MEDICATION BELIEFS AMONG ADVANCED CANCER PATIENTS RECEIVING ORAL ONCOLYTIC AGENTS

By

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ABSTRACT

MEDICATION BELIEFS AMONG ADVANCED CANCER PATIENTS RECEIVING ORAL ONCOLYTIC AGENTS

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The purpose of this dissertation is to examine how medication beliefs among advanced stage cancer patients receiving oral oncolytic agents (OAs) change over the first 12 weeks after initiating a new OA and determine factors associated with these changes. Manuscript one introduces a conceptual model derived from the Extended Common-Sense Model of Self-Regulation to explain the phenomenon of medication beliefs using a theory derivation approach.

Manuscript two examines: 1) whether positive and negative components of medication beliefs change over time; 2) summed symptom severity and interference indices on the positive and negative components of medication beliefs over time and; 3) the influence of depression and cognitive effectiveness on the positive and negative components of medication beliefs over time and over and above the summed symptom severity and interference indices. A total of 272 participants completed the baseline interview. The sample was predominantly Caucasian (91%), diagnosed with stage four cancer (71%), and had a mean age of 61.39 (SD = 2.22) years. The most prevalent cancers were gastrointestinal (32%) and breast cancer (21%). Kinase inhibitors (47%) and cytotoxics (35%) were the most frequent forms of OA treatment. Linear mixed models (LME) revealed Necessity beliefs increased over time, mean difference 0.112, SE=0.055, p = .04. Concern beliefs only changed when symptom severity and interference were introduced into the LME. A decrease in Necessity beliefs was significantly associated with higher levels of depressive symptoms (B = -0.012, SE = 0.004, p = <.01). Increased Concern beliefs were significantly associated with patient-reported symptom severity (B = 0.009, SE = 0.001, p = <.01), symptom interference (B = 0.010, SE = 0.001, p = <.01), depressive symptoms (B =

0.021, SE = 0.003, p = <.01), cognitive effectiveness (B = -0.006, SE = 0.001, p = <.01) and chronic conditions requiring medications (B = 0.048, SE = 0.014, p = <.01).

Manuscript three aimed to: 1) explore the relationship of documented adverse events on positive and negative components of medication beliefs 12 weeks after initiating a new OA and 2) determine whether patients who experience a permanent physician-directed OA stoppage differ in their medication beliefs compared to those with no permanent physician-directed OA stoppage. A total of 164 participants were included in the study. Mean age was 62.60 (SD = 10.46) years. The sample was predominantly Caucasian (88%). Breast (26%) and gastrointestinal cancers (23%) were the most prevalent types of cancer and 72% had stage four cancer. A regression analysis showed patients experiencing zero (B = 0.50, SE = 0.21, p = .02), one (B = 0.70, SE = 0.21, p = <.01), or two (B = 0.82, SE = 0.23, p = <.01) adverse events had significantly higher Necessity beliefs compared to those with three or more adverse events. Independent t-tests followed by a regression analysis revealed patients not experiencing a physician-directed OA stoppage had significantly higher Necessity beliefs (B = 0.80, SE = 0.23, p = <.01) compared to those who had experienced a permanent physician-directed OA stoppage.

Results support that the two components of medication beliefs are influenced by different factors. Nurses should elicit medication beliefs at each clinic visit, especially when patients experience increasing levels of symptom severity/interference or adverse events, depressive symptoms, compromised cognitive effectiveness, and when patients experience a permanent physician-directed OA stoppage. Screening medication beliefs can also serve to address ethical issues regarding how long patients remain on OAs that cause more harm than benefit at the end of life. Future research on medication beliefs is needed with more diverse ethnic backgrounds.

This dissertation is dedicated to my husband, David and four children, Ireland, Benjamin, Weston, and Anniston who have offered continuous support and made considerable sacrifices in order for me to see the completion of the doctoral program to fruition.

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CHAPTER 1: INTRODUCTION

Medication beliefs are a critical component to medication taking behavior and are important in establishing a foundation for how individuals cope with their illness (Banning, 2012; Chambers et al., 2011; Heisig et al., 2016; Horne, 2003). Medication beliefs have been consistently linked to patient outcomes, such as symptoms, side effects, and adherence across chronic diseases, including cancer (Banning, 2012; Bhattacharya, Easthall, Willoughby, Small, & Watson, 2012; Corter, Findlay, Broom, Porter, & Petrie, 2013; Iskandarsyah et al., 2014; Saratsiotou et al., 2010; Spoelstra et al., 2013; Thuné-Boyle, Myers, & Newman, 2006).

Oral oncolytic agents (OAs) have changed the cancer care delivery model and shifted the responsibility of cancer medication administration to the patient and their family caregivers (Given, Spoelstra, & Grant, 2011; Weingart et al., 2008). OAs have narrow therapeutic ranges (Neuss et al., 2013), making adherence essential to prevent unnecessary medication changes, drug resistance, disease progression, and loss of survival time (Geynisman & Wickersham, 2013). As patients are managing their OA administration at home, medication beliefs among patients with advanced cancer warrant examination by both oncology professionals and researchers to determine what factors influence medication beliefs over time. The goal of this research is to examine, using a derived conceptual model, how medication beliefs among advanced stage cancer patients receiving OAs change over the first 12 weeks since initiating a new OA medication and to determine what factors are associated with changes in those beliefs.

Background & Significance

Oral Oncolytic Agents

OAs are often prescribed as a last available line of treatment for patients with advanced cancer. The development of new OAs has broadened the treatment options for patients with

various solid tumors who have not responded to other anti-cancer treatment options (American Society of Clinical Oncology, n.d.; Matsuyama, Reddy, & Smith, 2006; Mohammed, Peter, Gastaldo, & Howell, 2016). Of the newly approved Food and Drug Administration (FDA) cancer treatments in 2017, 70% are supplied in oral form (Center Watch, 2017) and that number is expected to increase as more clinical trials involving OAs are in the pipeline.

Research continues to improve the scientific understanding of genetics, genomics, and molecular changes involved in tumor progression (Geynisman & Wickersham, 2013). Such research has led to the development of new OAs specifically targeting the abnormal proteins and signaling pathways of cancer cells (Geynisman & Wickersham, 2013) and, has increased the treatment options for patients with advanced cancer.

The American Cancer Society estimates that in 2018, over 1.7 million individuals will be diagnosed with cancer (American Cancer Society, 2018). The National Cancer Institute projects individuals living beyond their cancer diagnoses will increase nearly 25% between 2014 and 2024 (National Cancer Institute, 2017). Cancer has now been deemed a chronic illness and more patients are receiving continuous and long-term treatment with OAs. Cancer patients receiving OAs require the self-management of cancer treatment in the home environment (Given et al., 2011; Hess et al., 2017) and medication taking behavior has been consistently reported to be influenced by medication beliefs (Arlt, Nestoriuc, & Rief, 2017; Banning, 2012; Bhattacharya et al., 2012). Differences among traditional cancer therapies and OAs are described below, with a focus on the implications that specific route of administration has on medication beliefs.

Differences Between Traditional Cancer Therapies and OAs Affecting Medication Beliefs

Traditional cancer therapies and OAs differ in the way the medication is administered, the way in which the medication works to treat cancer, and the patient's responsibility for

administration. Such differences among the routes of administration have an impact on how patients' medication beliefs regarding cancer treatment are formed and change over time. Traditional cancer therapies can entail intermittent invasive treatments administered by trained oncology personnel in a hospital or oncology-based clinic, under the close observation of clinical oncology personnel (Hess et al., 2017). Patients taking OAs are required to self-manage their cancer therapy, while oncology professionals deliver and monitor the administration of traditional cancer therapies (Tipton, 2012). Because cancer patients are not responsible for self-administration of traditional cancer therapies, such as intravenous chemotherapy, medication beliefs do not affect medication-taking behavior in the same way as with OAs.

Treatment with OAs allow advanced cancer patients or their caregivers to self-administer cancer medication in the home environment (Given et al., 2011; Hess et al., 2017). Over the past two decades, it has been reported that cancer patients prefer OAs to traditional cancer therapies most often because of convenience (Liu, Franssen, Fitch, & Warner, 1997; Simchowitz, Brouillard, & Weingart, 2010; Tipton, 2015). Patients receiving OAs enjoy the comfort of administering cancer medication in the home (Liu et al., 1997), a more manageable treatment schedule for work and family, and some patients report less side effects with oral cancer treatment (Eek et al., 2016). Additionally, patients receiving OAs appreciate not having to endure invasive cancer treatments, such as intravenous chemotherapy. Despite the speculated convenience of OAs, there are disadvantages to this treatment (Given, et al., 2011; Tipton, 2015; Weingart et al., 2008) that affect medication beliefs and lead to undesirable patient outcomes, such as nonadherence and symptom burden at the end of cancer care.

