites with 73.0% having more than five sites of pain, and the majority (63.4%) had several co-occurring chronic cancer-related pain syndromes. To the best of our knowledge, this study is the first that demonstrates the common occurrence of multisite pain in cancer survivors with cancer-related pain without pre-existing non-cancer pain. This finding should be further explored because it has important implications for management and pain phenotyping. Multisite pain, similar to pain catastrophizing, limits the effectiveness of pharmacologic treatments and is associated with long-term opioid use and challenges with opioid tapering (Coggon et al., 2013).

The non-significant relationship between chronic cancer-related pain interference and cancer-specific psychosocial factors was surprising and may reflect our small sample size and participant characteristics. Approximately half our sample experienced moderate FCR, matching the reported prevalence in the literature (Luigjes-Huizer et al., 2022). Still, few rigorous longitudinal studies capture our study population, the majority of which were > 6 years' post-curative treatment (Simard et al., 2013). The relationship between FCR and pain interference may diminish as pain persists and people are further along in the cancer survivorship continuum. Additionally, the relationship between fear of cancer recurrence and pain may be modulated by

the location of pain and whether the location could signal recurrent disease. Most of our participants had diffuse pain persisting many years' post-treatment, so perhaps this is less likely to trigger thoughts of cancer recurrence. Given the diffuse nature of pain and participants being nearly a decade since initial treatment, fear of cancer recurrence may be less important to the pain experience than we hypothesized in long-term survivors with multisite pain.

Using the impact events scale to measure cancer trauma, we hoped to capture cancer trauma accurately. However, whether or not cancer is a single traumatic event is a source of debate (Leano et al., 2019), with some researchers suggesting cancer is more akin to a chronic stressor (Abbey et al., 2015; Cordova et al., 2017). Only a small portion of our sample had clinically significant levels of trauma, likely because post-traumatic stress disorder is most pronounced shortly after treatment (Abbey et al., 2015). Our study does not clarify the role of cancer trauma and the chronic cancer-related pain experience in cancer survivors, but the surrounding literature identifies that early childhood trauma and other forms of trauma can influence cancer-related pain in cancer survivors (Novy & Aigner, 2014; Sager et al., 2020).

In our study, cancer-specific factors, pain catastrophizing, and the number of sites of pain combined accounted for less variance in the pain severity outcome, our secondary measure, than in pain interference. A possible explanation is this was a cross-sectional study, and average pain severity may be a less meaningful measure in cancer survivors who have been living with pain for many years. Likely examining pain severity trajectories over time would be a more meaningful indicator of pain severity within persons. Other evidence also points to pain severity remaining stable in cancer survivors receiving and not receiving cancer treatment, suggesting pain severity may be less of a dynamic measure of cancer-related pain (Shi et al., 2011).

As a first step to understanding the unique aspect of the chronic cancer-related pain experience, we attempted to offset the weaknesses of our study design by using validated and psychometrically sound measures previously used in cancer survivors. Nonetheless, data was only collected at one-time point and likely influenced our findings. Many of our participants were nearly a decade from cancer treatment, a population rarely captured in the existing literature making our study an important contribution to the literature. Future studies on chronic cancer-related pain should consider pain, psychosocial measures, and treatment over time since psychosocial factors and management strategies frequently change (Nekhlyudov et al., 2017). Our findings may have also been influenced by the COVID-19 pandemic that has had significant ramifications for cancer survivors and people living with chronic pain (Edmond et al., 2022; Jammu et al., 2021).

Despite our attempts to include a broad group of cancer survivors because they are grouped together in national pain management guidelines (Paice et al., 2016), our small sample was predominantly compromised of female breast cancer survivors. The role of sex can influence the findings since females are more likely to experience pain catastrophizing and chronic pain (Bartley & Fillingim, 2013). Additionally, although we rigorously screened and excluded people with pre-existing non-cancer pain or pain unrelated to cancer, some pain may be attributed to non-cancer conditions common in the age represented in our cohort (i.e., musculoskeletal pain). This may impact the fidelity of our study findings but also reflects the reality that the etiology of chronic pain can be difficult to pinpoint, with 22.0% of our sample lacking a chronic cancer-related or other formal pain diagnoses (Ahuja et al., 2017). Lastly, we captured nearly fifty percent of explained variance of pain interference in cancer survivors (as measured by the BPI-

PI); but numerous factors can influence chronic pain in cancer survivors (Novy & Aigner, 2014), and we have only accounted for pain catastrophizing and the number of sites of pain. Using a parsimonious approach, we may have overlooked additional factors that would have provided insights into our findings and the cancer-related pain experience.

Implications for Nursing

Nurses are ideally suited to provide formal education on pain self-management and interventions targeting pain catastrophizing and addressing multisite pain. Cognitive behavioral therapies (CBT) and other non-pharmacologic treatments can improve pain and other distress symptoms commonly experienced by cancer survivors such as fatigue, insomnia, anxiety, and depression. Evidence supports the use of nurse-led psychosocial interventions such as CBT or directing patients to self-directed resources (Dean et al., 2020).

The study findings also suggest that assessing and managing pain catastrophizing can be an aspect of distress screening, often under the purview of nurses in cancer care. Interventions to improve cancer distress delivered by nurses are often accepted, and nurses are the preferred clinician to help with psychosocial distress among cancer survivors (Brebach et al., 2016). Nurses are also well positioned to deliver non-pharmacologic treatment that target pain and distress in patient-centered ways. Such as telehealth, group treatments, one-time interventions, or a triage system that allows nurses to deliver brief interventions and referrals to mental health clinicians as needed (Daniels, 2015; Turner et al., 2011). Mindfulness approaches and exercise were commonly used by participants in our sample and should be encouraged because they appear to have similar efficacy in people with cancer who are further along the survivorship continuum (Blumenstein et al., 2022). Nurses are critical to bridging the gap of improving access

to interventions to improve pain catastrophizing and multisite pain across cancer and pain care. There are a limited number of clinicians trained in chronic pain, and there is less awareness and access to evidenced-based psychological pain treatments than pharmacologic treatment (Jena et al. 2015). Nursing advocacy and policy change is needed to improve equitable access and consistent insurance coverage for multimodal pain treatment (Darnall et al., 2016; Ludwick et al., 2020)

Conclusion

This study demonstrated that the non-cancer-specific factors of pain catastrophizing and the number of sites of pain are significantly associated with chronic cancer-related pain, with cancer-specific psychosocial factors playing a lesser role in the pain experience of cancer survivors. The results suggest a greater need to attend to pain catastrophizing in survivorship care. Nurses can be instrumental in championing multimodal pain treatments that target pain catastrophizing for cancer survivors with chronic cancer-related pain. Further research should seek to understand the role of multisite pain in cancer survivors as a unique pain phenotype that may differ from acute cancer-related pain and contribute to higher rates of long-term opioid use in cancer survivors.

Appendix C

Figure 1. Conceptual Model and Study Variables

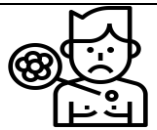
	Biological	Psychosocial	Cancer-Specific Psychosocial Factors: Reactions to cancer diagnosis and treatment			Outcome: Pain Experience	
							
Construct	Multisite Pain	Pain Catastrophizing	Cancer Trauma	Cancer Distress	Fear of Cancer Recurrence	Pain Inference	Pain Severity
Measure	CHOIR body map	PCS	IES	CSS	FCR-7	BPI-PI	Average Pain over the past 7 days
Definition	Pain in more than one anatomical location.	Negative emotional or cognitive response to pain.	A measure of the impact of cancer on thoughts and behaviors.	Cancer survivors assessment of concern related psychosocial distress in psychosocial, practical, and physical domains.	Fear, worry, or concern that cancer will come back.	A measure of the degree that chronic pain interferes with activities of daily living.	A measure of the average pain severity over the past 7 days
Clinical Relevance	A greater extent of pain distribution is associated with worse clinical outcomes.	Scores <10 is the recommended therapeutic target for people with chronic pain	A cut-off score of >33 identifies clinically significant traumatic distress	Reported mean of cancer distress in the literature is 27.9. Higher CSS scores suggest a need to assess for depression or anxiety	Scores > 15 indicate moderate FCR Scores > 27 indicate high levels of FCR	Higher scores indicate more interference of pain with activities	Higher scores indicate more pain severity
Baken &Wooley, 2011; Darnall, 2019; Custer et al., 2014 Lebel et al., 2016; Rosenbaum, 2015							

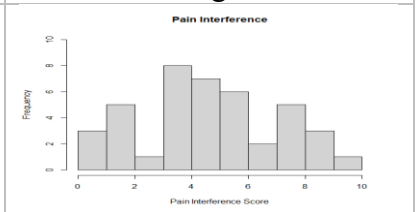
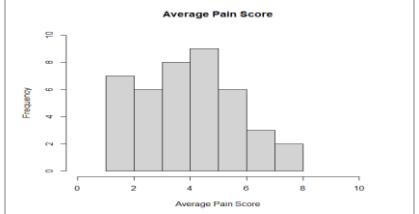
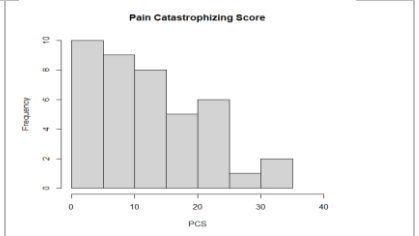
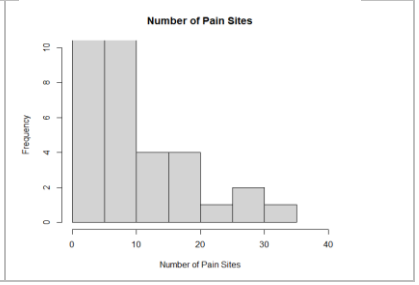
Table 1: Participant Demographics and Clinical Characteristics (n=41)

Sample	No. (%)
Age (Mean, (SD), years)	59.58 (9.07)
Gender Self-report	
Man	3 (7.3)
Women	38 (92.7)
Education	
Less than Bachelor's	10 (24.4)
Bachelor's Degree	10 (24.3)
Graduate Degree	21 (51.2)
Financial Status	
Comfortable	20 (48.8)
Have enough to make ends meet	18 (43.9)
Do not have enough	2 (4.9)
Prefer not to say	1 (2.4)
Partnered Status	
Single	5 (12.2)
Married or Partnered	26 (63.4)
Divorced	10 (24.3)
Employment	
Employed	23 (56.1)
Retired	12 (29.3)
Unemployed	3 (7.3)
Sick Leave	3 (7.3)
Cancer Type	
Breast	27 (65.9)
Head and Neck	5 (12.2)
Lung	1 (2.4)
Sarcoma	4 (9.8)

GYN	2 (4.9)
GI	1 (2.4)
Time since treatment	
3 months-1 year	2 (4.9)
Between 1-3 years	7 (17.1)
Between 3- 6 years	8 (19.5)
Between 7-10 years	8 (19.5)
More than 11 years	16 (39.0)
Treatment History	
Surgery	39 (95.1)
Radiation	34 (82.9)
Chemotherapy	27 (65.9)
Hormonal therapy or Immunotherapy	17 (41.5)
More than one cancer treatment	41(100.0)
Two cancer treatments	13 (31.7)
More than three cancer treatments	28(68.3)
Pain Diagnosis	
CIPN	10 (24.4)
Surgery	20 (48.8)
Bone Pain	9 (22.0)
Radiation	16 (39.0)
Lymphedema	16 (39.0)
No Pain Diagnosis	9 (22.0)
Other	13 (31.7)
More than one pain syndrome	26 (63.4)
Pharmacologic Treatments	
Opioids	11 (26.8)
Gabapentinoids	8 (19.5)
Cannabis	5 (12.2)
Nonsteroidal Anti-inflammatories	8 (19.5)
Acetaminophen	12 (29.3)
Antidepressants	12 (29.3)
Lidocaine patches or infusion	4 (9.8)

None	8 (19.5)
Nonpharmacologic Treatments	
Physical Therapy	9 (22.0)
Acupuncture	4 (9.8)
Massage	14 (34.2)
Cognitive Behavioral Therapy	0 (0)
Yoga	7(17.1)
Mindfulness-Based Approaches (mediation or prayer)	11 (26.8)
None	20 (48.8)

Table 2: Descriptive Statistics

	Mean (SD)	Median	Range	Histogram
Pain Interference	4.69 ±2.38	4.86	0.14-9.14	
Pain Severity (Mean, Range, SD)	4.39 ±1.80	4.00	1.00-8.00	
Pain Catastrophizing (PCS)	12.93±8.94	12.00	0.00-35.00	
Number of Sites of Pain	9.29±7.72	7.00	1.00-31.00	

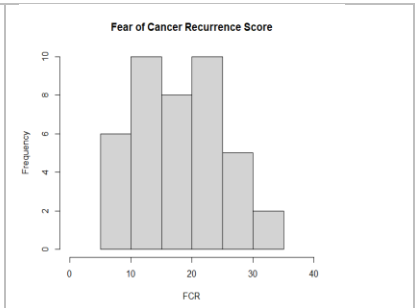
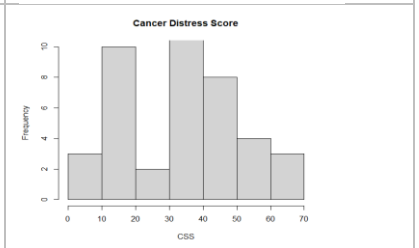
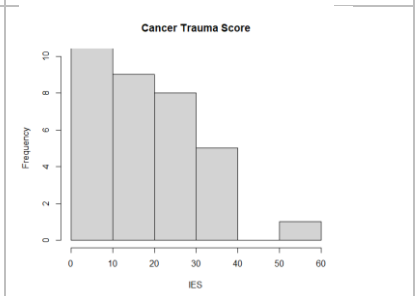
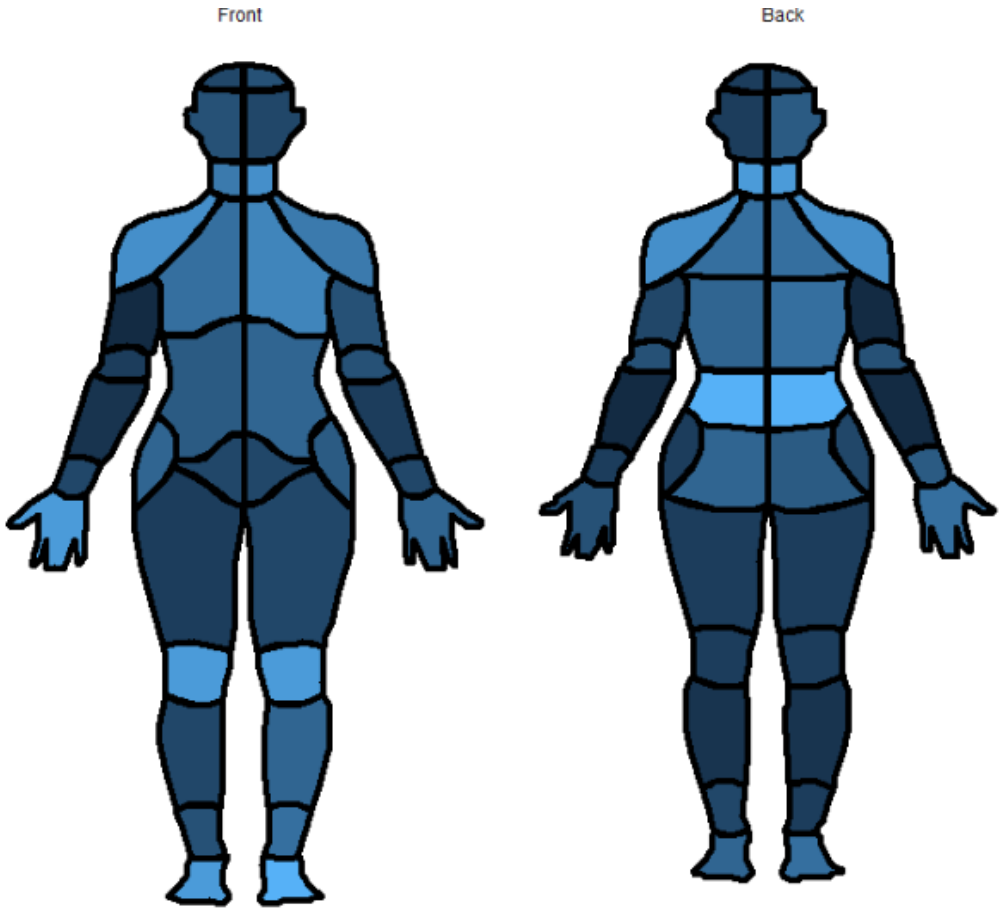
Fear of Cancer Recurrence (FCR)	18.29±6.92	19.00	6.00-32.00	
Cancer Distress (CSS)	33.68 ±16.43	35.00	2.00-63.00	
Cancer Trauma (IES)	14.88±13.23	12.00	0.00-52.00	

Figure 2: Pain Distribution using CHOIR Body Map



Number of people (n) indicating pain in a specific body region.