First, patients receiving OAs are required to self-manage complex medication regimens (Given et al., 2011), which can negatively influence activities of daily life. Treatment with OAs

entails fluctuating dosages, medication cycling, and temporary or even permanent OA stoppages. The complexity of treatment for cancer patients receiving OAs leave patients susceptible to developing negative medication beliefs and subsequent nonadherence.

Another major challenge facing patients receiving OAs is that the medications are toxic and patients or their family caregivers are responsible for independently self-managing symptoms in the home environment (Given et al., 2011; Spoelstra et al., 2013). OAs are associated with adverse events such as toxicities, symptoms, and side effects (Neuss et al., 2013; Shimada et al., 2014; Spoelstra et al., 2013; Tipton, 2015), which influence the development of negative medication beliefs. Such negative medication beliefs could lead to a change in medication taking behavior, resulting in nonadherence (Bhattacharya et al., 2012). Alterations in adherence to the OA can lead to unfavorable outcomes (Geynisman & Wickersham, 2013). Patients who develop new symptoms or experience adverse events after initiating an OA may attribute new symptoms or adverse events to the medication. Further, patients who cannot manage these symptoms and adverse events effectively at home can develop increasing concern about taking an OA.

In summary, a shift in the responsibility of cancer care continues to move from oncology clinics to patients and their caregivers. Patients are now accountable for administration of their own oral cancer medication. Challenges of OA medications include complex dosing regimens, symptoms, and adverse events. However, it is not understood how these treatment-related challenges influence medication beliefs over time. Medication beliefs and their link to patient outcomes in cancer illness are briefly described below.

Antecedents

A patient's memory including prior experiences with their illness, medications, and physical, emotional, and cognitive health can influence future medication beliefs (Horne, 2003). For example, cancer patients are often confronted with comorbid conditions requiring additional medications, especially patients 65 years of age and older (Sarfati, Koczwara, & Jackson, 2016). Patients with advanced cancer have also often undergone other cancer treatments. Patients then appraise these experiences positively or negatively, which can lead to the development of positive or negative medication beliefs. When a new medication is prescribed, medication beliefs are activated and prior experiences with illness and medications will influence medication beliefs regarding the newly prescribed OA.

Medication Beliefs

Medication beliefs are cognitive structures (Anderson, 2015; Turk & Salovey, 1985), which implies that a patient's memory of past experiences with their OA impact the development of mediation beliefs over time (Horne, 2003). Medication beliefs are activated by cognitive processing. Cognitive processing is ongoing when receiving and interpreting information, such as education delivered by the oncologist, oncology nurse, or informative printed materials regarding the OA medication (Anderson, 2015; Turk & Salovey, 1985).

Typically, patients with advanced stage cancers have experienced prior failed cancer treatments and are often confronted with a last treatment option in the form of OAs (Mohammed et al., 2016). Because medication beliefs develop from prior experiences, patients with advanced stage cancers already have established medication beliefs regarding cancer medication. If medication beliefs are to be fully understood, they must be evaluated in the larger domain of cognitive representation of illness associated with advanced stage cancer (Horne, 2003).

Medication beliefs are defined as an individual's perception regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003). Medication beliefs have two separate components, one positive and one negative (Horne, Weinman, & Hankins, 1999), that may be held at the same time (Phillips, Diefenbach, Kronish, Negron, & Horowitz, 2014). The positive component of medication beliefs includes beliefs that medication is beneficial (Horne et al., 1999), valued, and the patient's health will be improved or maintained in some way as a result of taking medication. For example, taking an OA to treat advanced cancer is expected to deliver some benefit to the patient, perhaps by way of delayed disease progression or symptom control. If such benefits of medication are appraised favorably, the positive medication beliefs are reinforced through the experience of symptom relief or through knowledge of delayed disease progression via information received from the oncology professional.

The negative component of medication beliefs among cancer patients receiving OAs represent concern for taking medication (Horne et al., 1999). Negative medication beliefs are challenged and vulnerable to change over time in response to treatment-related assaults, such as symptoms and adverse effects of the medication. Treatment-related assaults involving adverse events may be present in the form of symptoms, side effects, or toxicities that interrupt a patient's routine or daily schedule (Bhattacharya et al., 2012; Corter et al., 2013; Chen, Chen, Huang, & Chang, 2014; Salgado et al., 2017). Patients experiencing treatment-related assaults are vulnerable to the development or reinforcement of negative medication beliefs, which alter health behaviors such as adherence (Fink, Gurwitz, Rakowski, Guadagnoli, & Silliman, 2005; Grunfeld, Hunter, Sikka, & Mittal, 2005; Lin, Clark, Tu, Bosworth, & Zullig, 2017; Moon, Moss-Morris, Hunter, Carlisle, & Hughes, 2017). In addition, cancer patients are vulnerable to

experiencing depressive symptoms or altered cognitive functioning (cognitive effectiveness) that can further contribute to the development of negative medication beliefs and the inability to perceive the positive benefits of medication (Belzung, Willner, & Philippot, 2015; DiMatteo, Lepper, & Croghan, 2000; Salgado et al., 2017).

Medication beliefs have often been the center of adherence studies and are examined as independent variables to predict medication adherence (Foot et al., 2016; Horne et al., 2013). Less is known about the factors that influence medication beliefs, especially how or if patients' medication beliefs change over time as most studies are cross sectional (Arriola et al., 2014; Bhattacharya et al., 2012; Corter et al., 2013; Grunfeld et al., 2005; Heisig et al., 2016). Understanding the factors that can give rise to medication beliefs over time can inform oncology interventions (Arlt et al., 2017). Such interventions can enhance and support positive medication beliefs while decreasing negative medication beliefs in order to maintain medication adherence, achieve delayed disease progression, and successfully manage symptoms towards the end of cancer care.

The following section describes the development of a conceptual framework among advanced cancer patients receiving OAs that will address gaps in the current theoretical and empirical knowledge surrounding medication beliefs. Through the process of theory derivation, a derived conceptual framework utilizes a pertinent model grounded in cognitive psychology, the Extended Common-Sense Model of Self-Regulation (Horne, 2003), as a guide to advance nursing science in order to explain and describe how patients perceive their OA cancer medication over the treatment trajectory with a new OA prescription.

Theoretical/Conceptual Framework

Using theory derivation, as outlined by Walker & Avant (2011), a review of the literature surrounding medication beliefs among different disciplines and across various chronic illnesses, including cancer, was conducted. The derivation process allows for creativity by the author in order to select the parts or structure of a parent theory that can be modified or redefined in order to advance the theoretical understanding of a phenomenon (Walker & Avant, 2011). One commonly used theoretical framework integrating the concept of medication beliefs is the Extended Common-Sense Model of Self-Regulation (ECSM), which integrates both treatment perceptions (medication beliefs) and illness representations to predict behavior (Horne, 2003). The ECSM lays significant groundwork for defining medication beliefs and understanding how medication beliefs can change based on appraisals over the treatment trajectory and is used as the parent theoretical framework. The way an individual perceives their illness is critical to understanding how they perceive the medication used to treat the illness (Horne, 2003). In addition, the ECSM incorporates both cognitive and emotional response to illness and treatment (Horne, 2003), which is important to the development of medication beliefs among cancer patients who can face a number of threats to their cognitive and emotional well-being. Patients face challenges with cancer treatment that can give rise to depressive symptoms (Salgado et al., 2017) and decreased cognitive effectiveness (Cimprich, 1992) that negatively influence the ability self-regulate personal cancer care in the home environment. This section will discuss the concepts and components of the ECSM to provide conceptual grounding for the development of the derived conceptual model (See Appendix for copyright permission).

The ECSM (Figure 1.1) is fundamental in explaining how cancer patients' medication beliefs can be formed and change over time as patients cope and adapt with their illness. The dynamic interaction between patient illness, treatment beliefs, and behavior are emphasized in this model as the patient attempts to achieve a state of health (Horne, 2003). The ECSM identifies that individuals form cognitive representations of their illness and treatment (illness representations), participate in coping procedures (medication adherence or nonadherence), and evaluate their coping procedures via an appraisal process. The appraisals inform future illness and treatment beliefs and can modify existing beliefs. Beliefs can change as the effectiveness of their coping procedures, such as medication-taking behavior, are appraised and deemed either effective or ineffective (Horne, 2003). Individuals then adapt coping behavior accordingly (Horne, 2003).