- Head n=11
- Neck n= 15
- Chest n=13
- Abdomen n=5
- Back n=19
- Left hip, buttock, or leg n=25
- Left Arm n=19
- Right hip, buttock, or leg n=25
- Right Arm n=23

Number of sites of pain reported
Range 1-31, Mean 9.29 ± 7.73

- One site of pain n=5
- Two to four sites of pain n=6
- Five to Seven sites of pain n=10
- Eight to Ten sites of pain n=8
- Eleven to Thirteen sites of pain n=2
- Fourteen to Sixteen sites of pain n=4
- Seventeen to Nineteen sites of pain n=2
- > 20 sites of pain n=4

Lighter blue indicate less participant reported pain in the location; Darker Blue indicates more people reported pain in the location.

Table 3: Multivariable Regression and Likelihood ratio test for pain interference

	Model 1a			Model 2a			Model 3a			Model 4a			Model 5a		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	1.89	0.85 – 2.92	**0.001**	1.23	0.01 – 2.45	**0.048**	1.67	0.07 – 3.28	**0.041**	1.79	0.75 – 2.84	**0.001**	1.48	-0.21 – 3.18	0.084
PCS	0.13	0.06 – 0.19	**<0.001**	0.08	0.01 – 0.16	**0.034**	0.13	0.06 – 0.19	**0.001**	0.11	0.04 – 0.18	**0.003**	0.08	0.00 – 0.16	**0.041**
Number of Pain Sites	0.12	0.05 – 0.20	**0.002**	0.11	0.03 – 0.18	**0.005**	0.12	0.04 – 0.20	**0.003**	0.12	0.04 – 0.19	**0.004**	0.11	0.03 – 0.19	**0.006**
CSS				0.04	-0.00 – 0.08	0.065							0.04	-0.01 – 0.10	0.124
FCR							0.02	-0.07 – 0.10	0.721				-0.02	-0.12 – 0.07	0.633
IES										0.03	-0.02 – 0.07	0.284	0.00	-0.06 – 0.06	0.950
R^2 / R^2 adjusted	0.521 / 0.496			0.564 / 0.528			0.523 / 0.484			0.523 / 0.498			0.567 / 0.505		
AIC	164.371			162.535			166.23			165.08			166.26		
Change in R^2 [a]	X			0.04			0.001			0.010			0.05		
Cohen's f^2 [a]	X			0.10			0.002			0.030			0.110		
likelihood ratio p-value [a]	X			0.065			0.721			0.284			0.313		

[a] Compared to Model 1a

Table 4: Multivariable Regression and Likelihood ratio test for average pain severity

	Model 1b			Model 2b			Model 3b			Model 4b			Model 5b		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	2.96	1.97 – 3.94	**<0.001**	3.18	1.97 – 4.39	**<0.001**	3.14	1.61 – 4.66	**<0.001**	2.92	1.91 – 3.93	**<0.001**	3.50	1.85 – 5.16	**<0.001**
PCS	0.06	-0.00 – 0.12	0.056	0.07	-0.00 – 0.15	0.059	0.06	-0.00 – 0.13	**0.058**	0.05	-0.02 – 0.12	0.126	0.07	-0.01 – 0.15	0.068
Number of Pain sites	0.07	0.00 – 0.14	**0.048**	0.08	0.00 – 0.15	**0.041**	0.08	0.00 – 0.15	**0.048**	0.07	-0.00 – 0.14	0.066	0.07	-0.00 – 0.15	0.052
CSS				-0.01	-0.06 – 0.03	0.524							-0.03	-0.08 – 0.03	0.306
FCR							-0.01	-0.09 – 0.07	0.755				-0.01	-0.11 – 0.08	0.765
IES										0.01	-0.04 – 0.06	0.666	0.03	-0.03 – 0.09	0.287
R^2 / R^2 adjusted	0.243 / 0.203			0.251 / 0.190			0.245 / 0.183			0.246 / 0.185			0.275 / 0.172		
AIC	160.197			161.741			162.088			161.988			164.393		
Change in R^2 a	X			0.008			0.002			0.004			0.030		
Cohens f^2 [a]	X			0.010			0.002			0.005			0.040		
Likelihood Ratio p-value [a]	X			0.524			0.755			0.666			0.668		

[a] Compared to Model 1b

Chapter V

Discussion

The overarching goal of this manuscript dissertation was to develop a deeper understanding of the unique factors associated with the chronic cancer-related pain experience in cancer survivors. The goal was addressed by: 1) evaluating evidence of the published and peer-reviewed literature regarding patient and disease-specific factors associated with long-term opioid therapy in cancer survivors, 2) gaining a deeper understanding of the daily lived experience of cancer survivors with chronic cancer-related pain, and 3) quantifying the contribution of cancer-specific psychosocial factors to the chronic-cancer pain experience in cancer survivors. Three manuscripts were successfully developed, supported by a multidisciplinary team of clinicians and researchers, to fill the existing knowledge gap. There are several areas where chronic cancer-related pain is unique. Chronic cancer-related pain uses an opioid-centric approach, multisite pain is common, and cancer survivors perceive chronic cancer-related pain as the cost of survival associated. There are also several key areas where chronic cancer-related pain shares similar features with other chronic pain syndromes. Such as the role of pain catastrophizing, communication challenges with clinicians, family, peers, and the need to largely self-navigate treatment (Bernard et al., 2018; Miaskowski et al., 2019).

The first manuscript, an integrative review, summarized and evaluated the evidence of the published and peer-reviewed literature regarding patient and disease-specific factors associated with long-term opioid therapy (LTOT) in cancer survivors. The study found several terms for opioid use after curative treatment, including chronic opioid use, persistent opioid use, prolonged opioid use, late opioid use, post-treatment opioid use, or long-term opioid therapy (LTOT). In this dissertation, we favored using the term long-term opioid therapy because it is used in the

general literature on opioid benefits and harms (Chou et al., 2015). However, a mapping review was completed following the integrative review and recommended using the term persistent opioid use to mirror the term used in the surgery literature (Check et al., 2022). Future work should consider a consensus definition with an agreed-upon term that captures the phenomenon of opioid use that is longer than anticipated or potentially avoidable.

Additionally, manuscript one demonstrated that LTOT in cancer survivors is influenced by several biopsychosocial factors, such as cancer type, cancer treatment, medical comorbidities, opioid characteristics, mental health diagnoses, and socioeconomic factors (Jones et al., 2021). The integrative review also highlighted the lack of prospective studies investigating the influence of cancer-specific biopsychosocial factors on pain characteristics (i.e., pain severity and interference) and how cancer survivors view long-term opioid use. This gap led us to conduct a prospective study to examine cancer-specific biological and psychosocial factors associated with pain experience (manuscript 3) and the lived experience of chronic cancer-related pain (manuscript 2).

The second manuscript provides a deeper understanding of the lived experience of cancer survivors with chronic cancer-related pain using a qualitative approach. This approach expanded the knowledge of chronic cancer-related pain beyond the BPS framework constructs and enriched the understanding of cancer survivors' daily lived experiences with chronic cancer-related pain. Several themes emerged to describe cancer survivors’ perception and management of chronic cancer-related pain. Participants perceived chronic cancer-related pain caused invisible suffered and viewed pain as the cost of surviving. Cancer survivors characterized the management of chronic cancer-related pain as revolving around opioid decisions and a need to

try everything by self-navigating treatments. The study's findings demonstrate how the biomedical model of seeing pain as a purely nociceptive phenomenon to be fixed or requiring external medical treatment (i.e. opioids) -may contribute to poor psychological well-being and suboptimal pain management in cancer survivors (Azizoddin et al., 2021). Common psychological aspects of pain include pain catastrophizing (further explored in manuscript three), ascribing meaning and belief about the pain, fear pain will never improve, and excessive attention focused on pain (Cohen et al., 2008). If left unaddressed, these factors can result in worsening suffering and suboptimal pain management (Bushnell et al., 2013). Many of these factors were named in manuscript two, including pain "consuming your life," a sense that pain was a reminder of cancer, and cancer survivors feeling "lesser" than other people because of pain. These psychosocial factors could be uniquely targeted with psychological pain treatments such as cognitive behavioral therapy, mindfulness, or acceptance and commitment therapy (Thompson et al., 2022). Additionally, the second manuscript suggested that multisite pain in cancer survivors may be an important area of future research. The third manuscript builds on the findings in manuscript two by quantifying the cancer-specific psychosocial aspects of chronic cancer-related pain, pain catastrophizing, and the role of multisite pain.

The third manuscript identified pain catastrophizing and chronic multisite pain as critical drivers of the variability in the chronic cancer-related pain experience. Pain catastrophizing and the number of sites of pain had a more significant influence on pain interference and severity than cancer-specific psychosocial factors of cancer distress, fear of cancer recurrence, and cancer trauma. On average, cancer survivors in our sample had nine sites of pain. The number of pain sites pain and pain catastrophizing accounted for 50% of explained variance in pain interference.

The results provide additional evidence that pain catastrophizing is an important psychosocial factor involved in the chronic cancer-related pain experience and multisite pain is an underappreciated feature of chronic pain in cancer survivors (Akbas et al., 2021; Leysen et al., 2021).

The three dimensions of pain catastrophizing are rumination, magnification, and feelings of helplessness leading to activity avoidance and distress (Petrini & Arendt-Nielsen, 2020). These dimensions can be directly targeted by psychosocial pain treatments such as cognitive restricting that occurs with cognitive behavioral therapy and intervention that address pain avoidance behaviors such as physical therapy and exercise (Driscoll et al., 2021). Pain catastrophizing has also been referred to as pain distress and is seen as a negative mindset, including an inability to inhibit pain-related thoughts during, following, or in anticipation of pain. Supporting research in cancer populations indicates ignoring psychosocial aspects of pain (including pain catastrophizing) can lead to increase reliance on pharmacologic treatments, particularly opioids (Azizoddin et al., 2022). This, in turn, can increase opioid harm and undermine their effectiveness (Darchuk et al., 2010). Whereas addressing psychosocial dimension of pain can reduce pain intensity. For example, a randomized controlled trial demonstrated improvement in pain from chemotherapy-induced peripheral neuropathy using a self-guided online cognitive behavioral program (Knoerl et al., 2018). Likewise, a randomized controlled trial testing an innovative model of "telerehabiltation" using a combination of nursing and physical therapy virtual visits improved pain and function in people with advanced cancer (Cheville et al., 2019). The results from manuscripts two and three, suggest more significant

attention to multisite pain, pain catastrophizing, including activity avoidance, has the potential to improve chronic cancer-related pain.

Across all three studies, cancer survivors with chronic cancer-related pain experienced high rates of opioid use. LTOT was up to 45% in manuscript one, 46% in manuscript two, and 25% in manuscript three. These rates are significantly higher than the reported prevalence rate of 6.8% in the general population to manage chronic pain (Mojtabai, 2018), but similar to what is reported in the oncology literature (Check et al., 2022). Predictors of LTOT are outlined in manuscript one, including comorbidities, prior substance use, low socioeconomic status, and mental health conditions. These are shared risks for LTOT in the general population, as well as risks for opioid harm (Karmali et al., 2020). There are several reasons for the elevated opioid use in cancer survivors, elucidated by the findings in manuscripts two and three.

Communication about chronic pain and opioid treatment is often frustrating for clinicians and patients (Matthias & Henry, 2022). In our study, participants largely felt their pain was dismissed, and opioids were the focus of pain assessment. Lack of validation of pain can also contribute to greater pain catastrophizing (Darnall, 2019). Pain catastrophizing and associated vigilance has been described as behavior that attempts to elicit social support (Matthias et al., 2022) and, in some cases, may be a necessary response to get appropriate care (Thompson et al., 2022). Insufficient or poor communication about chronic cancer-related pain appears to increase suffering in cancer survivors. Participants were mainly navigating the process of trial and error of chronic cancer-related pain management on their own. For cancer survivors with chronic cancer-related pain, there is a breakdown in communication and therapeutic relationships if pain persists after treatment. The dissertation underscores that high-quality communication focused on the

pain experience is needed to actualize the goal of improving cancer-related pain and opioid care (Carmona-Bayonas et al., 2017). Indeed, patients with chronic pain have identified fostering an atmosphere of caring, concern, and trust is paramount to effective pain care (Henry & Matthias, 2018). Investigating the link between cancer-related pain outcomes in cancer survivors and clinician communication regarding pain and opioid use is an important area of future research.

The findings across the three manuscripts highlight many key similarities between chronic non-cancer pain and chronic cancer-related pain. Chronic non-cancer pain is associated with catastrophizing, multisite pain, communication challenges, and invisible suffering (Darnall, 2019; Merlin et al., 2017). The collective findings are thought-provoking because clinically and in national guidelines, cancer-related pain is often seen and managed as an entirely different condition from non-cancer pain (Dowell et al., 2016). The dissertation findings raise questions on how dichotomizing chronic cancer–related and chronic non-cancer pain may harm people with cancer. The lack of attention to common chronic pain factors such as pain catastrophizing and multisite pain may explain why some clinicians and patients rely on opioids for pain management since there are few other options integrated into cancer care (Meghani & Vapiwala, 2018). The dissertation results suggest the general literature can be a starting point for tailoring chronic cancer-related pain treatments to cancer survivors (Jones & Merlin, 2021).