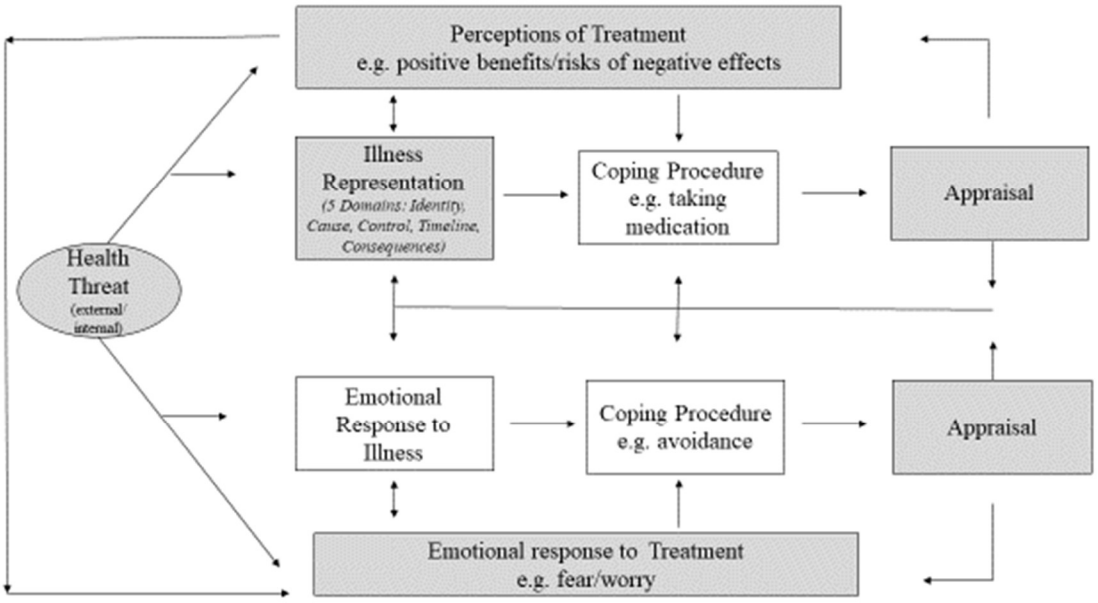

Figure 1.1 The Extended Common-Sense Common of Self-Regulation (Horne, 2003). *Components shaded in gray are used in the derived conceptual model.*

The self-regulation of the ECSM refers to attempts by an individual to adjust or adapt their cognitions, emotions, and coping behaviors in order to achieve goals of maintaining health

and wellness (Cameron & Leventhal, 2003). One key feature of the ECSM is the parallel processing of cognitive and emotional aspects of health threats (Leventhal et al., 2003). This is important to consider among advanced cancer patients who may experience a decline in cognitive effectiveness (Andreotti, Root, Ahles, McEwen, & Compas, 2014; Merriman et al., 2013), fears related to illness, treatment, or recurrence (Corter et al., 2013; Horne, 2003; Salgado et al., 2017), and depressive symptoms (Salgado et al., 2017).

Extended Common-Sense Model of Self-Regulation: Concepts and Components

This section will explain all ECSM model concepts, components, and relationships as presented in Figure 1.1. A description of limitations of the model to explain the phenomenon of medication beliefs among advanced stage cancer patients receiving OAs is provided.

Health threat. The ECSM begins with a stimulus, described as a health threat, to activate both illness representations and subsequently treatment perceptions once treatment for the illness is sought by the patient or prescribed by a healthcare professional (Figure 1.1). Perceived health threats can be external or internal (Horne, 20003). For example, an external health threat may be the physician delivering news of an illness diagnosis, prescribing a new medication, or providing information regarding potential side effects of a new prescription medication. An internal health threat may represent somatic symptoms the patient experiences to indicate they are facing illness (Horne, 2003). In the derived conceptual model (Figure 1.2), prescription of the new oral oncolytic agent will activate medication beliefs and may or may not act as a health threat.

Illness representations. Illness representations are defined as a patient's perceptions regarding an illness or somatic symptom (Cameron & Leventhal, 2003). Illness representations include five domains (identity, cause, control, timeline, and consequences) and comprise the patient's cognitive response to treatment (Cameron & Leventhal, 2003). Identity is described as

the characteristics associated with illness and reflects how the illness presents itself, such as specific symptoms (Horne, 2003). Identity is important in the development of medication beliefs, specifically for determining whether treatment would be beneficial or raise concern for taking the medication. Cause represents an individual's impression of how the illness was triggered or the sources of their symptoms (Horne, 2003). Patients with advanced cancer can face aggressive treatments (Earle, et al., 2004; Earle et al., 2008). Having advanced stage cancer, which necessitates treatment, can give rise to positive medication beliefs as patients strive for survival, but also the cause of illness may be perceived as a result of the cancer treatment itself. Control refers to the extent to which the individual believes that their illness can be managed or controlled by treatment and/or medication (Horne, 2003). Control entails patients' perceptions that the medication is appropriate, necessary, effective to treat the illness (Horne, 2003). Timeline indicates how long the individual perceives the illness will last, such as an illness that is chronic or terminal vs. acute/cyclical (Horne, 2003). Lastly, the consequences component of illness indicates how the individual believes the illness will impact them and how the patient perceives the consequences of treating versus not treating their illness (Horne, 2003).

Each domain of the illness representation plays a key role in perceptions of treatment with medication (Horne, 2003). The derived conceptual model incorporates illness representations to explain that medication beliefs are defined within the larger domain of illness representation (Figure 1.2). The five domains of illness within the ECSM allow the patient to interpret a health threat and cope with the health threat using common sense actions, or behaviors that make sense to the patient, in order to maintain health (Horne, 2003).

Perceptions of treatment (medication beliefs). Perceptions of treatment include cognitive representations of medication beliefs, which occurs in parallel with an emotional

response to treatment. Horne (2003) describes treatment perceptions as having two components. Patients determine whether they need medication (positive) as well as hold concerns that reflect the medication as a health threat, causing adverse effects (negative). Horne (2003) discusses balancing beliefs that medication is needed against concern for taking the medication in relation to coping procedures such as adherence. In his description of weighing beliefs about benefits of medication with concerns about medication, Horne (2003) hints at the interplay between these two separate components. Horne (2003) suggests previous empirical data, quantifying the two medication belief components, can be used to compute a single numerical value to demonstrate the interplay of the two medication belief components of need and concern to predict adherence. Use of such computations of the two medication belief components are not theoretically sound and have resulted in the misconception that the two components of medication beliefs have an inverse relationship, when they are independent constructs (Phillips et al., 2014). Patients may hold positive and negative medication beliefs simultaneously, but they are distinct constructs influenced by different factors and influence patient outcomes, such as adherence, differently (Aikens, Nease, & Klinkman, 2008; Horne et al., 1999; Horne & Weinman, 2002; Kalichman, Kalichman, & Cherry, 2016; Neame & Hammond, 2005; Phillips et al., 2014).

A major contribution of this research is to approach each of the two components of medication beliefs as theoretically distinct constructs, that are not polar opposite constructs (Horne et al., 1999; Kalichman et al., 2016; Phillips et al., 2014), and to examine these components as dependent variables. Using a derived model, medication beliefs will be examined independently to determine how each component of medication beliefs may change over time, while exploring how treatment-related events along the first 12 weeks of the new OA treatment trajectory influence each component separately. The derived model will also introduce the

important role of cognitive effectiveness in development and change of medication beliefs over time (Figure 1.2).

Emotional response to illness and treatment. The emotional response to illness, as described in the ECSM, refers to the activation of emotions when illness or treatment health threats are perceived (Horne, 2003). Patients diagnosed with advanced cancer experience emotional responses in the form of worry, fear, depression, and anxiety in relation to both stress of illness and its treatment. Patients taking OAs need to self-manage the illness, treatment, and its effects, which may aggravate the adverse emotional responses. Emotional and cognitive representations are distinct concepts that occur in parallel; however, influence one another (Horne, 2003).

Such emotional responses can affect medication beliefs by decreasing one's ability to perceive positive medication beliefs (DiMatteo et al., 2010) or reinforcing negative medication beliefs (Salgado et al., 2017). The derived conceptual model (Figure 1.2) will use depressive symptoms to represent the emotional response to treatment as depression is common among patients with advanced cancer (Fitzgerald et al., 2013; Hung et al., 2017).

Coping procedures. Coping procedures include actions or behaviors exhibited by the individual in order to maintain a state of health (Horne, 2003). Examples of coping behavior include taking medication to treat an illness or adhering to a medication regimen (Horne, 2003). In the ECSM, coping procedures are appraised to evaluate the effectiveness of the medication taking behavior, and these appraisals inform future medication beliefs. The goal of this dissertation research is not to examine outcomes of medication beliefs, but rather *medication beliefs as the outcome* and the factors that influence medication beliefs across the first 12 weeks

of the new OA treatment trajectory. Thus, coping was not one of the ECSM model components retained in the derived model (Figure 1.2).

Appraisals. Horne (2003) describes the appraisal in the ECSM as the evaluation of outcomes of adherence or non-adherence. Appraisals either reinforce and/or change illness or treatment representations based on evaluations of those outcomes (Horne, 2003). In the derived model, specific OA treatment-related events are appraised and ultimately change medication beliefs over time in cancer patients receiving OAs. Adherence or non-adherence is not explored in this research as adherence at the end of life may not have the same implications as earlier stage cancers; thus, appraisals of these medication-taking behaviors are not included in the derived model (Figure 1.2).

Limitations of the ECSM to Explain and Describe Medication Beliefs

The ECSM has not been used to explain how the positive and negative components of medication beliefs may change independently over time among patients with advanced cancer receiving OAs. Additionally, the ECSM does not explain what factors may influence each of the two components of medication beliefs. Much of the literature using the ECSM to guide studies of various chronic illnesses often involves adherence as the outcome variable but fail to fully recognize the factors contributing and giving rise to an individual's medication beliefs (Krauskopf et al., 2015; Kung, Koschwanez, Painter, Honeyman, & Broadbent, 2012; Morgan et al., 2015). Medication beliefs are not examined as dependent variables; therefore, it is unknown what factors are influencing medication beliefs. Understanding how medication beliefs are influenced over the course of treatment with OAs is critical given that medication beliefs are closely linked with medication adherence and patients are expected to self-manage their OAs in

the home without the close observation of oncology professionals. Thus, the phenomena of medication beliefs have not been fully recognized or explored.

Medication beliefs are cognitive representations of treatment (Horne, 2003). These beliefs are vulnerable to change over time as cancer patients face a number of emotional responses to the illness and treatment as well as alterations in cognitive effectiveness secondary to the cancer disease and treatment effects, or the stress and emotions that come with managing cancer care in the home environment. Compromised cognitive effectiveness may contribute to both the development and change of medication beliefs. A decline in cognitive effectiveness can negatively impact directed attention and the ability to inhibit specific behaviors, thoughts, and emotions (Kaplan, 1995; Pennebaker, 1992). A decline in cognitive effectiveness negatively affects directed attention and influences a patient's ability to self-regulate and manage cancer care (e.g. self-administration of cancer medication in the home environment), yet this critical component is not discussed in the ECSM.

Using the ECSM as a theoretical underpinning, a derived conceptual model was developed to 1) describe how medication beliefs are formed prior to being prescribed an oral oncolytic agent; 2) describe how the positive and negative components of medication beliefs can change differently over time in relation to appraisals of treatment-related events; 3) explain the positive and negative components of medication beliefs and the relationship between the two separate components and; 4) explain how treatment-related factors can influence each of the medication components differently.

Medication beliefs are defined within a larger domain of illness representation for which medication is prescribed. It is important to understand how a patient perceives their illness in order to understand how they perceive the medication used to treatment the illness. Therefore,

the ECSM was used as a guide to develop a derived conceptual model. New conceptual knowledge can advance nursing science, including the contribution to the development of interventions that can enhance or improve medication beliefs and decrease negative medication beliefs to improve patient outcomes such as adherence.

In summary, the ECSM has not been used to fully explain the rise and formation of both positive and negative medication beliefs over time among advanced-stage cancer patients receiving OAs. Introducing a derived conceptual model can advance the science by providing conceptual clarity regarding how individuals perceive their medication over time, especially those with advanced cancer receiving OA medication and who experience devastating symptoms and adverse events that can result in treatment disruption. The derived conceptual model (Figure 1.2) is presented below.

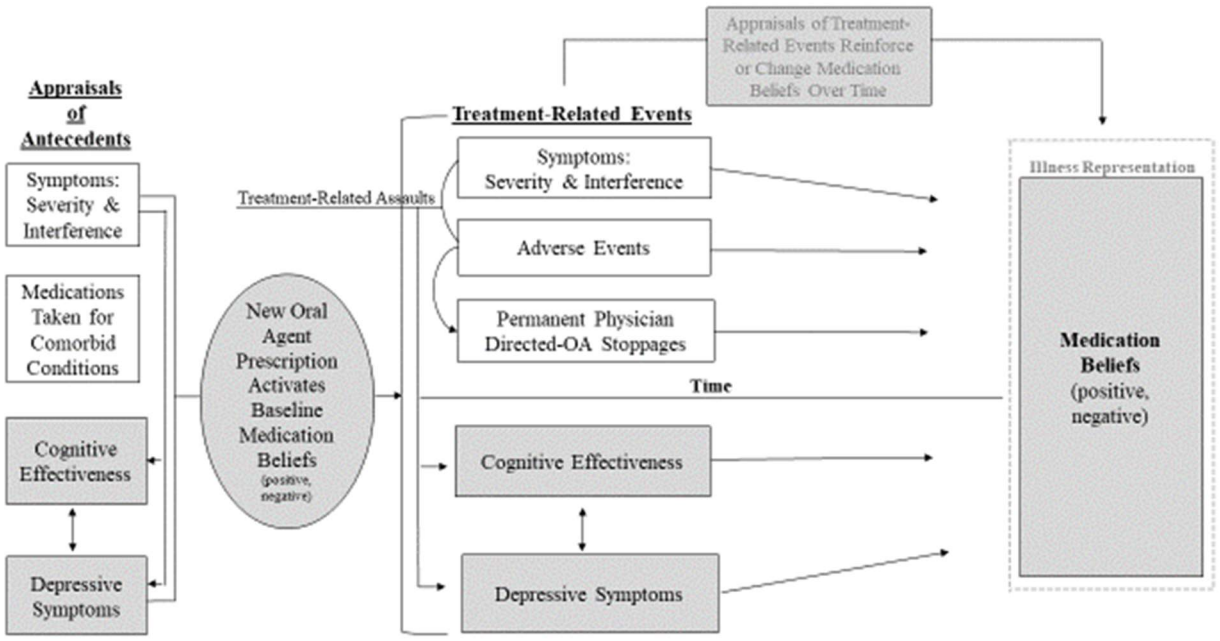

Figure 1.2 The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). *This model is derived from Extended Common-Sense Model of Self-Regulation. Horne, R. (2003). Derived components from the ECSM that are redefined or modified are highlighted in gray.*

Introduction of a Derived Conceptual Model

Given the limitations of the ECSM to explain how the positive and negative components of medication beliefs may change separately over time and what factors impact each component among advanced cancer patients receiving OAs, a derived conceptual model was developed using theory derivation as outlined by Walker & Avant (2011). Some of the ECSM model concepts (Figure 1.1) were redefined as analogies were drawn from the field of cognitive psychology to the field of nursing; those components are highlighted in gray in the derived model (Figure 1.2). In addition, the ECSM structure was adapted by adding or eliminating model concepts and components to better explain the phenomenon of medication beliefs. One of the most innovative areas of derivation involved using medication beliefs as the outcome variable in the model. See Table 1.1 for descriptions of model derivations.

Table 1.1

Description of ECSM and Derived Model Concepts

ECSM Concepts/Components	**Theory/Concept Derivations**	**Derived Model Concepts/Components**
Health Threat	Health threat in the ECSM activates perceptions of treatment. In the derived conceptual model, the new oral oncolytic agent prescription activates treatment perceptions in the form of medication beliefs.	*New Oral OA Prescription* activates medication beliefs and may or may not act as a health threat.
Perceptions of Treatments (needs and concerns)	In the ECSM, treatment perceptions, including the need for treatment and concern for treatment, are activated from the health threat.	*Medication Beliefs* are activated when a patient receives a new oral oncolytic agent. Medication beliefs have both a positive component (represents benefit of taking medication to improve or maintain health) and a negative component (representing concern for taking medication).
Illness Representations	Illness Representations in the ECSM are a main focus of the model in relation to treatment perceptions. Illness Representation in the derived model are displayed only to define medication beliefs within the domain of cancer illness representation for which the oral oncolytic agent was prescribed.	*Illness Representations* in the derived model are displayed to explain that medication beliefs are defined within a larger domain of illness representation for which the medication was prescribed to treat.
Emotional Response to Illness	Emotional Response to Illness is deleted in the derived model as illness representations are not the focus of the derived model.	Emotional Response to Illness is deleted in the derived model because the focus is treatment perceptions in the form of medication beliefs, not perceptions of illness.
Emotional Response to Treatment	Emotional Response to Treatment in the ECSM acts in parallel with Cognitive Representations of Treatment in the form of Treatment Perceptions.	The derived conceptual model also displays parallel processing of emotional response to the oral oncolytic agent via *Depressive Symptoms* and cognitive response to the oral oncolytic agent via *Cognitive Effectiveness*, both affecting medication beliefs over time and interfering with the patient's ability to inhibit behaviors, thoughts, and emotions. Both components inhibit the capacity to view positive aspects of medication beliefs and introduce cognitive bias towards negative aspects of medication.
Coping Procedures	Coping procedures in the ECSM were removed and are not included in the derived conceptual model.	Coping procedures in the ECSM were removed in the new conceptual model as the focus is to explain and predict medication beliefs, not outcomes of medication beliefs.
Appraisals	The appraisal is described, in the ECSM, as "the outcome of adherence or non-adherence is appraised with subsequent reinforcement or change in treatment representations" (Horne, 2003, pg. 147).	The derived model describes the *Appraisals* as evaluating treatment-related events (e.g. symptom severity & interference/adverse events) experienced along the oral oncolytic agent treatment trajectory that can reinforce or change medication beliefs over time.