Summary and Implications

. Our findings have urgent implications for increasing the adoption of individualized opioid care as an aspect of holistic pain care for cancer survivors with chronic cancer-related

pain. There is a need to develop an alternative paradigm that provides greater access to psychosocial treatment modalities, prioritizes high-quality communication, and may decrease reliance on opioids. There is also a need for equity in access to psychosocial treatments, including insurance coverage and availability within cancer centers, given the findings of our study and others (Jones et al., 2021; Liou et al., 2019; Ludwick et al., 2020).

The dissertation findings have significant potential to improve the pain experience in cancer survivors by adopting the essential structures of pain self-management and better access to multimodal pain treatment (Azizoddin et al., 2021; ElMokhallalati et al., 2018; Hernandez et al., 2019). Pain self-management should be individualized and tailored to the patient and circumstance; our study findings highlight that balancing different pain sites is essential to developing a treatment plan. Second, cancer survivors must develop a treatment plan through high-quality communication with clinicians. This study suggests that communication between clinicians and cancer survivors is impeded by a focus on opioids and not acknowledging the pain experience. These aspects of the cancer-related pain experience must be overcome to adopt a patient-centered approach. Third, cancer survivors with chronic cancer-related pain would benefit from more information to improve their self-efficacy in managing their pain (ElMokhallalati et al., 2018). Over the past several years, there have been promising results using telephone and mobile health to improve self-manage of common cancer-related symptoms, including lymphedema, cancer-related fatigue, and cancer distress- but there is limited evidence for pain self-management education for cancer-related pain in people without active disease (Azizoddin et al., 2021; Fu et al., 2016; Ream et al., 2020). Future work on implementing pain

self-management and pain education as a part of routine care of cancer survivors with chronic cancer-related pain is needed.

The research findings have implications for nursing and other disciplines. Cancer survivorship care is shared between oncology practices, including survivorship programs, palliative care teams, and primary care practices (Nekhlyudov et al., 2017). Who is best positioned to provide chronic cancer-related pain and long-term opioid care is an area of debate among clinicians from these specialties (Check et al., 2022). Future research should help identify "a healthcare home" for cancer survivors to best address pain, while simultaneously improving clinicians' knowledge and comfort in managing chronic cancer-related pain and LTOT in cancer survivors (Carmona-Bayonas et al., 2017; Chow et al.,, 2017; Merlin et al., 2012). During COVID-19, innovative treatments that optimize pain management and opioid safety by leveraging telehealth and interdisciplinary care were piloted at the Veterans Health Administration with feasibility and acceptability (Edmond et al., 2022). Similar interventions could be tailored to cancer survivors. Nurses are ideally positioned to contribute to a dedicated treatment model for cancer survivors, given the importance of providing whole-person care and fostering a trusting relationship (Ream et al., 2020; Willis et al., 2008).

Nurses are increasingly valued members of the cancer care team, with survivorship programs often led and exclusively staffed by APNs (Sun et al., 2015). Nursing contributions to pain and opioid management can include novel nurse-led care models that advance patient education on chronic pain and opioid safety (Courtenay & Carey, 2008; Finnell et al., 2019; Van Cleave et al., 2021). Optimal pain and opioid care are interdisciplinary, and a large body of

evidence supports nurses' role in leading pain and opioid care (Darawad et al., 2019; Darnall et al., 2016; Van Cleave et al., 2021).

Advance Practice Nurse (APN) led cancer survivorship pain programs would be novel and may offer value over registered nurse support services that have not been consistently effective in cancer care because of the volume of tasks required of oncology-based nurses (Schenker et al., 2021b). Nurse lead survivorship, pain, and opioid programs demonstrate high levels of satisfaction and improvement in cancer survivor's physical and emotional functioning (Cooper et al.,, 2010; Feldenzer et al.,, 2019). Despite the critical role APNs play in survivorship, palliative, and chronic pain care, APNs continue to have a restricted or reduced scope of practice in more than 50% of states (American Academy of Nurse Practitioners, 2021). These scope of practice restrictions are particularly relevant in chronic pain care, opioid prescribing, and treating opioid harms, such as opioid use disorder or misuse (Tierney et al., 2020). APN scope of practice restrictions also exists in the context of state-based opioid limitations that potentially impact cancer survivors more than people with active disease (Bulls et al., 2021). Although the impact of practice laws on cancer survivors with cancer-related pain managed with opioids was outside this study's scope, it is an essential area for future work and advocacy. Over half the states in the United States have restricted or reduced the scope of practice for Advance Practice Providers (APPs) (Spetz et al., 2021). Likewise, 36 states have opioid prescribing restrictions (Bulls et al., 2021; Jones et al.). State-based scope of practice and opioid prescribing limitations are likely to have an unintended effect of further complicating opioid access and contribute to the communication challenges described by participants. During the COVID-19 pandemic, many

states suspended practice barriers, including restrictions related to opioid prescribing, resulting in a perceived ability to meet patient's needs better (O'Reilly-Jacob et al.,, 2021).

Strengths and Limitations

The results of the dissertation should be interpreted in recognition of its strengths and limitations. The use of a multimethod approach is a strength of the dissertation; several different methods can overcome any inherent limitations of using a strictly qualitative or quantitative approach (Doyle et al., 2016). Second, a strength of the sample described in manuscripts two and three excluded people with pre-cancer chronic pain, which allowed a greater understanding of the phenomenon of chronic cancer-related pain. Prior studies of people with cancer have not delineated between cancer-specific pain syndromes and non-cancer pain syndromes (Paice, 2018; Paice, 2019c), making this dissertation a novel contribution to the literature. Furthermore, the dissertation focused on the collective burden of pain in cancer survivors from more than one cancer-pain syndrome.

As a first step to understanding the unique aspect of the cancer experience on chronic cancer-related pain, our study has several limitations. Most participants were female breast cancer survivors, which is important since females are more likely to experience pain catastrophizing and chronic pain (Bartley & Fillingim, 2013). Although the study was not designed to examine racial disparities in pain characteristics or pain care, these disparities are a significant issue in cancer pain care that is likely to influence pain interference and severity due to racism effects (Meghani et al., 2012). We were unable to characterize how disease-related differences (such as breast cancer compared to head and neck cancer) and pain etiology

differences (such as chemotherapy-induced peripheral neuropathy compared to post-surgical pain) may influence the chronic cancer-related pain experience. Many of our cancer survivors were >6 years post cancer treatment, which may limit the generalizability of our findings since psychosocial factors and pain characteristics often change over time (Nekhlyudov et al., 2017). The measure of opioid therapy differed across all manuscripts. Numerous factors can influence chronic pain in cancer survivors (Novy & Aigner, 2014) that were not accounted for across the three studies. The cross-sectional design and single interview recruited within one cancer center was also a limitation of studies two and three because pain, psychosocial measures, and daily lived experience change over time and across cancer centers.

Conceptual Model and Future Directions

A conceptual model, Figure 1, illustrated the dissertation's findings of the cancer survivor's experience of chronic cancer-related pain. This model incorporates several cancer-specific, individual, and external contextual factors that highlight the complexity of chronic cancer-related pain. The model highlights key study findings informed by the perspective of cancer survivors. The conceptual model helps to inform areas of improvement, future research, innovation, and policy changes.

This dissertation provides a solid foundation to build my research program and identifies multiple future directions to strengthen nursing research in chronic cancer-related pain in cancer survivors. In future work, I intend to craft a nursing psychosocial-based intervention blending existing interventions for pain catastrophizing, acceptance and commitment therapy, and gratitude training. I will continue my research training as a post-doctoral fellow with Dr. Merlin on her funded R01 NIH-funded study “Skills TO Manage Pain” (STOMP) which aims to

improve pain and function in people living with HIV. People living with HIV share many similarities with cancer survivors, including high rates of multisite pain, substance use or misuse, and depression with psychosocial distress (Merlin et al., 2013; Merlin et al., 2014; Merlin et al., 2017; Merlin et al., 2019).

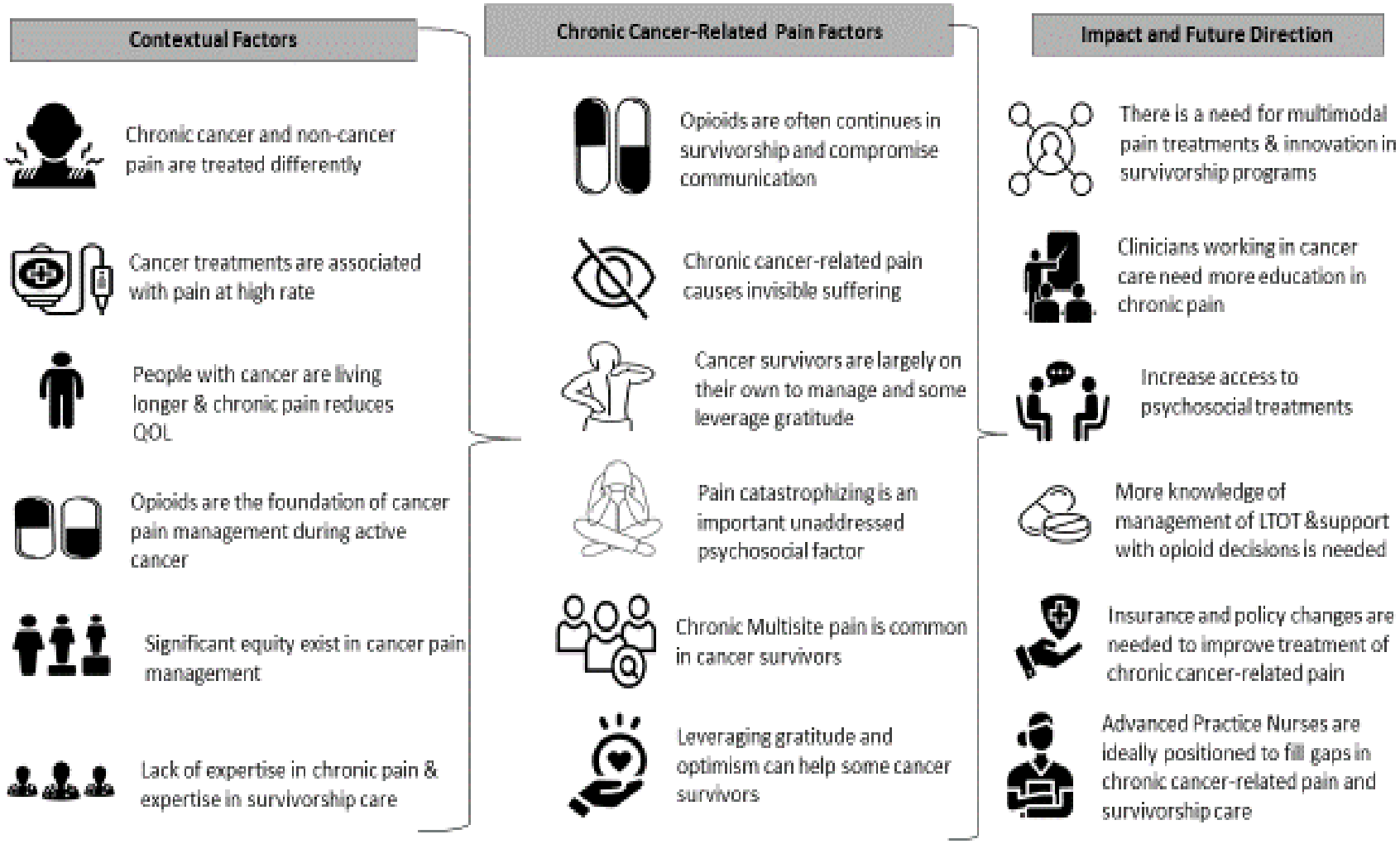
As demonstrated in our study, using opioids to manage chronic cancer-related pain is common. However, there is limited evidence on the long-term safety and efficacy of opioids for chronic-cancer-related pain (Meghani & Vapiwala, 2018; Schatz et al., 2020). During my post-doctoral training, I will contribute to a grant funded by Dr. Merlin and Dr. Christine Ritchie MD, to understand opioid benefits and harms from the perspectives of key stakeholders (patient, family, caregiver, and clinicians) using quantitative and qualitative methods.

Lastly, the false dichotomy of pain and addiction was illustrated in manuscript one, where a prior history of substance use disorder was associated with LTOT. I have made additional contributions to the literature on the imprecise policy delineation of opioids for pain and opioid use disorder (Ho et al., 2022; Jones & Mason, 2022). Likewise, Dr. Merlin and I have developed consensus based-guidance on opioid decisions for people with advanced cancer with substance use disorder that were published in two separate JAMA publications (Jones et al., 2022; Merlin et al., 2021). In future work, I intend to expand on these findings by understanding how experts make and communicate opioid decisions in cancer survivors (as opposed to advanced cancer).

In summary, the findings from the dissertation and past and future work help fill critical knowledge and research gaps on optimizing chronic pain, opioid safety, and quality of life in cancer survivors.

Appendix D

Figure 1: Conceptual Model of Chronic Cancer-Related Pain in Cancer Survivors



Acknowledgment

Katie Fitzgerald Jones received grants from the National Institute of Nursing Research F31NR019929-01 and Jonas Philanthropies as a 2021-2023 Mental Health Scholar.

The funders had no role in the designs and conduct of the studies; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript and decision to submit the manuscript for publication.

Master Reference List

Abahussin, A. A., West, R. M., Wong, D. C., & Ziegler, L. E. (2019). PROMs for Pain in Adult Cancer Patients: A Systematic Review of Measurement Properties. *Pain practice: the official journal of World Institute of Pain, 19*(1), 93-117. doi:10.1111/papr.12711

Abbey, G., Thompson, S. B. N., Hickish, T., & Heathcote, D. (2015). A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psycho-Oncology, 24*(4), 371-381. doi:https://doi.org/10.1002/pon.3654

Adler, R. H. (2009). Engel's biopsychosocial model is still relevant today. *Journal of Psychosomatic Research, 67*(6), 607-611. doi:https://doi.org/10.1016/j.jpsychores.2009.08.008

Ahuja, D., Bharati, S. J., Mishra, S., & Bhatnagar, S. (2017). Chronic Cancer Pain: Diagnostic Dilemma and Management Challenges. *Indian Journal of Palliative Care, 23*(4), 480-483. doi:https://dx.doi.org/10.4103/IJPC.IJPC_74_17

Akbas, A., Dagmura, H., Daldal, E., Dasiran, F. M., Deveci, H., & Okan, I. (2021). Association between Shoulder Range of Motion and Pain Catastrophizing Scale in Breast Cancer Patients after Surgery. *Breast Care (Basel), 16*(1), 66-71. doi:10.1159/000506922

Alexander, M. J., Kiang, M. V., & Barbieri, M. (2018). Trends in black and white opioid mortality in the United States, 1979–2015. *Epidemiology (Cambridge, Mass.), 29*(5), 707.