Table 1.1 (cont'd)

Newly Added Model Concepts		
ECSM Concepts/Components	**Theory/Concept Derivations**	**Derived Model Concepts/Components**
N/A	Past experiences with health, illness, and medications act as antecedent to medication belief structure.	*Past Experiences with Health, Illness, and Medications* are important in the development of medication beliefs and are fundamental in the experiences that formulate beliefs of new medications, thus are added *antecedents* and appear at the beginning of the model.
N/A	Oral Oncolytic Treatment Trajectory *(Time)* was added to the derived conceptual model to depict the concept of time (12 weeks).	*Oral Oncolytic Treatment Trajectory (Time)* was added to the derived conceptual model to represent how medication beliefs change over time as patients appraise treatment-related events that either reinforce or change existing medication beliefs. The model displays the first 12 weeks of treatment since initiating a new OA medication.
N/A	Treatment-related assaults were added to the derived conceptual model to signify the influence of symptom severity and adverse events on medication beliefs across the oral oncolytic agent treatment trajectory.	*Treatment-Related Assaults* were added to the derived conceptual model to signify the effect of *Symptom Severity* & *Interference* (patient-reported) and *Adverse Events* (documented in the medical record audit) on medication beliefs across the oral oncolytic agent treatment trajectory.
N/A	Physician-directed stoppages are specific to oral oncolytic agent treatment and were added to conceptualize how such medication stoppages can influence medication beliefs.	*Physician-Directed Stoppages,* which are experienced by patients with advanced cancer along treatment trajectory, affect medication beliefs after patients appraise and evaluate oral oncolytic agents after the medication is no longer beneficial to improving or maintaining health.
N/A	Cognitive Effectiveness was added to the derived model to represent the cognitive response to treatment in addition to medication beliefs. As described in the ECSM, cognitive response occurs in parallel with emotional response to treatment. In the ECSM, cognitive response to treatment is depicted in treatment perceptions.	*Cognitive Effectiveness* is important for cognitive processing and the formation of medication beliefs. As patients face treatment-related events along the oral oncolytic agent treatment trajectory, cognitive effectiveness is challenged, decreasing the ability to inhibit stimuli and, therefore, affecting medication beliefs. Specifically, declining cognitive effectiveness can alter one's ability to inhibit behaviors, thoughts, and emotions and can interrupt the ability to self-regulate cancer care and medication taking in the home environment.

A Derived Conceptual Model: The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents

Table 1.1 provides an overview of ECSM derivations completed to form the derived conceptual model. Advanced stage cancer patients have evaluated each domain of their cancer illness representation and treatment perceptions as described in the ECMS as they have experienced and appraised cancer and cancer treatment before being prescribed a new OA (Horne, 2003). Given these domains of illness and treatment representation, appraisals have been made in order to adjust cognitions, emotions and/or behavior with the overall intent to either maintain current health or prevent a decline in current health. The derived conceptual model and its components are described below and illustrated in Figure 1.2. Specific derived components from the ECSM that have been redefined or modified are highlighted in gray (Figure 1.1) as not all the ECSM model components were utilized in the derived model (Figure 1.2). The derived model has renamed some of the ECSM concepts to make the model reflective of advanced cancer patients and are described below.

Model Concepts & Components

Antecedents. A patient's prior experiences with physical, cognitive, and emotional health, illness, and medications can give rise to future medication beliefs (Horne, 2003). Patients with cancer often have other comorbid conditions requiring medications beyond cancer treatments (Sarfati et al., 2016). In addition, patients with advanced cancer have often been exposed to other cancer treatments before they are prescribed an OA, which influence medication beliefs regarding the new OA. Patients with advanced cancer often enter into treatment with a new OA prescription with symptoms stemming from either the cancer or previous treatment with medications prescribed for cancer or other comorbid conditions. In

addition, patients can experience depressive symptoms and altered cognitive effectiveness as they self-manage their cancer, comorbid conditions, various medications and cope with their cancer prognosis. Such depressive symptoms and decreased cognitive effectiveness influence the development of new medication beliefs and impair the ability to inhibit negative perceptions or the ability to perceive the positive aspects of OA treatment.

New oral oncolytic agent prescription. In the ECSM a health threat acts as a stimulus to activate illness and treatment perceptions (Figure 1.1). In the derived conceptual model, the new OA acts as a stimulus and potential health threat to activate medication beliefs (Figure 1.2). When a cancer patient receives a prescription for a new OA, medication beliefs are activated in one of two ways. First, medication beliefs are cognitive structures, which can be triggered by a patient's memory of prior experiences with treatment that influence future medication beliefs. Secondly, medication beliefs can also be activated by cognitive processing of current treatment information (Anderson, 2015; Turk & Salovey, 1985). Cognitive processing involves the patient's ability to take in new external information regarding the medication such as education delivered by the oncologist, oncology nurse, or via informative printed materials and may include cognitive processing of somatic symptoms (Anderson, 2015; Turk & Salovey, 1985).

Positive medication beliefs. Medication beliefs are defined within a larger domain of illness representation for the cancer illness in which the OA was prescribed. Positive medication beliefs represent the belief that treatment is beneficial (Horne, 2003). Examples of the positive beliefs about the benefit of taking medication include improvement of disease symptoms or delayed disease progression (Jansen et al., 2005; Jansen, Otten, & Stiggelbout, 2004). Positive medication beliefs are based on and grow out of larger, long-standing beliefs and past

experiences with the positive benefit of medication that are not as vulnerable to change in relation to OA treatment-related assaults.

Negative medication beliefs. Medication beliefs are defined within a larger domain of illness representation for the caner illness in which the OA was prescribed. Negative medication beliefs represent the concern for taking medication (Horne et al., 1999). Negative medication beliefs are vulnerable to change as patients appraise their experiences with various treatment-related assaults such as symptoms and adverse effects that cause interruptions in a patient's routine or daily schedule (Bhattacharya et al., 2012; Corter et al., 2013; Chen et al., 2014; Salgado, 2017).

Oral oncolytic agent treatment trajectory (Time). The oral oncolytic agent trajectory is placed in the model to denote time. Patients are taking OAs long term and medication beliefs can change over the treatment trajectory as treatment-related events are appraised to either reinforce or change existing medication beliefs. The treatment trajectory that will be examined for the derived model includes the first 12 weeks since initiating a new OA (Figure 1.2).

Treatment-related events. There are several treatment-related events that occur along the OA treatment trajectory such as treatment-related assaults (symptoms, adverse events), permanent physician-directed OA stoppages, depressive symptoms and decreased cognitive effectiveness. These events are highlighted and described below.

Treatment-related assaults: symptoms & adverse events. Over the course of the cancer treatment trajectory, patients may experience a number of treatment-related assaults such as symptoms and adverse events. Symptoms are defined as a perceived physical or psychological disturbance experienced by the patient and have been linked to negative medication beliefs (Bhattacharya et al., 2012; Salgado et al., 2017). Adverse events are defined by the National

Cancer Institute as "any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure" (US Department of Health and Human Services, 2009, pg.2). Adverse events, if confirmed by oncologists, could reinforce current negative beliefs about medications. The experience of symptoms and adverse events can fluctuate over time. As patients appraise these treatment-related assaults, medication beliefs are either reinforced and/or change over time.

Permanent physician-directed oral agent stoppage. Permanent physician-directed OA stoppages are defined as the discontinuation of an oral agent without the intent to restart the medication. Permanent physician-directed OA stoppages are often a result of disease progression, lack of response to the medication, or when the adverse events are deemed to outweigh the benefit of continued treatment (Chan et al., 2016). If the OA is permanently stopped by the physician, it is hypothesized that positive medication beliefs will weaken because the medication is no longer benefiting the patient. However, it is unknown how permanent OA stoppages impact the negative medication beliefs and will be an exploratory aim of this research.

Cognitive effectiveness & depressive symptoms. When patients are prescribed a new medication, both emotional and cognitive responses to treatment occur in parallel (Horne, 2003). Cognitive effectiveness is the capability to efficiently focus concentration on activities of daily living that necessitate attention or working memory (Cimprich, 1992) and can be compromised in individuals with cancer (Asher & Myers, 2015). The relationship of cognitive and emotional processing is highlighted in the derived model. Emotional responses to illness and treatment can include depression, anxiety, stress (Asher & Myers, 2015; Merriman et al., 2017), and worry (Berman et al., 2014) and are associated with cognitive changes.

There are several pathways in which cancer and cancer treatment can cause cognitive changes among patients including effects from the cancer and its treatment, attentional fatigue, affective symptoms (e.g. depression), and sleep disturbances (Merriman, Von Ah, Miaskowski, & Aouizerat, 2013). When prolonged and/or repeated stressors are imposed on individuals with cancer, their cognitive effectiveness declines (Andreotti et al., 2014). Increased cognitive demands are placed on a patient with cancer, especially during diagnosis or learned changes in current prognosis. Eventually, cognitive resources such as directed attention capacity become drained as patients must manage their cancer care including complex dosing regimens, management of symptoms or adverse events, oncology appointments, and managing comorbid conditions and related treatments (Cimprich, 1992). Compromised directed attentional capacities can negatively influence the cognitive reappraisals, decision making, and promote loss of ability to inhibit distracting and negative perceptions and emotions, which are critical in coping with cancer and cancer treatment (Andreotti et al., 2014).

Cognitive changes have been described in patients diagnosed with cancer *prior* to undergoing treatment (Berman et al., 2014; Cimprich et al., 2010), suggesting that emotional responses to the diagnosis and impending treatment, such as worry, impact an individual's cognitive effectiveness (Berman et al., 2014). Such distress and worry can affect illness perceptions and influence adaptive coping (Lehto & Cimprich, 2009). Emotional responses such depressive symptoms can result in pessimistic distortion or the inability to perceive positive benefits treatment and to focus on the negative effects of treatment (Belzung et al., 2015). Depressive symptoms are common to patients facing a terminal illness and who are experiencing treatment related assaults (Fitzgerald et al., 2013). Prolonged emotional distress such as worry, stress, or depression can begin to negatively affect cognitive functioning, specifically attention

and working memory, that can influence higher-level executive functions such as decision making and problem solving (Berman et al., 2014). Patients become increasingly unable to inhibit specific behaviors, thoughts, and emotions when cognitive effectiveness is compromised (Kaplan, 1995; Pennebaker, 1992). This is extremely important for patients who are attempting to self-regulate and manage their cancer care in the home environment. For example, patients with declining cognitive function may not be able to inhibit negative perceptions about their medication and this can negatively affect their medication taking behavior. As emotional responses to illness and treatment increases, cognitive effectiveness decreases, making it difficult for patients to carry out tasks that require concentration (Berman et al., 2014) and inhibitory control. In conclusion, patients with decreased cognitive effectiveness have alterations in their ability concentrate, focus, inhibit unneeded information, and inhibit negative thoughts and emotions, which negatively influences medication beliefs.

Impaired cognitive effectiveness and depressive symptoms can synergistically strengthen negative medication beliefs and inhibit the ability to perceive the positive benefit of medication (Belzung et al., 2015; DiMatteo, Lepper, & Croghan, 2000; Hilliard, Eakin, Borrelli, Green, & Riekert, 2015; Kalichman et al., 2016; Kalichman, Pellowski, Kegler, Cherry, & Kalichman, 2015; Maguire, Hughes, & McElnay, 2008; Reynolds et al., 2004; Salgado et al., 2017). The emotional and cognitive responses to treatment are distinct yet associated concepts influencing one another.

Appraisals. Appraisals are noted to reflect that patients taking OAs evaluate treatment-related events over time and continuously evaluate and interpret information that results in subsequent reinforcement and/or change in medication beliefs (Horne, 2003). Appraisals therefore strengthen or weaken a medication belief.

Relationship among Model Concepts & Components

The positive and negative components of medication beliefs are independent, given they can be held simultaneously (Horne et al., 1999; Kalichman et al., 2016; Phillips et al., 2014). A review of the literature found cancer patients taking oral cancer medications had various factors influencing positive and negative components of medication beliefs in different ways (Bender et al., 2014; Jansen et al., 2005; Bhattacharya et al., 2012; Salgado et al., 2017).

Positive medication beliefs among cancer patients receiving treatment are associated with factors such as previous exposure to chemotherapy, a greater number of prescribed medications and clinical or diagnostic indicators that the cancer medication was effective (Bender et al., 2014; Del Castillo, Godoy-Izquierdo, Vasquez, & Godoy, 2011; Jansen et al., 2005; Jansen et al., 2004). Negative medication beliefs are associated with factors such as depression, interruptions to cancer treatment, and symptoms and side effects (Bhattacharya et al., 2012; Corter et al., 2013; Salgado et al., 2017).

Based on a review of the cancer literature concerning medication beliefs among cancer patients, positive medication beliefs are less likely to be affected by cancer treatment-related assaults (Heisig et al., 2016; Salgado et al., 2017). For example, the experience of symptoms and side effects do not influence positive components of cancer medication beliefs (Heisig et al., 2016; Salgado et al., 2017). However, the negative components of medication beliefs are influenced by treatment-related assaults, changing in intensity when experiencing symptoms and adverse events (Bhattacharya et al., 2012; Salgado et al., 2017). Therefore, the derived conceptual model (Figure 1.2) depicts the appraisals of treatment-related events, including treatment-related assaults that either reinforce and/or change medication beliefs over time. Negative medication beliefs are conceptualized to be more vulnerable to change as compared to

positive medications beliefs when patients experience various treatment-related assaults over the course of the treatment trajectory and can also negatively influence depressive symptomatology and cognitive effectiveness.

Gaps in the Literature

Studies investigating medication beliefs among cancer patients are cross sectional in nature (Arriola et al., 2014; Bhattacharya et al., 2012; Corter et al., 2013; Grunfeld et al., 2005; Heisig et al., 2016). Longitudinal studies explaining how medication beliefs among cancer patients change over time are limited. Only two longitudinal studies evaluate medication beliefs among cancer patients and neither study reported findings as medication beliefs were either not significant in the final model (Bender et al., 2014) or medication beliefs were only measured at baseline (Llewellyn et al., 2007). Literature examining medication beliefs among late-stage cancer patients receiving cancer treatment is also scarce. In addition, some studies assess medication beliefs among cancer patients before initiating treatment (Llewellyn et al. 2006; Llewellyn et al., 2007), while others assessed medication beliefs following treatment exposure, making it difficult to compare results. Medication beliefs about cancer treatment are also measured by differing methods, which can make comparison among studies challenging.

Research reporting longitudinal data on medication beliefs in other chronic illnesses is limited due to the examination of general medication beliefs rather than medication beliefs that were specific to one type of medication prescribed (Porteous, Francis, Bond, & Hannaford, 2010). Additionally, some studies only examine the negative components of medication beliefs and fail to report on the positive components of medication beliefs (Shiyanbola et al., 2013) or only explore medication beliefs in patients within specific age populations (Shiyanbola et al., 2013). There is also limited research describing potential changes in the positive and negative

components of medication beliefs and the factors associated with potential changes in medication beliefs.

Comparing changes can be difficult as different criteria are chosen to detect temporal changes in medication beliefs, even when the same measurement to quantify medication beliefs is used (Lapointe et al., 2010; Shiyanbola et al., 2013). Studies depicting oral cancer medication beliefs among patients receiving targeted OAs are also not well represented. Lack of research involving OAs could be a result of the fairly recent rise in use of these medications or the assumption that patients receiving oral cancer medication are mostly adherent. Additionally, there may be a failure to link medication beliefs about OAs to patient outcomes. Much of the literature examining medication beliefs among cancer patients is limited to breast cancer patients taking adjuvant endocrine or hormone therapy (Arriola et al., 2014; Corter et al., 2013; Bender et al., 2014; Heisig et al., 2016; Salgado et al., 2017). There is also a lack of conceptual framework that describes the phenomena of medications beliefs and the factors that can influence changes in medication beliefs over time.

In summary, the science currently lacks both conceptual clarity and empirical evidence regarding how positive and negative components of medication beliefs change over time among advanced cancer patients receiving OAs, the factors associated with changes in medication beliefs over time, such as treatment-related assaults, and the effects permanent physician-directed stoppages of OAs have on medication beliefs. The dissertation study outlined to address these gaps is presented in the following section.