Altekruse, S. F., Cosgrove, C. M., Altekruse, W. C., Jenkins, R. A., & Blanco, C. (2020). Socioeconomic risk factors for fatal opioid overdoses in the United States: Findings from the Mortality Disparities in American Communities Study (MDAC). *PloS one, 15*(1), e0227966-e0227966. doi:10.1371/journal.pone.0227966

Alter, B. J., Anderson, N. P., Gillman, A. G., Yin, Q., Jeong, J. H., & Wasan, A. D. (2021). Hierarchical clustering by patient-reported pain distribution alone identifies distinct chronic pain subgroups differing by pain intensity, quality, and clinical outcomes. *PloS one, 16*(8), e0254862. doi:10.1371/journal.pone.0254862

American Academy of Nursing Practitioners. (April, 2022). *Issues at a Glance: Full Practice Authority*. https://www.aanp.org/advocacy/advocacy-resource/policy-briefs/issues-full-practice-brief

American Cancer Society (2020). ACS Survivorship Compendium. https://www.asco.org/practice-policy/cancer-care-initiatives/prevention-survivorship/survivorship/survivorship-compendium.

Armoogum, J., Harcourt, D., Foster, C., Llewellyn, A., & McCabe, C. S. (2020). The experience of persistent pain in adult cancer survivors: A qualitative evidence synthesis. *European Journal of Cancer Care, 29*(1), e13192. doi:10.1111/ecc.13192

Atkinson, T. M., Mendoza, T. R., Sit, L., Passik, S., Scher, H. I., Cleeland, C., & Basch, E. (2010). The Brief Pain Inventory and Its "Pain At Its Worst in the Last 24 Hours" Item: Clinical Trial Endpoint Considerations. *Pain Medicine, 11*(3), 337-346. doi:10.1111/j.1526-4637.2009.00774.x

Azizoddin, D. R., Adam, R., Kessler, D., Wright, A. A., Kematick, B., Sullivan, C., Enzinger, A. C. (2021). Leveraging mobile health technology and research methodology to optimize patient education and self-management support for advanced cancer pain. *Supportive Care in Cancer, 29*(10), 5741-5751. doi:10.1007/s00520-021-06146-4

Azizoddin, D. R., Beck, M., Flowers, K. M., Wilson, J. M., Chai, P., Johnsky, L., Schreiber, K. L. (2022). Psychological Evaluation of Patients With Cancer Presenting to the Emergency Department With Pain: Independent Predictors of Worse Pain Severity, Interference, and Higher Hourly Opioid Administration. *JCO Oncology Practice*, OP.22.00142. doi:10.1200/OP.22.00142

Azizoddin, D. R., Knoerl, R., Adam, R., Kessler, D., Tulsky, J. A., Edwards, R. R., & Enzinger, A. C. (2021). Cancer pain self-management in the context of a national opioid epidemic: Experiences of patients with advanced cancer using opioids. *Cancer, 127*(17), 3239-3245. doi:10.1002/cncr.33532

Azizoddin, D. R., Schreiber, K., Beck, M. R., Enzinger, A. C., Hruschak, V., Darnall, B.. Mackey, S. (2021). Chronic pain severity, impact, and opioid use among patients with cancer: An analysis of biopsychosocial factors using the CHOIR learning health care system. *Cancer*. doi:10.1002/cncr.33645

Baken, D. M., & Woolley, C. (2011). Validation of the Distress Thermometer, Impact Thermometer and combinations of these in screening for distress. *Psycho-Oncology, 20*(6), 609-614. doi:10.1002/pon.1934

Baker, T. A., Krok-Schoen, J. L., & McMillan, S. C. (2016). Identifying factors of psychological distress on the experience of pain and symptom management among cancer patients. *BMC psychology, 4*(1), 52-52. doi:10.1186/s40359-016-0160-1

Bao, T., Seidman, A., Li, Q., Seluzicki, C., Blinder, V., Meghani, S., Mao, J. (2018). Living with chronic pain: perceptions of breast cancer survivors. *Breast Cancer Research and Treatment, 169*(1), 133-140. doi:10.1007/s10549-018-4670-9

Barbera, L., Sutradhar, R., Howell, D., Corn, E., O'Brien, M. A., Seow, H., Sussman, J. (2019). Factors Associated With Opioid Use in Long-term Cancer Survivors. *Journal of Pain and Symptom Management, 58*(1), 100-107.e102. doi:https://doi.org/10.1016/j.jpainsymman.2019.02.024

Baria, A. M., Pangarkar, S., Abrams, G., & Miaskowski, C. (2018). Adaption of the Biopsychosocial Model of Chronic Noncancer Pain in Veterans. *Pain Medicine, 20*(1), 14-27. doi:10.1093/pm/pny058

Bartley, E. J., & Fillingim, R. B. (2013). Sex differences in pain: a brief review of clinical and experimental findings. *Br J Anaesth, 111*(1), 52-58. doi:10.1093/bja/aet127

Belfer, I., Schreiber, K. L., Shaffer, J. R., Shnol, H., Blaney, K., Morando, A., Bovbjerg, D. H. (2013). Persistent Postmastectomy Pain in Breast Cancer Survivors: Analysis of Clinical, Demographic, and Psychosocial Factors. *The Journal of Pain, 14*(10), 1185-1195. doi:https://doi.org/10.1016/j.jpain.2013.05.002

Bennett, M. I., Eisenberg, E., Ahmedzai, S. H., Bhaskar, A., O'Brien, T., Mercadante, S., Morlion, B. (2019). Standards for the management of cancer-related pain across Europe-

A position paper from the EFIC Task Force on Cancer Pain. *European Journal of Pain, 23*(4), 660-668. doi:10.1002/ejp.1346

Berger, J. M., Longhitano, Y., Zanza, C., & Sener, S. F. (2020). Factors affecting the incidence of chronic pain following breast cancer surgery: Preoperative history, anesthetic management, and surgical technique. *Journal of Surgical Oncology, 122*(7), 1307-1314. doi:https://dx.doi.org/10.1002/jso.26176

Bernard, S. A., Chelminski, P. R., Ives, T. J., & Ranapurwala, S. I. (2018). Management of Pain in the United States—A Brief History and Implications for the Opioid Epidemic. *Health Services Insights, 11*, 1-1. doi:10.1177/1178632918819440

Björkman, B., Arnér, S., & Hydén, L.-C. (2008). Phantom breast and other syndromes after mastectomy: eight breast cancer patients describe their experiences over time: a 2-year follow-up study. *The Journal of Pain, 9*(11), 1018-1025.

Block, S. D. (2001). Psychological considerations, growth, and transcendence at the end of life: the art of the possible. *JAMA, 285*(22), 2898-2905.

Blumenstein, K. G., Brose, A., Kemp, C., Meister, D., Walling, E., DuVall, A. S., & Zhang, A. (2022). Effectiveness of cognitive behavioral therapy in improving functional health in cancer survivors: A systematic review and meta-analysis. *Crit Rev Oncol Hematol, 175*, 103709. doi:10.1016/j.critrevonc.2022.103709

Boyd, R., Lindo, E., Weeks, L. McLemore, M. (July 2, 2020). On Racism: A New Standard foR

Publishing on Racial Health Inequities. doi: 10.1377/hblog20200630.939347

Brebach, R., Sharpe, L., Costa, D. S. J., Rhodes, P., & Butow, P. (2016). Psychological intervention targeting distress for cancer patients: a meta-analytic study investigating uptake and adherence. *Psycho-Oncology, 25*(8), 882-890. doi:https://doi.org/10.1002/pon.4099

Brummett, C. M., Waljee, J. F., Goesling, J., Moser, S., Lin, P., Englesbe, M. J., . . . Nallamothu, B. K. (2017). New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surgery, 152*(6), e170504-e170504.

Bugada, D., Lorini, L. F., & Lavand'homme, P. (2021). Opioid free anesthesia: evidence for short and long-term outcome. *Minerva Anestesiologica, 87*(2), 230-237. doi:https://dx.doi.org/10.23736/S0375-9393.20.14515-2

Bulls, H. W., Bell, L. F., Orris, S. R., Goodin, B. R., Liebschutz, J. M., Wozniak, A., Schenker, Y. (2021). Exemptions to state laws regulating opioid prescribing for patients with cancer-related pain: A summary. *Cancer, n/a*(n/a). doi:https://doi.org/10.1002/cncr.33639

Burke, H., Chow, E., Chow, R., Saunders, K., & Belanger, A. (2017). Needs assessment of primary care physicians in the management of chronic pain in cancer survivors. *Supportive Care in Cancer, 25*(11), 3505-3514. doi:10.1007/s00520-017-3774-9

Bushnell, M. C., Ceko, M., & Low, L. A. (2013). Cognitive and emotional control of pain and its disruption in chronic pain. *Nat Rev Neurosci, 14*(7), 502-511. doi:10.1038/nrn3516

Butera, K. A., Roff, S. R., Buford, T. W., & Cruz-Almeida, Y. (2019). The impact of multisite pain on functional outcomes in older adults: biopsychosocial considerations. *Journal of pain research, 12*, 1115-1125. doi:10.2147/jpr.S192755

Buzaglo, J. S., Zaleta, A. K., McManus, S., Golant, M., & Miller, M. F. (2020). CancerSupportSource®: validation of a revised multi-dimensional distress screening program for cancer patients and survivors. *Supportive Care in Cancer, 28*(1), 55-64.

Carmona-Bayonas, A., Jimenez-Fonseca, P., Castanon, E., Ramchandani-Vaswani, A., Sanchez-Bayona, R., Custodio, A.,Virizuela, J. A. (2017). Chronic opioid therapy in long-term cancer survivors. *Clinical & Translational Oncology, 19*(2), 236-250. doi:10.1007/s12094-016-1529-6

Cass, A. S., Alese, J. T., Kim, C., Curry, M. A., LaFollette, J. A., Chen, Z. J., & Alese, O. B. (2018). Analysis of Opioid Use Following Curative Cancer Treatment at a Large Urban Safety-net Hospital. *Clinical Journal of Pain, 34*(10), 885-889. doi:10.1097/ajp.0000000000000612

Cata, J. P., Patino, M., Gorur, A., Du, K. N., Uhelski, M. L., Myers, J., Owusu-Agyemang, P. (2019). Persistent and Chronic Postoperative Opioid Use in a Cohort of Patients with Oral Tongue Squamous Cell Carcinoma. *Pain Medicine*. doi:10.1093/pm/pnz242

Center for Disease Control prescribing trends (2019). *Drug Overdose Deaths and Prescribing Practices.* https://www.cdc.gov/drugoverdose/data/prescribing/prescribing-practices.htmlhealthcare.

Chandrasekar, D., Tribett, E., & Ramchandran, K. (2016). Integrated Palliative Care and Oncologic Care in Non-Small-Cell Lung Cancer. *Current Treatment Options in Oncology, 17*(5). doi:10.1007/s11864-016-0397-1

Chaturvedi, S. K. (2012). Psychiatric oncology: Cancer in mind. *Indian Journal of Psychiatry, 54*(2), 111-118. doi:10.4103/0019-5545.99529

Check, D. K., Avecilla, R. A. V., Mills, C., Dinan, M. A., Kamal, A. H., Murphy, B., . . . Oeffinger, K. C. (2022). Opioid Prescribing and Use Among Cancer Survivors: A Mapping Review of Observational and Intervention Studies. *Journal of Pain and Symptom Management, 63*(4), e397-e417. doi:10.1016/j.jpainsymman.2021.10.015

Check, D., Jones, KF., Fish, L, Dinan, M., Dunbar, T., Farley, S., Ma, J., Merlin, J., O'Regan, A., Oeffinger, K. JCO Oncology Practice (2022, in press). Clinician Perspectives on Managing Chronic Pain after Curative-Intent Cancer Treatment.

Chen, I., Kurz, J., Pasanen, M., Faselis, C., Panda, M., Staton, L.,Wood, J. (2005). Racial differences in opioid use for chronic nonmalignant pain. *Journal of General Internal Medicine, 20*(7), 593-598.

Chen, L., Chubak, J., Yu, O., Pocobelli, G., Ziebell, R. A., Aiello Bowles, E. J., Boudreau, D. M. (2019). Changes in use of opioid therapy after colon cancer diagnosis: a population-based study. *Cancer Causes & Control, 30*(12), 1341-1350. doi:10.1007/s10552-019-01236-5

Chen, L., Chubak, J., Yu, O., Pocobelli, G., Ziebell, R. A., Bowles, E. J. A., Boudreau, D. M. (2019). Changes in use of opioid therapy after colon cancer diagnosis: a population-based study. *Cancer Causes & Control, 30*(12), 1341-1350. doi:10.1007/s10552-019-01236-5

Cheng, J., Rutherford, M., & Singh, V. (2019). The HHS Pain Management Best Practice Inter-Agency Task Force Report Calls for Patient-Centered and Individualized Care. *Pain Medicine, 21*(1), 1-3. doi:10.1093/pm/pnz303

Cheville, A. L., Moynihan, T., Herrin, J., Loprinzi, C., & Kroenke, K. (2019). Effect of Collaborative Telerehabilitation on Functional Impairment and Pain Among Patients With

Advanced-Stage Cancer: A Randomized Clinical Trial. *JAMA Oncology, 5*(5), 644-652. doi:10.1001/jamaoncol.2019.0011

Chou, R., Turner, J. A., Devine, E. B., Hansen, R. N., Sullivan, S. D., Blazina, I., Deyo, R. A. (2015). The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop. *Annals of Internal Medicine, 162*(4), 276-286. doi:10.7326/m14-2559

Chow, R., Saunders, K., Burke, H., Belanger, A., & Chow, E. (2017). Needs assessment of primary care physicians in the management of chronic pain in cancer survivors. *Support Care Cancer, 25*(11), 3505-3514. doi:10.1007/s00520-017-3774-9

Chwistek, M., Ewerth, N., Amrhein, S. G., & Ebersole, B. (2016). "Why do I still hurt?" an integrated model of survivorship and palliative care. *Journal of Pain and Symptom Management, 51*(2), 396. Retrieved from http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L72204758

Clarke, H., Soneji, N., Ko, D. T., Yun, L., & Wijeysundera, D. N. (2014). Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ,* 348:g1251.

Coggon, D., Ntani, G., Palmer, K. T., Felli, V. E., Harari, R., Barrero, L. H., Gray, A. (2013). Patterns of multisite pain and associations with risk factors. *Pain, 154*(9), 1769-1777. doi:10.1016/j.pain.2013.05.039

Cohen, E., Botti, M., Hanna, B., Leach, S., Boyd, S., & Robbins, J. (2008). Pain beliefs and pain management of oncology patients. *Cancer Nursing, 31*(2), E1-8. doi:https://dx.doi.org/10.1097/01.NCC.0000305693.67131.7d

Cohen, J. (2013). *Statistical power analysis for the behavioral sciences*: Routledge: Lawrence Erlbaum Associate Publishers.