Dissertation Format & Study Purpose

A three-manuscript format is presented for this dissertation. The following three chapters represent each of the three manuscripts formatted per author guidelines in preparation for

submission for journal publication (Figure 1.3). The purpose of the studies included in the dissertation project is to address significant gaps in the current literature describing medication beliefs.

Manuscript 1 (Chapter 2)

Manuscript 1 aims to reconceptualize medication beliefs by highlighting factors that influence positive and negative components of these beliefs among advanced stage cancer patients receiving OA medication during the first 12 weeks after initiating a new OA. This work introduces a conceptual model using the theory derivation approach to explain and describe the phenomenon of medication beliefs across the first 12 weeks of the treatment trajectory, thus adding to nursing science. Manuscript 1 is formatted to meet author guidelines according to the European Journal of Cancer Care.

Manuscript 2 (Chapter 3)

Manuscript 2 examines relationships among portions of the derived conceptual model introduced in Manuscript 1 by examining how positive and negative components of medication beliefs change over the first 12 weeks after the initiation of a new oral oncolytic medication by measuring medication beliefs at baseline, 4, 8, and 12 weeks. Additionally, the influence of patient-reported symptom severity and symptom interference, depressive symptoms, and cognitive effectiveness on medication beliefs over 12 weeks since initiating a new oral oncolytic medication are examined. A secondary analysis was completed using data derived from a National Cancer Institute study, *Improving Adherence to Oral Cancer Agents and Self Care of Symptoms Using an IVR* (Given & Given, 2013-2017). The parent study is a two-arm randomized controlled trial of a symptom management and OA adherence intervention over 12 weeks using an interactive voice response (IVR) system (Given & Given, 2013-2017).

Patient sociodemographics, including age, sex, race, ethnicity and education, and patient cancer and cancer treatment characteristics including cancer site, cancer stage, cancer diagnosis as recurrent disease, oral agent drug classification, and whether patients received either concurrent intravenous chemotherapy or radiation is evaluated and used to describe the sample.

Medication beliefs are the dependent variables and operationalized using an adapted Beliefs about Medicine Questionnaire (BMQ), an 11-item instrument measuring both positive and negative components of medication beliefs (Horne et al., 1999). Baseline medication beliefs were adjusted for. Three repeated measures of medication beliefs were investigated in relation to three repeated measures of independent variables, including patient-reported symptom severity and interference as measured by the Cancer Symptom Experience Inventory (Given et al., 2008), cognitive effectiveness measured by the Attentional Function Index (Cimprich 1992), and depressive symptomatology measured by the Center for Epidemiologic Studies-Depression (CES-D) scale (Radloff, 1977). Number of comorbid conditions requiring medication, verified via medical record audit, were also evaluated.

SPSS was used to complete data analyses. The analysis used descriptive statistics to summarize the distributions of age, sex, race, ethnicity, level of education, site of cancer, and cancer medication characteristics. Next, distributions of the 12-week interview BMQ subscales scores (outcome variables) were evaluated. The analysis included linear mixed effects models (LME) to relate each BMQ subscale at the four data collection points (baseline, 4, 8, & 12 weeks) to the fixed explanatory covariates (age, sex, race, ethnicity, level of education, site of cancer, cancer medication drug category, cancer medication as continuous or intermittent, and study group assignment). Baseline BMQ was adjusted for in the study. Time was entered as a categorical value in reference to the three data collection points (4, 8, & 12 weeks) to capture

potential non-linear change patterns among study participants over the course of the 12-week study. Least squares means of each BMQ subscale at each time point was output from the LME and differences tested to evaluate if positive and negative dimensions of medication beliefs change over time.

In addition, patient-reported summed symptom severity and interference indices were added to the LME separately as explanatory time varying-covariates. If an effect was found on medication beliefs, an exploratory analysis examining the influence of the five most prevalent symptoms on the BMQ were completed. The outcome of the exploratory analysis was used as a guide to select and narrow the number of symptom severity and interference scores used in the LME analyses. Each symptom severity and interference score from this exploratory analysis was entered one at a time instead of the summed severity and interference in the model. Finally, additional explanatory time-varying covariates of depressive symptoms and cognitive effectiveness, and fixed covariates of the number of comorbid conditions requiring medication were added to the LME separately one at a time to determine their influence on positive and negative medication beliefs. Manuscript 2 is formatted to meet author guidelines according to Psycho-Oncology.

Manuscript 3 (Chapter 4)

Manuscript 3 builds on Manuscript 2 by examining additional relationships in the derived conceptual model. Secondary analysis of data derived from a National Cancer Institute study, *Improving Adherence to Oral Cancer Agents and Self Care of Symptoms Using an IVR* (Given & Given, 2013-2017), explores the relationship of adverse events documented in the medical record on medication beliefs at 12 weeks post-initiation of a new oral oncolytic agent. This manuscript also explores the effect that permanent physician-directed OA stoppages have on the positive and

negative components of medication beliefs by comparing differences in medication beliefs between those who had permanent physician-directed OA stoppages and those who did not.

Patient sociodemographics, including age, sex, race, ethnicity, and education, and patient cancer and cancer treatment characteristics, including cancer site, cancer stage, cancer diagnosis as recurrent disease, oral agent drug classification, and whether patients received either concurrent intravenous chemotherapy or radiation, are evaluated and used to describe the sample.

Medication beliefs are operationalized using an adapted 11-item BMQ (Horne et al., 1999) at 12 weeks. Medication beliefs are the dependent variables. Adverse events are the independent variable, measured by the Common Terminology Criteria for Adverse Events (U.S. Department of Health and Human Services, 2009) and collected via medical record audit at the end of the 12-week parent study, not over time. The effect of number of comorbid conditions requiring medication, verified by medical record audit, was controlled for in the analyses.

Medical record audits confirmed physician-directed OA stoppages and reason for OA stoppage. Physician-directed stoppages are defined as discontinuation of at least one oral agent, listed within the parent study protocol, without the intent to restart the medication. Physician-directed OA stoppages, reasons for OA stoppages, and patient referrals to hospice were measured via medical record audit.

SPSS was used to complete data analyses. The analysis uses descriptive statistics to summarize the distributions of age, sex, race, ethnicity, level of education, site of cancer, and cancer medication characteristics. Next, distributions of the 12-week interview BMQ subscales scores (outcome variables) and explanatory variables, including selected adverse events and physician-directed oral oncolytic stoppages was also evaluated. A regression analysis evaluated the relationship of the total number of adverse events with each of the BMQ subscales

(dependent variables) at the 12-week interview, adjusting for baseline BMQ. Demographic and cancer/oral agent medication characteristics are adjusted for and the effect of number of comorbid conditions requiring medication are controlled.

Next, the relationship that permanent physician-directed OA stoppages have on the positive and negative dimension of medication beliefs at 12 weeks after initiation of a new oral agent is examined. For study participants completing the 12-week BMQ after a documented permanent physician-directed OA stoppage, a t-test determined differences in positive and negative components of medication beliefs between those who had permanent OA stoppages and those who did not. This unadjusted analysis was followed by the adjusted analysis, in which positive and negative components of medications beliefs at week 12 are related to medication beliefs at baseline, demographic and cancer/oral agent medication characteristics, and permanent physician-directed oral agent stoppage. Manuscript three is formatted to meet author guidelines according to Oncology Nursing Forum.

Chapter 5: Conclusion

The final chapter of this dissertation provides a summary of the three manuscripts. A collaborative discussion regarding findings, interpretations, limitations and implications for future nursing research and practice will be provided as well.