Center for Diease Control Prevention and Control. (2017). Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Wkly Rep 2017; 66:265-269.

Cook, R. D. (1977). Detection of influential observation in linear regression. *Technometrics, 19*(1), 15-18.

Cooper, J. M., Loeb, S. J., & Smith, C. A. (2010). The primary care nurse practitioner and cancer survivorship care. *Journal of the American Association of Nurse Practitioners, 22*(8). Retrieved from https://journals.lww.com/jaanp/Fulltext/2010/08000/The_primary_care_nurse_practitioner_and_cancer.2.aspx

Cordova, M. J., Riba, M. B., & Spiegel, D. (2017). Post-traumatic stress disorder and cancer. *Lancet Psychiatry, 4*(4), 330-338. doi:10.1016/s2215-0366(17)30014-7

Courtenay, M., & Carey, N. (2008). The impact and effectiveness of nurse-led care in the management of acute and chronic pain: a review of the literature. *Journal of Clinical Nursing, 17*(15), 2001-2013. doi:https://doi.org/10.1111/j.1365-2702.2008.02361.x

Cramer, J. D., Johnson, J. T., & Nilsen, M. L. (2018). Pain in Head and Neck Cancer Survivors: Prevalence, Predictors, and Quality-of-Life Impact. *Otolaryngology–Head and Neck Surgery, 159*(5), 853-858. doi:10.1177/0194599818783964

Creţu, I., Bojincă, M., Milicescu, M., Cursaru, A., Șerban, B., Crețu, B., . . . Ionescu, R. (2021). Musculoskeletal adverse reactions after immunotherapy for cancer: A case series. *Experimental and Therapeutic Medicine, 22*(3), 1027-1027. doi:10.3892/etm.2021.10459

Custers, J. A., van den Berg, S. W., van Laarhoven, H. W., Bleiker, E. M., Gielissen, M. F., & Prins, J. B. (2014). The Cancer Worry Scale: detecting fear of recurrence in breast cancer survivors. *Cancer Nurs, 37*(1), E44-50. doi:10.1097/NCC.0b013e3182813a17

Daitch, D., Daitch, J., Novinson, D., Frey, M., Mitnick, C., & Pergolizzi, J., Jr. (2014). Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients. *Pain Medicine, 15*(12), 2087-2094. doi:10.1111/pme.12520

Daniels, S. (2015). Cognitive Behavior Therapy for Patients With Cancer. *Journal of the advanced practitioner in oncology, 6*(1), 54-56.

Darawad, M., Alnajar, M. K., Abdalrahim, M. S., & El-Aqoul, A. M. (2019). Cancer Pain Management at Oncology Units: Comparing Knowledge, Attitudes and Perceived Barriers Between Physicians and Nurses. *Journal of Cancer Education, 34*(2), 366-374. doi:10.1007/s13187-017-1314-4

Darchuk, K. M., Townsend, C. O., Rome, J. D., Bruce, B. K., & Hooten, W. M. (2010). Longitudinal treatment outcomes for geriatric patients with chronic non-cancer pain at an

interdisciplinary pain rehabilitation program. *Pain medicine (Malden, Mass.), 11*(9), 1352-1364. doi:https://dx.doi.org/10.1111/j.1526-4637.2010.00937.x

Darnall, B. D. (2019). *Psychological Treatments for Patients with Chronic Pain*. Washington, DC: American Psychological Association.

Darnall, B.D, Juurlink, D., Kerns, R. D., Mackey, S., Van Dorsten, B., Humphreys, K., Lovejoy, T. (2018). International Stakeholder Community of Pain Experts and Leaders Call for an Urgent Action on Forced Opioid Tapering. *Pain Medicine, 20*(3), 429-433. doi:10.1093/pm/pny228

Darnall, B. D., Roy, A., Chen, A. L., Ziadni, M. S., Keane, R. T., You, D. S., Mackey, S. C. (2021). Comparison of a Single-Session Pain Management Skills Intervention With a Single-Session Health Education Intervention and 8 Sessions of Cognitive Behavioral Therapy in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. *JAMA Network Open, 4*(8), e2113401-e2113401. doi:10.1001/jamanetworkopen.2021.13401

Darnall, B. D., Scheman, J., Davin, S., Burns, J. W., Murphy, J. L., Wilson, A. C., Mackey, S. C. (2016). Pain Psychology: A Global Needs Assessment and National Call to Action. *Pain medicine (Malden, Mass.), 17*(2), 250-263. doi:10.1093/pm/pnv095

Darnall, B. D., Ziadni, M. S., Krishnamurthy, P., Flood, P., Heathcote, L. C., Mackey, I. G., . . . Wheeler, A. (2019). "My Surgical Success": Effect of a Digital Behavioral Pain Medicine Intervention on Time to Opioid Cessation After Breast Cancer Surgery-A Pilot Randomized Controlled Clinical Trial. *Pain medicine (Malden, Mass.), 20*(11), 2228-2237. doi:https://dx.doi.org/10.1093/pm/pnz094

Dassieu, L., Heino, A., Develay, E., Kabore, J. L., Page, M. G., Moor, G., Choiniere, M. (2021). "They think you're trying to get the drug": Qualitative investigation of chronic pain patients' health care experiences during the opioid overdose epidemic in Canada. *Canadian journal of pain, 5*(1), 66-80. doi:https://dx.doi.org/10.1080/24740527.2021.1881886

Dean, G. E., Weiss, C., Jungquist, C. R., Klimpt, M. L., Alameri, R., Ziegler, P. A., . . . Dickerson, S. S. (2020). Nurse-Delivered Brief Behavioral Treatment for Insomnia in Lung Cancer Survivors: A Pilot RCT. *Behav Sleep Med, 18*(6), 774-786. doi:10.1080/15402002.2019.1685523

Delgado-Guay, M., Parsons, H. A., Li, Z., Palmer, J. L., & Bruera, E. (2009). Symptom distress in advanced cancer patients with anxiety and depression in the palliative care setting. *Supportive Care in Cancer, 17*(5), 573-579. doi:10.1007/s00520-008-0529-7

Desai, R., Camacho, F., Tan, X., LeBaron, V., Blackhall, L., & Balkrishnan, R. (2019). Mental health comorbidities and elevated risk of opioid use in elderly breast cancer survivors using adjuvant endocrine treatments. *Journal of oncology practice, 15*(9), E777-E786. doi:10.1200/JOP.18.00781

Deyo, R. A., Hallvik, S. E., Hildebran, C., Marino, M., Dexter, E., Irvine, J. M., Millet, L. M. (2017). Association Between Initial Opioid Prescribing Patterns and Subsequent Long-Term Use Among Opioid-Naïve Patients: A Statewide Retrospective Cohort Study. *Journal of General Internal Medicine, 32*(1), 21-27. doi:10.1007/s11606-016-3810-3

Dory, G., Qiu, Z., Qiu, C. M., Fu, M. R., & Ryan, C. E. (2017). A phenomenological understanding of residents' emotional distress of living in an environmental justice

community. *International Journal of Qualitative Studies on Health and Well-being, 12*(1), 1269450. doi:10.1080/17482631.2016.1269450

Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. *JAMA: Journal of the American Medical Association, 315*(15), 1624-1645. doi:10.1001/jama.2016.1464

Doyle, L., Brady, A.-M., & Byrne, G. (2016). An overview of mixed methods research – revisited. *Journal of Research in Nursing, 21*(8), 623-635. doi:10.1177/1744987116674257

Driscoll, M. A., Edwards, R. R., Becker, W. C., Kaptchuk, T. J., & Kerns, R. D. (2021). Psychological Interventions for the Treatment of Chronic Pain in Adults. *Psychological Science in the Public Interest, 22*(2), 52-95. doi:10.1177/15291006211008157

Dworkin, R. H., Turk, D. C., Farrar, J. T., Haythornthwaite, J. A., Jensen, M. P., Katz, N. P., Witter, J. (2005). Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain, 113*(1), 9-19. doi:10.1016/j.pain.2004.09.012

Edmond, S. N., Currie, S., Gehrke, A., Falker, C. G., Sung, M., Abelleira, A., Becker, W. C. (2022). Optimizing Interdisciplinary Virtual Pain Care and Buprenorphine Initiation During COVID-19: A Quality Improvement Study. *Pain Med, 23*(6), 1043-1046. doi:10.1093/pm/pnab348

ElMokhallalati, Y., Mulvey, M. R., & Bennett, M. I. (2018). Interventions to support self-management in cancer pain. *Pain reports, 3*(6), e690. doi:10.1097/pr9.0000000000000690

Feldenzer, K., Rosenzweig, M., Soodalter, J. A., & Schenker, Y. (2019). Nurses' perspectives on the personal and professional impact of providing nurse-led primary palliative care in outpatient oncology settings. *International Journal of Palliative Nursing, 25*(1), 30-37. doi:10.12968/ijpn.2019.25.1.30

Ferrell, B. R., & Coyle, N. (2008). The nature of suffering and the goals of nursing. *Oncol Nurs Forum, 35*(2), 241-247. doi:10.1188/08.Onf.241-247

Finlayson, C. S., Chen, Y. T., & Fu, M. R. (2015). The impact of patients' awareness of disease status on treatment preferences and quality of life among patients with metastatic cancer: a systematic review from 1997–2014. *Journal of Palliative Medicine, 18*(2), 176-186. doi: 10.1089/jpm.2014.0222. PMID: 25259624

Finnell, D. S., Tierney, M., & Mitchell, A. M. (2019). Nursing: Addressing substance use in the 21st century. *Substance abuse, 40*(4), 412-420. doi:10.1080/08897077.2019.1674240

Fishbain, D. A., & Pulikal, A. (2018). Does Opioid Tapering in Chronic Pain Patients Result in Improved Pain or Same Pain vs Increased Pain at Taper Completion? A Structured Evidence-Based Systematic Review. *Pain Medicine, 20*(11), 2179-2197. doi:10.1093/pm/pny231

Fredheim, O. M., Skurtveit, S., Handal, M., & Hjellvik, V. (2019). A complete national cohort study of prescriptions of analgesics and benzodiazepines to cancer survivors in Norway 10 years after diagnosis. *Pain, 160*(4), 852-859. doi:10.1097/j.pain.0000000000001459

Fu, M. R. (2005). Breast cancer survivors' intentions of managing lymphedema. *Cancer Nursing, 28*(6), 446-457; quiz 458-449. doi:10.1097/00002820-200511000-00007

Fu, M. R., Axelrod, D., Guth, A. A., Rampertaap, K., El-Shammaa, N., Hiotis, K., Wang, Y. (2016). mHealth self-care interventions: managing symptoms following breast cancer treatment. *mHealth, 2*, 28. doi:10.21037/mhealth.2016.07.03

Fu, M. R., Ridner, S. H., Hu, S. H., Stewart, B. R., Cormier, J. N., & Armer, J. M. (2013). Psychosocial impact of lymphedema: a systematic review of literature from 2004 to 2011. *Psycho-Oncology, 22*(7), 1466-1484. doi:10.1002/pon.3201

Fu, M. R., & Rosedale, M. (2009). Breast cancer survivors' experiences of lymphedema-related symptoms. *Journal of Pain and Symptom Management, 38*(6), 849-859. doi:10.1016/j.jpainsymman.2009.04.030

Fu, M. R., Xu, B., Liu, Y., & Haber, J. (2008). 'Making the best of it': Chinese women's experiences of adjusting to breast cancer diagnosis and treatment. *Journal of Advanced Nursing, 63*(2), 155-165.

Gallaway, M. S., Townsend, J. S., Shelby, D., & Puckett, M. C. (2020). Pain Among Cancer Survivors. *Prev Chronic Dis, 17*, E54. doi:10.5888/pcd17.190367

Ganju, R., Neeranjun, R., Morse, R., Lominska, C., TenNapel, M., & Chen, A. (2019). Incidence and Predictors of Persistent Opioid Use in Long-term Survivors of Head and Neck Cancer Treated with Radiation. *International Journal of Radiation Oncology Biology Physics, 103*(5), E2. doi:10.1016/S0360-3016(19)30405-5

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull, 133*(4), 581-624. doi:10.1037/0033-2909.133.4.581

Generaal, E., Milaneschi, Y., Jansen, R., Elzinga, B. M., Dekker, J., & Penninx, B. W. J. H. (2016). The brain-derived neurotrophic factor pathway, life stress, and chronic multi-site musculoskeletal pain. *Molecular Pain, 12*, 1744806916646783. doi:10.1177/1744806916646783

Glare, P. A., Davies, P. S., Finlay, E., Gulati, A., Lemanne, D., Moryl, N., Syrjala, K. L. (2014). Pain in cancer survivors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 32*(16), 1739-1747. doi:10.1200/JCO.2013.52.4629

Golan-Vered, Y., & Pud, D. (2013). Chemotherapy-Induced Neuropathic Pain and Its Relation to Cluster Symptoms in Breast Cancer Patients Treated with Paclitaxel. *Pain Practice, 13*(1), 46-52. doi:10.1111/j.1533-2500.2012.00554.x

Gomes, T., Juurlink, D. N., Antoniou, T., Mamdani, M. M., Paterson, J. M., & van den Brink, W. (2017). Gabapentin, opioids, and the risk of opioid-related death: a population-based nested case–control study. *PLoS medicine, 14*(10), e1002396.

Goodlev, E. R., Discala, S., Darnall, B. D., Hanson, M., Petok, A., & Silverman, M. (2019). Managing Cancer Pain, Monitoring for Cancer Recurrence, and Mitigating Risk of Opioid Use Disorders: A Team-Based, Interdisciplinary Approach to Cancer Survivorship. *Journal of Palliative Medicine, 22*(11), 1308-1317.

Grace, P. &Zumstein, M. (2019). Using Ockham's razor to redefine "nursing science". *Nursing Philosophy*(e12246), 1-8.

Green, C. R., Hart-Johnson, T., & Loeffler, D. R. (2011). Cancer-related chronic pain. *Cancer, 117*(9), 1994-2003. doi:10.1002/cncr.25761

Hah, J., Mackey, S. C., Schmidt, P., McCue, R., Humphreys, K., Trafton, J., Carroll, I. (2018). Effect of Perioperative Gabapentin on Postoperative Pain Resolution and Opioid Cessation in a Mixed Surgical Cohort: A Randomized Clinical Trial. *JAMA Surgery, 153*(4), 303-311. doi:10.1001/jamasurg.2017.4915

Hefner, J., Kapp, M., Drebinger, K., Dannenmann, A., Einsele, H., Grigoleit, G. U., Mielke, S. (2014). High prevalence of distress in patients after allogeneic hematopoietic SCT: Fear of progression is associated with a younger age. *Bone Marrow Transplantation, 49*(4), 581-584. doi:10.1038/bmt.2013.228

Hellerstedt-Börjesson, S., Nordin, K., Fjällskog, M.-L., Holmström, I. K., & Arving, C. (2016). Women treated for breast cancer experiences of chemotherapy-induced pain: memories, any present pain, and future reflections. *Cancer Nursing, 39*(6), 464.

Henry, M., Alias, A., Frenkiel, S., Richardson, K., Hier, M., Zeitouni, A., Rosberger, Z. (2019). Contribution of psychiatric diagnoses to extent of opioid prescription in the first year post-head and neck cancer diagnosis: A longitudinal study. *Psycho-Oncology, 28*(1), 107-115. doi:10.1002/pon.4917

Henry, S. G., & Matthias, M. S. (2018). Patient-Clinician Communication About Pain: A Conceptual Model and Narrative Review. *Pain Medicine, 19*(11), 2154-2165. doi:10.1093/pm/pny003

Hermesdorf, M., Berger, K., Baune, B. T., Wellmann, J., Ruscheweyh, R., & Wersching, H. (2016). Pain Sensitivity in Patients With Major Depression: Differential Effect of Pain Sensitivity Measures, Somatic Cofactors, and Disease Characteristics. *The Journal of Pain, 17*(5), 606-616. doi:https://doi.org/10.1016/j.jpain.2016.01.474

Hernandez Silva, E., Lawler, S., & Langbecker, D. (2019). The effectiveness of mHealth for self-management in improving pain, psychological distress, fatigue, and sleep in cancer survivors: a systematic review. *Journal of cancer survivorship : research and practice, 13*(1), 97-107. doi:10.1007/s11764-018-0730-8

Ho, J., Jones, K. F., Sager, Z., Neale, K., Childers, J. W., Loggers, E., & Merlin, J. (2022). Barriers to Buprenorphine Prescribing for Opioid Use Disorder in Hospice and Palliative Care. *J Pain Symptom Manage*. doi:10.1016/j.jpainsymman.2022.05.004

Hoffman, K. M., Trawalter, S., Axt, J. R., & Oliver, M. N. (2016). Racial bias in pain assessment and treatment recommendations, and false beliefs about biological differences between blacks and whites. *Proceedings of the National Academy of Sciences*, 201516047. doi:10.1073/pnas.1516047113

Hooten, W. M., Brummett, C. M., Sullivan, M. D., Goesling, J., Tilburt, J. C., Merlin, J.,. Warner, D. O. (2017). A Conceptual Framework for Understanding Unintended Prolonged Opioid Use. *Mayo Clin Proc, 92*(12), 1822-1830. doi:10.1016/j.mayocp.2017.10.010

Hovind, I. L., Bredal, I. S., & Dihle, A. (2013). Women's experience of acute and chronic pain following breast cancer surgery. *Journal of Clinical Nursing, 22*(7-8), 1044-1052.

Husserl, E. (1931). Sciences of the dogmatic and sciences of the philosophical standpoint Ideas: General Introduction to Pure Phenomenology. In: New York: Routledge.

James, J. R., Scott, J. M., Klein, J. W., Jackson, S., McKinney, C., Novack, M., Merrill, J. O. (2019). Mortality After Discontinuation of Primary Care-Based Chronic Opioid Therapy for Pain: a Retrospective Cohort Study. *J Gen Intern Med, 34*(12), 2749-2755. doi:10.1007/s11606-019-05301-2

Institute of Medicine (2005). *From Cancer Patient to Cancer Survivor: Lost in Translation*. Washington, DC: The National Academies Press.

Jammu, A. S., Chasen, M. R., Lofters, A. K., & Bhargava, R. (2021). Systematic rapid living review of the impact of the COVID-19 pandemic on cancer survivors: update to August 27, 2020. *Supportive Care in Cancer, 29*(6), 2841-2850. doi:10.1007/s00520-020-05908-w

Jaremka, L. M., Fagundes, C. P., Glaser, R., Bennett, J. M., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2013). Loneliness predicts pain, depression, and fatigue: Understanding the role of immune dysregulation. *Psychoneuroendocrinology, 38*(8), 1310-1317. doi:https://doi.org/10.1016/j.psyneuen.2012.11.016

Jena, M., Mishra, S., Pradhan, S., Jena, S., & Mishra, S. S. (2015). Chronic pain, its management and psychological issues: A review. *Asian Journal of Pharmaceutical and Clinical Research, 8*(5), 42-47. Retrieved from https://www.embase.com/search/results?subaction=viewrecord&id=L605918427&from=export

Jiang, C., Wang, H., Wang, Q., Luo, Y., Sidlow, R., & Han, X. (2019). Prevalence of Chronic Pain and High-Impact Chronic Pain in Cancer Survivors in the United States. *JAMA Oncology, 5*(8), 1224-1226. doi:10.1001/jamaoncol.2019.1439

Jones, K. F. (2019). Buprenorphine Use in Palliative Care. *J Hosp Palliat Nurs, 21*(6), 540-547. doi:10.1097/njh.0000000000000598

Jones, K. F., Abdulhay, L. B., Orris, S. R., Merlin, J. S., Schenker, Y., & Bulls, H. W. The Relevance of State Laws Regulating Opioid Prescribing for People Living with Serious

Illness. *Journal of Pain and Symptom Management*. doi:10.1016/j.jpainsymman.2022.05.001

Jones, K. F., Fu, M. R., Merlin, J. S., Paice, J. A., Bernacki, R., Lee, C., & Wood, L. J. (2021). Exploring Factors Associated With Long-Term Opioid Therapy in Cancer Survivors: An Integrative Review. *Journal of Pain and Symptom Management, 61*(2), 395-415. doi:https://doi.org/10.1016/j.jpainsymman.2020.08.015

Jones, K. F., & Mason, D. J. (2022). The False Dichotomy of Pain and Opioid Use Disorder. *JAMA Health Forum, 3*(4), e221406-e221406. doi:10.1001/jamahealthforum.2022.1406

Jones, K. F., & Merlin, J. S. (2021). Approaches to opioid prescribing in cancer survivors: Lessons learned from the general literature. *Cancer*. doi:10.1002/cncr.33961

Jones, K.F., Khodyakov, D., Arnold, R., Bulls, H., Dao, E., Kapo, J., Merlin, J. (2022). Consensus-Based Guidance on Opioid Management in Individuals With Advanced Cancer-Related Pain and Opioid Misuse or Use Disorder. *JAMA Oncology*. doi:10.1001/jamaoncol.2022.2191

Kadan-Lottick, N. S., Vanderwerker, L. C., Block, S. D., Zhang, B., & Prigerson, H. G. (2005). Psychiatric disorders and mental health service use in patients with advanced cancer. *Cancer, 104*(12), 2872-2881. doi:10.1002/cncr.21532

Karmali, R. N., Bush, C., Raman, S. R., Campbell, C. I., Skinner, A. C., & Roberts, A. W. (2020). Long-term opioid therapy definitions and predictors: A systematic review. *Pharmacoepidemiology and drug safety, 29*(3), 252-269. doi:10.1002/pds.4929

Kaur, A., Doberstein, T., Amberker, R. R., Garje, R., Field, E. H., Singh, N., & Sinnberg, T. (2019). Immune-related adverse events in cancer patients treated with immune

checkpoint inhibitors: A single-center experience. *Medicine (United States), 98*(41). doi:10.1097/MD.0000000000017348

Kawi, J., Duke, A., & Maduka, G. (2020). Self-Efficacy and Multisite Pain Predictors among Economically Disadvantaged Women with Back Pain. *Pain Manag Nurs, 21*(4), 307-313. doi:10.1016/j.pmn.2020.03.001

Kligler, B., Buonora, M., Gabison, J., Jacobs, E., Karasz, A., & McKee, M. D. (2015). "I Felt Like It Was God's Hands Putting the Needles In": A Qualitative Analysis of the Experience of Acupuncture for Chronic Pain in a Low-Income, Ethnically Diverse, and Medically Underserved Patient Population. *J Altern Complement Med, 21*(11), 713-719. doi:10.1089/acm.2014.0376

Klimas, J., Gorfinkel, L., Fairbairn, N., Amato, L., Ahamad, K., Nolan, S., Wood, E. (2019). Strategies to Identify Patient Risks of Prescription Opioid Addiction When Initiating Opioids for Pain: A Systematic Review. *JAMA Network Open, 2*(5), e193365-e193365. doi:10.1001/jamanetworkopen.2019.3365

Knoerl, R., Smith, E. M., Barton, D. L., Williams, D. A., Holden, J. E., Krauss, J. C., & LaVasseur, B. (2018). Self-guided online cognitive behavioral strategies for chemotherapy-induced peripheral neuropathy: A multicenter, pilot, randomized, wait-list controlled trial. *The Journal of Pain, 19*(4), 382-394.

Kong, J. T., You, D. S., Law, C. S. W., Darnall, B. D., Gross, J. J., Manber, R., & Mackey, S. (2021). Association between temporal summation and conditioned pain modulation in chronic low back pain: baseline results from 2 clinical trials. *Pain reports, 6*(4), e975. doi:10.1097/pr9.0000000000000975

Kroenke, K., Theobald, D., Wu, J., Loza, J. K., Carpenter, J. S., & Tu, W. (2010). The Association of Depression and Pain with Health-Related Quality of Life, Disability, and Health Care Use in Cancer Patients. *Journal of Pain and Symptom Management, 40*(3), 327-341. doi:https://doi.org/10.1016/j.jpainsymman.2009.12.023

Kwon, J. H., Hui, D., Chisholm, G., & Bruera, E. (2013). Predictors of long-term opioid treatment among patients who receive chemoradiation for head and neck cancer. *The oncologist, 18*(6), 768.

Lagisetty, P. A., Ross, R., Bohnert, A., Clay, M., & Maust, D. T. (2019). Buprenorphine Treatment Divide by Race/Ethnicity and Payment. *JAMA Psychiatry, 76*(9), 979-981. doi:10.1001/jamapsychiatry.2019.0876

Laroche, F., Perrot, S., Medkour, T., Cottu, P.-H., Pierga, J.-Y., Lotz, J.-P., Coste, J. (2017). Quality of life and impact of pain in women treated with aromatase inhibitors for breast cancer. A multicenter cohort study. *PloS one, 12*(11), e0187165. doi:10.1371/journal.pone.0187165

Leach, C. R., Weaver, K. E., Aziz, N. M., Alfano, C. M., Bellizzi, K. M., Kent, E. E., Rowland, J. H. (2015). The complex health profile of long-term cancer survivors: prevalence and predictors of comorbid conditions. *Journal of Cancer Survivorship, 9*(2), 239-251.

Leano, A., Korman, M. B., Goldberg, L., & Ellis, J. (2019). Are we missing PTSD in our patients with cancer? Part I. *Can Oncol Nurs J, 29*(2), 141-146.

Lebel, S., Simard, S., Harris, C., Feldstain, A., Beattie, S., McCallum, M., Devins, G. M. (2016). Empirical validation of the English version of the Fear of Cancer Recurrence Inventory. *Qual Life Res, 25*(2), 311-321. doi:10.1007/s11136-015-1088-2

Lee, J. S.-J., Hu, H. M., Edelman, A. L., Brummett, C. M., Englesbe, M. J., Waljee, J. F.,Dossett, L. A. (2017). New Persistent Opioid Use Among Patients With Cancer After Curative-Intent Surgery. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 35*(36), 4042-4049. doi:10.1200/JCO.2017.74.1363

Lee, J. S. J., Hu, H. M., Edelman, A. L., Brummett, C. M., Englesbe, M. J., Waljee, J. F., Dossett, L. A. (2017). New Persistent Opioid Use Among Patients With Cancer After Curative-Intent Surgery. *Journal of Clinical Oncology, 35*(36), 4042-+. doi:10.1200/jco.2017.74.1363

Leysen, L., Cools, W., Nijs, J., Adriaenssens, N., Pas, R., van Wilgen, C. P., Beckwée, D. (2021). The mediating effect of pain catastrophizing and perceived injustice in the relationship of pain on health-related quality of life in breast cancer survivors. *Supportive Care in Cancer, 29*(10), 5653-5661. doi:10.1007/s00520-021-06011-4

Li, H., Wu, J., Ni, Q., Zhang, J., Wang, Y., & He, G. (2021). Systematic review and meta-analysis of effectiveness of acceptance and commitment therapy in patients with breast cancer. *Nursing research, 70*(4), E152-E160.

Lincoln, Y. S., & Guba, E. G. (1985). *Naturalistic inquiry*. Sage Publications, Inc.

Liou, K. T., Hung, T. K. W., Meghani, S. H., Epstein, A. S., Li, Q. S., Romero, S. A. D., Mao, J. J. (2019). What if Acupuncture Were Covered by Insurance for Pain Management? A Cross-Sectional Study of Cancer Patients at One Academic Center and 11 Community Hospitals. *Pain Medicine, 20*(10), 2060-2068. doi:10.1093/pm/pnz087

Ludwick, A., Corey, K., & Meghani, S. (2020). Racial and Socioeconomic Factors Associated with the Use of Complementary and Alternative Modalities for Pain in Cancer

Outpatients: An Integrative Review. *Pain Management Nursing, 21*(2), 142-150. doi:https://doi.org/10.1016/j.pmn.2019.08.005

Luigjes-Huizer, Y. L., Tauber, N. M., Humphris, G., Kasparian, N. A., Lam, W. W. T., Lebel, S., van der Lee, M. L. (2022). What is the prevalence of fear of cancer recurrence in cancer survivors and patients? A systematic review and individual participant data meta-analysis. *Psycho-Oncology, 31*(6), 879-892. doi:https://doi.org/10.1002/pon.5921

Manchikanti, L., Manchikanti, K. N., Kaye, A. D., Kaye, A. M., & Hirsch, J. A. (2018). Challenges and concerns of persistent opioid use in cancer patients. *Expert Review of Anticancer Therapy, 18*(7), 705-718. doi:10.1080/14737140.2018.1474103

Martin, L. W., Sarosiek, B. M., Harrison, M. A., Hedrick, T., Isbell, J. M., Krupnick, A. S., Walters, D. M. (2018). Implementing a thoracic enhanced recovery program: lessons learned in the first year. *The Annals of thoracic surgery, 105*(6), 1597-1604.

Matthias, M. S., & Henry, S. G. (2022). Reducing Frustration and Improving Management of Chronic Pain in Primary Care: Is Shared Decision-making Sufficient? *Journal of General Internal Medicine, 37*(1), 227-228. doi:10.1007/s11606-021-06967-3

Matthias, M. S., Hirsh, A. T., Ofner, S., & Daggy, J. (2022). Exploring the Relationships Among Social Support, Patient Activation, and Pain-Related Outcomes. *Pain Medicine, 23*(4), 676-685. doi:10.1093/pm/pnab306

McDermott, J. D., Eguchi, M., Stokes, W. A., Amini, A., Hararah, M., Ding, D., Karam, S. D. (2019). Short- and Long-term Opioid Use in Patients with Oral and Oropharynx Cancer. *Otolaryngology--head and neck surgery : official journal of American Academy of*

Otolaryngology-Head and Neck Surgery, 160(3), 409-419. doi:10.1177/0194599818808513

Meghani, S. H., Byun, E., & Gallagher, R. M. (2012). Time to take stock: a meta-analysis and systematic review of analgesic treatment disparities for pain in the United States. *Pain Med, 13*(2), 150-174. doi:10.1111/j.1526-4637.2011.01310.x

Meghani, S. H., & Chittams, J. (2015). Controlling for Socioeconomic Status in Pain Disparities Research: All-Else-Equal Analysis When “All Else” Is Not Equal. *Pain Medicine, 16*(12), 2222-2225. doi:10.1111/pme.12829

Meghani, S. H., Kang, Y., Chittams, J., McMenamin, E., Mao, J. J., & Fudin, J. (2014). African Americans with cancer pain are more likely to receive an analgesic with toxic metabolite despite clinical risks: a mediation analysis study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 32*(25), 2773-2779. doi:10.1200/JCO.2013.54.7992

Meghani, S. H., & Vapiwala, N. (2018). Bridging the critical divide in pain management guidelines from the CDC, NCCN, and ASCO for cancer survivors. *JAMA Oncology, 4*(10), 1323-1324.

Mehta, A., & Chan, L. S. (2008). Understanding of the concept of" total pain": a prerequisite for pain control. *Journal of Hospice & Palliative Nursing, 10*(1), 26-32.

Merlin, J. S., Childers, J., & Arnold, R. M. (2012). Chronic Pain in the Outpatient Palliative Care Clinic. *American Journal of Hospice and Palliative Medicine®, 30*(2), 197-203. doi:10.1177/1049909112443587

Merlin, J. S., Khodyakov, D., Arnold, R., Bulls, H. W., Dao, E., Kapo, J. Liebschutz, J. M. (2021). Expert Panel Consensus on Management of Advanced Cancer–Related Pain in Individuals With Opioid Use Disorder. *JAMA Network Open, 4*(12), e2139968-e2139968. doi:10.1001/jamanetworkopen.2021.39968

Merlin, J. S., Patel, K., Thompson, N., Kapo, J., Keefe, F., Liebschutz, J., Ritchie, C. S. (2019). Managing Chronic Pain in Cancer Survivors Prescribed Long-Term Opioid Therapy: A National Survey of Ambulatory Palliative Care Providers. *Journal of Pain and Symptom Management, 57*(1), 20-27. doi:10.1016/j.jpainsymman.2018.10.493

Merlin, J. S., Tucker, R. O., Saag, M. S., & Selwyn, P. A. (2013). The role of palliative care in the current HIV treatment era in developed countries. *Topics in Antiviral Medicine, 21*(1), 20-26. Retrieved from https://www.embase.com/search/results?subaction=viewrecord&id=L369093210&from=exporthttps://www.iasusa.org/sites/default/files/tam/21-1-20.pdf

Merlin, J. S., Walcott, M., Ritchie, C., Herbey, I., Kertesz, S. G., Chamot, E., Turan, J. M. (2014). 'Two Pains Together': Patient Perspectives on Psychological Aspects of Chronic Pain while Living with HIV. *PloS one, 9*(11), e111765. doi:10.1371/journal.pone.0111765

Merlin, J. S., Westfall, A. O., Heath, S. L., Goodin, B. R., Stewart, J. C., Sorge, R. E., & Younger, J. (2017). Brief Report: IL-1beta Levels Are Associated With Chronic Multisite Pain in People Living With HIV. *Journal of acquired immune deficiency syndromes (1999), 75*(4), e99-e103. doi:https://dx.doi.org/10.1097/QAI.0000000000001377

Merlin, J. S., Young, S. R., Arnold, R., Bulls, H. W., Childers, J., Gauthier, L., Liebschutz, J. M. (2019). Managing Opioids, Including Misuse and Addiction, in Patients With Serious Illness in Ambulatory Palliative Care: A Qualitative Study. *Am J Hosp Palliat Care*, 1049909119890556. doi:10.1177/1049909119890556

Merlin, J. S., Young, S. R., Starrels, J. L., Azari, S., Edelman, E. J., Pomeranz, J., Liebschutz, J. M. (2018). Managing Concerning Behaviors in Patients Prescribed Opioids for Chronic Pain: A Delphi Study. *J Gen Intern Med, 33*(2), 166-176. doi:10.1007/s11606-017-4211-y

Miaskowski, C., Blyth, F., Nicosia, F., Haan, M., Keefe, F., Smith, A., & Ritchie, C. (2019). A Biopsychosocial Model of Chronic Pain for Older Adults. *Pain Medicine*. doi:10.1093/pm/pnz329

Miller, K. D., Nogueira, L., Mariotto, A. B., Rowland, J. H., Yabroff, K. R., Alfano, C. M., . . . Siegel, R. L. (2019). Cancer treatment and survivorship statistics, 2019. *CA: a cancer journal for clinicians, 69*(5), 363-385. doi:10.3322/caac.21565

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, a. t. P. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine, 151*(4), 264-269. doi:10.7326/0003-4819-151-4-200908180-00135

Mojtabai, R. (2018). National trends in long-term use of prescription opioids. *Pharmacoepidemiology and drug safety, 27*(5), 526-534.

Morse, J. M., & Field, P. A. (1996). Principles of data analysis. In J. M. Morse & P. A. Field (Eds.), *Nursing Research: The Application of Qualitative Approaches* (pp. 103-123). Boston, MA: Springer US.

Mory, N., Coyle, N., Essandoh, S., & Glare, P. (2010). Chronic pain management in cancer survivors. *JNCCN Journal of the National Comprehensive Cancer Network, 8*(9), 1104-1110. doi:10.6004/jnccn.2010.0079

Moschopoulou, E., Hutchison, I., Bhui, K., & Korszun, A. (2018). Post-traumatic stress in head and neck cancer survivors and their partners. *Supportive Care in Cancer, 26*(9), 3003-3011. doi:10.1007/s00520-018-4146-9

Murphy, C. C., Fullington, H. M., Alvarez, C. A., Betts, A. C., Lee, S. J. C., Haggstrom, D. A., & Halm, E. A. (2018). Polypharmacy and patterns of prescription medication use among cancer survivors. *Cancer, 124*(13), 2850-2857. doi:10.1002/cncr.31389

National Cancer Institute (2015). *Age and Cancer Risk*. https://www.cancer.gov/about-cancer/causes-prevention/risk/age

National Cancer Institute (2017). Adult Cancer Pain: Clinical Practice Guidelines in Oncology. https://www.nccn.org/guidelines/guidelines-detail?category=3&id=1413

Nekhlyudov, L., Ganz, P. A., Arora, N. K., & Rowland, J. H. (2017). Going Beyond Being Lost in Transition: A Decade of Progress in Cancer Survivorship. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology, 35*(18), 1978-1981. doi:10.1200/JCO.2016.72.1373

Nekhlyudov, L., Geerse, O. P., & Alfano, C. M. (2018). Opioid use among cancer survivors: A call to action for oncology and primary care providers. *Cancer, 124*(3), 648-649. doi:10.1002/cncr.31164

Nelson, D. B., Niu, J., Mitchell, K. G., Sepesi, B., Hofstetter, W. L., Antonoff, M. B., Rice, D. C. (2020). Persistent Opioid Use Among the Elderly After Lung Resection: A SEER-

Medicare Study. *The Annals of thoracic surgery, 109*(1), 194-202. doi:https://dx.doi.org/10.1016/j.athoracsur.2019.06.095

Novy, D. M., & Aigner, C. J. (2014). The biopsychosocial model in cancer pain. *Current opinion in supportive and palliative care, 8*(2), 117-123.

O'Reilly-Jacob, M., & Perloff, J. (2021). The Effect of Supervision Waivers on Practice: A Survey of Massachusetts Nurse Practitioners During the COVID-19 Pandemic. *Medical Care, 59*(4). Retrieved from https://journals.lww.com/lww-medicalcare/Fulltext/2021/04000/The_Effect_of_Supervision_Waivers_on_Practice__A.2.aspx

Oliva, E. M., Bowe, T., Manhapra, A., Kertesz, S., Hah, J. M., Henderson, P., Gordon, A. J. (2020). Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *bmj, 368*.

Opioids and Cancer Pain: Patient Needs and Access Challenges. (2019). *Journal of oncology practice, 15*(5), 225-225. doi:10.1200/JOP.19.00050

Pachman, D. R., Barton, D. L., Swetz, K. M., & Loprinzi, C. L. (2012). Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 30*(30), 3687-3696.

Paice, J. A. (2011). Chronic treatment-related pain in cancer survivors. *Pain, 152*(SUPPL.3), S84-S89. doi:10.1016/j.pain.2010.10.010

Paice, J. A. (2016). Cancer pain management: strategies for safe and effective opioid prescribing. *Journal of the National Comprehensive Cancer Network, 14*(5S), 695-697.

Paice, J. A. (2018). Navigating Cancer Pain Management in the Midst of the Opioid Epidemic. *Oncology (Williston Park, N.Y.), 32*(8), 386-403. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med15&NEWS=N&AN=30153316

Paice, J. A. (2019a). Managing Pain in Patients and Survivors: Challenges Within the United States Opioid Crisis. *Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw, 17*(5.5), 595-598. doi:10.6004/jnccn.2019.5010

Paice, J. A. (2019b). Pain in Cancer Survivors: How to Manage. *Curr Treat Options Oncol, 20*(6), 48. doi:10.1007/s11864-019-0647-0

Paice, J. A. (2019c). Risk assessment and monitoring of patients with cancer receiving opioid therapy. *The oncologist, 24*(10), 1294.

Paice, J. A. (2020). A delicate balance: risks vs benefits of opioids in cancer pain. *Pain, 161*(3). Retrieved from https://journals.lww.com/pain/Fulltext/2020/03000/A_delicate_balance__risks_vs_benefits_of_opioids.1.aspx

Paice, J. A., Mulvey, M., Bennett, M., Dougherty, P. M., Farrar, J. T., Mantyh, P. W., Smith, T. J. (2017). AAPT Diagnostic Criteria for Chronic Cancer Pain Conditions. *J Pain, 18*(3), 233-246. doi:10.1016/j.jpain.2016.10.020

Paice, J. A., Portenoy, R., Lacchetti, C., Campbell, T., Cheville, A., Citron, M., Bruera, E. (2016). Management of Chronic Pain in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. *Journal of clinical oncology : official*

journal of the American Society of Clinical Oncology, 34(27), 3325-3345. doi:10.1200/jco.2016.68.5206

Peck, K. R., Harman, J. L., & Anghelescu, D. L. (2018). Family and Peer-Group Substance Abuse as a Risk-Factor for Opioid Misuse Behaviors for a Young Adult with Cancer-Related Pain-A Case Study. *Journal of Adolescent and Young Adult Oncology, 7*(1), 137-140. doi:10.1089/jayao.2017.0055

Peretti-Watel, P., Bendiane, M.-K., Spica, L., & Rey, D. (2012). Pain narratives in breast cancer survivors. *Pain research and treatment, 2012*.

Petrini, L., & Arendt-Nielsen, L. (2020). Understanding Pain Catastrophizing: Putting Pieces Together. *Frontiers in Psychology, 11*. doi:10.3389/fpsyg.2020.603420

Porter, E. J. (1998). On" being inspired" by Husserl's phenomenology: Reflections on Omery's exposition of phenomenology as a method of nursing research. *Advances in Nursing Science, 21*(1), 16-28.

Porter, L. S., & Keefe, F. J. (2011). Psychosocial issues in cancer pain. *Curr Pain Headache Rep, 15*(4), 263-270. doi:10.1007/s11916-011-0190-6

Potosky, A. L., Han, P. K. J., Rowland, J., Klabunde, C. N., Smith, T., Aziz, N., . . . Stefanek, M. (2011). Differences Between Primary Care Physicians' and Oncologists' Knowledge, Attitudes and Practices Regarding the Care of Cancer Survivors. *Journal of General Internal Medicine, 26*(12), 1403-1410. doi:10.1007/s11606-011-1808-4

Rai, A. S., Khan, J. S., Dhaliwal, J., Busse, J. W., Choi, S., Devereaux, P. J., & Clarke, H. (2017). Preoperative pregabalin or gabapentin for acute and chronic postoperative pain among patients undergoing breast cancer surgery: A systematic review and meta-analysis of

randomized controlled trials. *J Plast Reconstr Aesthet Surg, 70*(10), 1317-1328. doi:10.1016/j.bjps.2017.05.054

Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain, 161*(9), 1976-1982. doi:10.1097/j.pain.0000000000001939

Ream, E., Hughes, A. E., Cox, A., Skarparis, K., Richardson, A., Pedersen, V. H., Bryant, A. (2020). Telephone interventions for symptom management in adults with cancer. *Cochrane Database Syst Rev, 6*(6), Cd007568. doi:10.1002/14651858.CD007568.pub2

Rice, D. C., Cata, J. P., Mena, G. E., Rodriguez-Restrepo, A., Correa, A. M., & Mehran, R. J. (2015). Posterior intercostal nerve block with liposomal bupivacaine: an alternative to thoracic epidural analgesia. *The Annals of thoracic surgery, 99*(6), 1953-1960.

Rights, J. D., & Sterba, S. K. (2020). New Recommendations on the Use of R-Squared Differences in Multilevel Model Comparisons. *Multivariate Behavioral Research, 55*(4), 568-599. doi:10.1080/00273171.2019.1660605

Roberts, A. W., Fergestrom, N., Neuner, J. M., & Winn, A. N. (2020). New-onset persistent opioid use following breast cancer treatment in older adult women. *Cancer, 126*(4), 814-822. doi:10.1002/cncr.32593

Robins, L. N., Helzer, J. E., Hesselbrock, M., & Wish, E. (2010). Vietnam Veterans Three Years after Vietnam: How Our Study Changed Our View of Heroin. *The American journal on addictions, 19*(3), 203-211. doi:10.1111/j.1521-0391.2010.00046.x

Rosenbaum, M., Lobas, J. , and Fergus, K. (2005). Using Reflection Activities to Enhance Teaching about End-of-Life Care. *Journal of Palliative Medicine, 8*(6), 1186-1195. doi:10.1089/jpm.2005.8.1186

Sager, Z. S., Wachen, J. S., Naik, A. D., & Moye, J. (2020). Post-Traumatic Stress Disorder Symptoms from Multiple Stressors Predict Chronic Pain in Cancer Survivors. *Journal of Palliative Medicine*. doi:10.1089/jpm.2019.0458

Salsman, J. M., Schalet, B. D., Andrykowski, M. A., & Cella, D. (2015). The impact of events scale: a comparison of frequency versus severity approaches to measuring cancer-specific distress. *Psycho-Oncology, 24*(12), 1738-1745. doi:https://doi.org/10.1002/pon.3784

Salz, T., Lavery, J. A., Lipitz-Snyderman, A. N., Boudreau, D. M., Moryl, N., Gillespie, E. F., & Korenstein, D. (2019). Trends in opioid use among older survivors of colorectal, lung, and breast cancers. *Journal of Clinical Oncology, 37*(12), 1001-1011. doi:10.1200/JCO.18.00938

Sandelowski, M. (2000). Whatever happened to qualitative description? *Research in Nursing & Health, 23*(4), 334-340. doi:https://doi.org/10.1002/1098-240X(200008)23:4<334::AID-NUR9>3.0.CO;2-G

Saraswathula, A., Chen, M. M., Mudumbai, S. C., Whittemore, A. S., & Divi, V. (2018). Persistent Postoperative Opioid Use in Older Head and Neck Cancer Patients. *Otolaryngology–Head and Neck Surgery, 160*(3), 380-387. doi:10.1177/0194599818778276

Schatz, A. A., Oliver, T. K., Swarm, R. A., Paice, J. A., Darbari, D. S., Dowell, D., Carlson, R. W. (2020). Bridging the gap among clinical practice guidelines for pain management in

cancer and sickle cell disease. *JNCCN Journal of the National Comprehensive Cancer Network, 18*(4), 392-399. doi:10.6004/jnccn.2019.7379

Schenker, Y., Althouse, A. D., Rosenzweig, M., White, D. B., Chu, E., Smith, K. J., Smith, T. J. (2021b). Effect of an Oncology Nurse–Led Primary Palliative Care Intervention on Patients With Advanced Cancer: The CONNECT Cluster Randomized Clinical Trial. *JAMA Internal Medicine, 181*(11), 1451-1460.

Schenker, Y., Hamm, M., Bulls, H. W., Merlin, J. S., Wasilko, R., Dawdani, A., Sabik, L. M. (2021a). This Is a Different Patient Population: Opioid Prescribing Challenges for Patients With Cancer-Related Pain. *JCO Oncology Practice, 17*(7), e1030-e1037. doi:https://dx.doi.org/10.1200/OP.20.01041

Schenker, Y., Merlin, J. S., & Quill, T. E. (2018). Use of Palliative Care Earlier in the Disease Course in the Context of the Opioid Epidemic: Educational, Research, and Policy Issues. *JAMA, 320*(9), 871-872. doi:10.1001/jama.2018.9739

Scherrer, K. H., Ziadni, M. S., Kong, J.-T., Sturgeon, J. A., Salmasi, V., Hong, J., . . . Mackey, S. (2021). Development and validation of the Collaborative Health Outcomes Information Registry body map. *Pain reports, 6*(1), e880-e880. doi:10.1097/PR9.0000000000000880

Schmidt-Hansen, M., Bromham, N., Taubert, M., Arnold, S., & Hilgart, J. S. (2015). Buprenorphine for treating cancer pain. *Cochrane Database of Systematic Reviews*(3). doi:10.1002/14651858.CD009596.pub4

Schreiber, K. L., Martel, M. O., Shnol, H., Shaffer, J. R., Greco, C., Viray, N., Belfer, I. (2013). Persistent pain in postmastectomy patients: Comparison of psychophysical, medical,

surgical, and psychosocial characteristics between patients with and without pain. *PAIN®, 154*(5), 660-668. doi:https://doi.org/10.1016/j.pain.2012.11.015

Shah, A., Hoffman, E. M., Mauermann, M. L., Loprinzi, C. L., Windebank, A. J., Klein, C. J., & Staff, N. P. (2018). Incidence and disease burden of chemotherapy-induced peripheral neuropathy in a population-based cohort. *Journal of Neurology Neurosurgery and Psychiatry, 89*(6), 636-641. doi:10.1136/jnnp-2017-317215

Shah, R., Chou, L. N., Kuo, Y. F., & Raji, M. A. (2019). Long-Term Opioid Therapy in Older Cancer Survivors: A Retrospective Cohort Study. *Journal of the American Geriatrics Society, 67*(5), 945-952. doi:10.1111/jgs.15945

Sharifzadeh, Y., Kao, M. C., Sturgeon, J. A., Rico, T. J., Mackey, S., & Darnall, B. D. (2017). Pain Catastrophizing Moderates Relationships between Pain Intensity and Opioid Prescription: Nonlinear Sex Differences Revealed Using a Learning Health System. *Anesthesiology, 127*(1), 136-146. doi:10.1097/aln.0000000000001656

Shi, Q., Smith, T. G., Michonski, J. D., Stein, K. D., Kaw, C., & Cleeland, C. S. (2011). Symptom burden in cancer survivors 1 year after diagnosis: a report from the American Cancer Society's Studies of Cancer Survivors. *Cancer, 117*(12), 2779-2790.

Simard, S., Thewes, B., Humphris, G., Dixon, M., Hayden, C., Mireskandari, S., & Ozakinci, G. (2013). Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. *Journal of Cancer Survivorship, 7*(3), 300-322. doi:10.1007/s11764-013-0272-z

Smith, T. G., Troeschel, A. N., Castro, K. M., Arora, N. K., Stein, K., Lipscomb, J., Ward, E. (2019). Perceptions of Patients With Breast and Colon Cancer of the Management of

Cancer-Related Pain, Fatigue, and Emotional Distress in Community Oncology. *Journal of Clinical Oncology, 37*(19), 1666-1676. doi:10.1200/jco.18.01579

Soneji, N., Clarke, H. A., Ko, D. T., & Wijeysundera, D. N. (2016). Risks of developing persistent opioid use after major surgery. *JAMA Surgery, 151*(11), 1083-1084.

Spetz, J., Chapman, S., Tierney, M., Phoenix, B., & Hailer, L. (2021). Barriers and Facilitators of Advanced Practice Registered Nurse Participation in Medication Treatment for Opioid Use Disorder: A Mixed Methods Study. *Journal of Nursing Regulation, 12*(2), 5-22.

Sun, V., Olausson, J. M., Fujinami, R., Chong, C., Dunham, R., Tittlefitz, T., . . . Grant, M. (2015). The Role of the Advanced Practice Nurse in Survivorship Care Planning. *Journal of the advanced practitioner in oncology, 6*(1), 64-70. doi:10.6004/jadpro.2015.6.1.7

Sutradhar, R., & Barbera, L. (2018). Reply to Opioid use among cancer survivors: A call to action for oncology and primary care providers. *Cancer, 124*(3), 649. doi:10.1002/cncr.31166

Sutradhar, R., Lokku, A., & Barbera, L. (2017). Cancer survivorship and opioid prescribing rates: A population-based matched cohort study among individuals with and without a history of cancer. *Cancer, 123*(21), 4286-4293. doi:10.1002/cncr.30839

Sztachańska, J., Krejtz, I., & Nezlek, J. B. (2019). Using a Gratitude Intervention to Improve the Lives of Women With Breast Cancer: A Daily Diary Study. *Front Psychol, 10*, 1365. doi:10.3389/fpsyg.2019.01365

Tauben, D. J., Langford, D. J., Sturgeon, J. A., Rundell, S. D., Towle, C., Bockman, C., & Nicholas, M. (2020). Optimizing telehealth pain care after COVID-19. *Pain, 161*(11), 2437-2445. doi:10.1097/j.pain.0000000000002048

Thompson, O. J., Powell-Roach, K., Taylor, J. L., Terry, E. L., & Booker, S. Q. (2022). Pain catastrophizing: A patient-centered approach to assessment. *Nursing2022, 52*(4), 26-30.

Tierney, M., Finnell, D. S., Naegle, M., Mitchell, A. M., & Pace, E. M. (2020). The Future of Nursing: Accelerating gains made to address the continuum of substance use. *Archives of Psychiatric Nursing, 34*(5), 297-303. doi:10.1016/j.apnu.2020.07.010

Tilley, C. P., Fu, M. R., Van Cleeve, J., Crocilla, B. L., & Comfort, C. P. (2020). Symptoms of Malignant Fungating Wounds and Functional Performance among Patients with Advanced Cancer: An Integrative Review from 2000 to 2019. *Journal of Palliative Medicine*.

Treede, R.-D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Wang, S.-J. (2019). Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain, 160*(1), 19-27. doi:10.1097/j.pain.0000000000001384

Treede, R. D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., Wang, S. J. (2015). A classification of chronic pain for ICD-11. Pain 156(6), 1003–1007.

Tripp, J. C., Jones, J. L., Back, S. E., & Norman, S. B. (2019). Dealing With Complexity and Comorbidity: Comorbid PTSD and Substance Use Disorders. *Current Treatment Options in Psychiatry, 6*(3), 188-197. doi:10.1007/s40501-019-00176-w

Turk, D. C., Dworkin, R. H., Allen, R. R., Bellamy, N., Brandenburg, N., Carr, D. B., Witter, J. (2003). Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain, 106*(3), 337-345. doi:https://doi.org/10.1016/j.pain.2003.08.001

Turner, J., Kelly, B., Clarke, D., Yates, P., Aranda, S., Jolley, D., McFadyen, L. (2011). A randomised trial of a psychosocial intervention for cancer patients integrated into routine care: the PROMPT study (promoting optimal outcomes in mood through tailored psychosocial therapies). *BMC cancer, 11*(1), 1-9.

Van Cleave, J. H., Booker, S. Q., Powell-Roach, K., Liang, E., & Kawi, J. (2021). A Scoping Review of Nursing's Contribution to the Management of Patients with Pain and Opioid Misuse. *Pain Management Nursing, 22*(1), 58-68. doi:https://doi.org/10.1016/j.pmn.2020.11.007

Van den Beuken-van Everdingen, M. H., Hochstenbach, L. M., Joosten, E. A., Tjan-Heijnen, V. C., & Janssen, D. J. (2016). Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis. *Journal of pain and symptom management*, *51*(6), 1070–1090.e9. https://doi.org/10.1016/j.jpainsymman.2015.12

Vatcheva, K. P., Lee, M., McCormick, J. B., & Rahbar, M. H. (2016). Multicollinearity in Regression Analyses Conducted in Epidemiologic Studies. *Epidemiology (Sunnyvale), 6*(2). doi:10.4172/2161-1165.1000227

Vitzthum, L. K., Riviere, P., Sheridan, P., Nalawade, V., Deka, R., Furnish, T., Murphy, J. D. (2019). Predicting Persistent Opioid Use, Abuse, and Toxicity Among Cancer Survivors. *JNCI: Journal of the National Cancer Institute*. doi:10.1093/jnci/djz200

Ward, K., Ramzan, A., Sheeder, J., Fischer, S., & Lefkowits, C. (2019). Persistent opioid use after radiation therapy in opioid-naive cervical cancer survivors. *International Journal of Gynecological Cancer, 29*(7), 1105-1109. doi:10.1136/ijgc-2019-000430

Webster, L., Gudin, J., Raffa, R. B., Kuchera, J., Rauck, R., Fudin, J., . . . Mallick-Searle, T. (2020). Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion. *Pain Medicine*. doi:10.1093/pm/pnz356

Wechsler, S., & Wood, L. (2021). The Effect of Chemotherapy on Balance, Gait, and Falls Among Cancer Survivors: A Scoping Review. *Rehabilitation Oncology, 39*(1), 6-22.

Weimer, M. B., Hartung, D. M., Ahmed, S., & Nicolaidis, C. (2016). A chronic opioid therapy dose reduction policy in primary care. *Substance abuse, 37*(1), 141-147.

Wertli, M. M., Burgstaller, J. M., Weiser, S., Steurer, J., Kofmehl, R., & Held, U. (2014). Influence of Catastrophizing on Treatment Outcome in Patients With Nonspecific Low Back Pain: A Systematic Review. *Spine, 39*(3), 263-273. doi:10.1097/brs.0000000000000110

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

Wilens, T. E., Kwon, A., Tanguay, S., Chase, R., Moore, H., Faraone, S. V., & Biederman, J. (2005). Characteristics of Adults with Attention Deficit Hyperactivity Disorder Plus Substance Use Disorder: The Role of Psychiatric Comorbidity. *The American journal on addictions, 14*(4), 319-327. doi:10.1080/10550490591003639

Willis, D. G., Grace, P. J., & Roy, C. (2008). A central unifying focus for the discipline: facilitating humanization, meaning, choice, quality of life, and healing in living and dying. *Advances in Nursing Science, 31*(1), E28-E40.

Wilsey, B. L., Fishman, S. M., Tsodikov, A., Ogden, C., Symreng, I., & Ernst, A. (2008). Psychological comorbidities predicting prescription opioid abuse among patients in

chronic pain presenting to the emergency department. *Pain Med, 9*(8), 1107-1117. doi:10.1111/j.1526-4637.2007.00401.x

Wilson, J. M., Schreiber, K. L., Mackey, S., Flowers, K. M., Darnall, B. D., Edwards, R. R., & Azizoddin, D. R. (2022). Increased pain catastrophizing longitudinally predicts worsened pain severity and interference in patients with chronic pain and cancer: A collaborative health outcomes information registry study (CHOIR). *Psycho-Oncology, n/a*(n/a). doi:https://doi.org/10.1002/pon.6020

Yang, Y., Li, W., Wen, Y., Wang, H., Sun, H., Liang, W., Humphris, G. (2019). Fear of cancer recurrence in adolescent and young adult cancer survivors: A systematic review of the literature. *Psychooncology, 28*(4), 675-686. doi:10.1002/pon.5013

Yau, W. H., Roeland, E. J., Revta, C., Ale-Ali, A., & Ma, J. D. (2018). Opioid and Benzodiazepine Relative Use in Breast Cancer Patients Before, During, and After Curative Chemotherapy. *Journal of Pain & Palliative Care Pharmacotherapy, 32*(1), 27-29. doi:10.1080/15360288.2018.1479328

Zabora, J., BrintzenhofeSzoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The prevalence of psychological distress by cancer site. *Psycho-Oncology, 10*(1), 19-28. doi:10.1002/1099-1611(200101/02)10:1<19::Aid-pon501>3.0.Co;2-6

Zaza, C., & Baine, N. (2002). Cancer Pain and Psychosocial Factors: A Critical Review of the Literature. *Journal of Pain and Symptom Management, 24*(5), 526-542. doi:https://doi.org/10.1016/S0885-3924(02)00497-9

Zedler, B., Xie, L., Wang, L., Joyce, A., Vick, C., Brigham, J., . . . Murrelle, L. (2015). Development of a risk index for serious prescription opioid-induced respiratory

depression or overdose in Veterans' Health Administration patients. *Pain Medicine, 16*(8), 1566-1579.

Zenda, S., Matsuura, K., Tachibana, H., Homma, A., Kirita, T., Monden, N., Asai, M. (2011). Multicenter phase II study of an opioid-based pain control program for head and neck cancer patients receiving chemoradiotherapy. *Radiotherapy and Oncology, 101*(3), 410-414. doi:https://doi.org/10.1016/j.radonc.2011.09.016

Ziadni, M. S., You, D. S., Cramer, E. M., Anderson, S. R., Hettie, G., Darnall, B. D., & Mackey, S. C. (2022). The impact of COVID-19 on patients with chronic pain seeking care at a tertiary pain clinic. *Sci Rep, 12*(1), 6435. doi:10.1038/s41598-022-10431-5