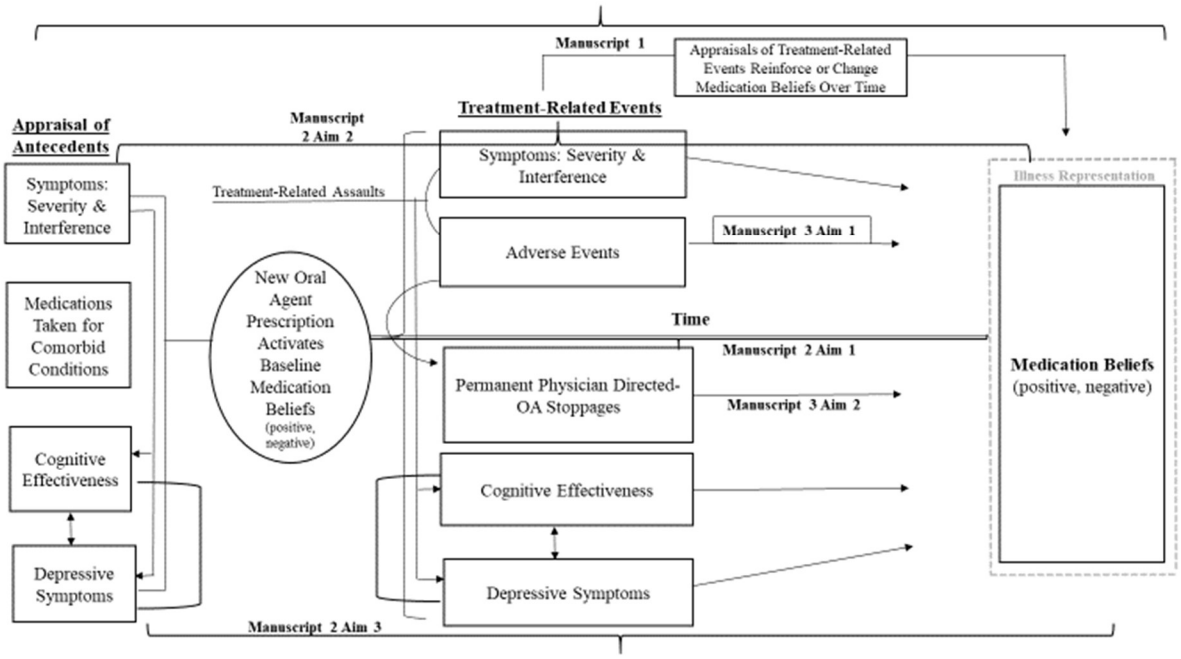

Figure 1.3 Manuscripts and aims highlighted within the Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). *Derived model from Extended Common-Sense Model of Self-Regulation (Horne, 2003).*

APPENDIX

APPENDIX

Routledge Copyright Permission: Extended Common-Sense Model of Self-Regulation

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REFERENCES

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Aikens, J. E., Nease, D. E., & Klinkman, M. S. (2008). Explaining patients' beliefs about the necessity and harmfulness of antidepressants. *The Annals of Family Medicine*, *6*(1), 23–29.

American Cancer Society. Cancer Facts & Figures. (2018). www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2018.html. Accessed on March 4, 2018.

American Society of Clinical Oncology. Cancer Progress. (n.d.). www.cancerprogress.net/cca/advances-cancer-treatment. Accessed September 28, 2017.

Andreotti, C., Root, J. C., Ahles, T. A., McEwen, B. S., & Compas, B. E. (2015). Cancer, coping, and cognition: A model for the role of stress reactivity in cancer-related cognitive decline. *Psycho-Oncology*, *24*(6), 617–623.

Arlt, A., Nestoriuc, Y., Rief, W. (2017). Why Current drug adherence programs fails: Addressing psychological risk factors of nonadherence. *Current Opinion in Psychiatry*, *30*(5), 326–333. Doi :10.1097/YCO.0000000000000345.

Arriola, K. R. J., Mason, T. A., Bannon, K. A., Holmes, C., Powell, C. L., Horne, K., & O'Regan, R. (2014). Modifiable risk factors for adherence to adjuvant endocrine therapy among breast cancer patients. *Patient Education and Counseling*, *95*(1), 98–103.

American Society of Clinical Oncology. (n.d.). Advances in Cancer Treatment Beyond Immunotherpay.progress/reports-studies/clinical-cancer-advances/advances-cancer-treatment-beyond. Accessed July 2017.

Anderson, J. R. (2015). *Cognitive Psychology and Its Implications*. New York, NY: Worth Publishers.

Asher, A., & Myers, J. S. (2015). The effect of cancer treatment on cognitive function. *Clinical Advances in Hematology Oncology*, *13*(7), 441–450.

Banning, M. (2012). Adherence to adjuvant therapy in post-menopausal breast cancer patients: A review. *European Journal of Cancer Care*, *21*(1), 10–19.

Belzung, C., Willner, P., & Philippot, P. (2015). Depression: From psychopathology to pathophysiology. *Current Opinion in Neurobiology*, *30*, 24–30. Doi: http://dx.doi.org/10.1016/j.conb.2014.08.013.

Bender, C. M., Gentry, A. L., Brufsky, A. M., Casillo, F. E., Cohen, S. M., Dailey, M. M., ... & Sereika, S. M. (2014, May). Influence of patient and treatment factors on adherence to adjuvant endocrine therapy in breast cancer. *Oncology Nursing Forum 41*(3), 274–285.

Berman, M. G., Askren, M. K., Jung, M., Therrien, B., Peltier, S., Noll, D. C., ... & Cimprich, B. (2014). Pretreatment worry and neurocognitive responses in women with breast cancer. *Health Psychology*, *33*(3), 222.

Bhattacharya, D., Easthall, C., Willoughby, K. A., Small, M., & Watson, S. (2012). Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. *Journal of Oncology Pharmacy Practice*, *18*(3), 333–342.

Cameron, L. D., & Leventhal, H. (Eds.). (2003). *The self-regulation of health and illness 39ehavior*. London: Routledge.

Center Watch. (2017). FDA Approved Drugs for Oncology. www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology.

Chambers, J. A., O'Carroll, R. E., Hamilton, B., Whittaker, J., Johnston, M., Sudlow, C., & Dennis, M. (2011). Adherence to medication in stroke survivors: A qualitative comparison of low and high adherers. *British Journal of Health Psychology*, *16*(3), 592–609. Doi:10.1348/2044-8287.00200.

Chan, W. L., Lam, K. O., Siu, W. K., & Yuen, K. K. (2016). Chemotherapy at end-of-life: An integration of oncology and palliative team. *Supportive Care in Cancer*, *24*(3), 1421–1427.

Chen, L. C., Chen, T. C., Huang, Y. B., & Chang, C. S. (2014). Disease acceptance and adherence to imatinib in Taiwanese chronic myeloid leukaemia outpatients. *International Journal of Clinical Pharmacy*, *36*(1), 120–127.

Cimprich B. (1992). Attentional fatigue following breast cancer surgery. *Research in Nursing & Health*, *15*:199–207. Doi: 10.1002/nur.4770150306.

Corter, A. L., Findlay, M., Broom, R., Porter, D., & Petrie, K. J. (2013). Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology*, *18*(1), 168–181.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, *160*(14), 2101–2107. Doi:10.1001/archinte.160.14.2101.

Del Castillo, A., Godoy-Izquierdo, D., Vázquez, M. L., & Godoy, J. F. (2011). Illness beliefs about cancer among healthy adults who have and have not lived with cancer patients. *International Journal of Behavioral Medicine*, *18*(4), 342–351.

Earle, C. C., Neville, B. A., Landrum, M. B., Ayanian, J. Z., Block, S. D., & Weeks, J. C. (2004). Trends in the aggressiveness of cancer care near the end of life. *Journal of Clinical Oncology*, *22*(2), 315–321.

Earle, C. C., Landrum, M. B., Souza, J. M., Neville, B. A., Weeks, J. C., & Ayanian, J. Z. (2008). Aggressiveness of cancer care near the end of life: Is it a quality-of-care issue?. *Journal of Clinical Oncology*, *26*(23), 3860–3866.

Eek, D., Krohe, M., Mazar, I., Horsfield, A., Pompilus, F., Friebe, R., & Shields, A. L. (2016). Patient-reported preferences for oral versus intravenous administration for the treatment of cancer: A review of the literature. *Patient Preference and Adherence*, *10*, 1609–1621. http://doi.org/10.2147/PPA.S106629.

Fink, A. K., Gurwitz, J., Rakowski, W., Guadagnoli, E., & Silliman, R. A. (2004). Patient beliefs and tamoxifen discontinuance in older women with estrogen receptor—positive breast cancer. *Journal of Clinical Oncology*, *22*(16), 3309–3315.

Fitzgerald, P., Lo, C., Li, M., Gagliese, L., Zimmermann, C., & Rodin, G. (2013). The relationship between depression and physical symptom burden in advanced cancer. *BMJ Supportive & Palliative Care*, *5*, 381–388.

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The necessity–concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling*, *99*(5), 706–717. doi:10.1016/j.pec.2015.11.004.

Geynisman, D. M., & Wickersham, K. E. (2013). Adherence to targeted oral anticancer medications. *Discovery Medicine*, *15*(83), 231–241.

Given, B.A., & Given, C.W. (2013–2017). *Improving adherence to oral cancer agents and self care of symptoms using an IVR (1R01CA162401-O1A1)*. [National Cancer Institute clinical trial]. Retrieved from https://clinicaltrials.gov/ct2/show/NCT02043184.

Given, C. W., & Given, B. A. (2016). Care of the Elderly Patient on Oral Oncolytics for Advanced Disease. *Current Geriatrics Reports*, *5*(3), 233–239.

Given, B., Given, C. W., Sikorskii, A., Jeon, S., McCorkle, R., Champion, V., & Decker, D. (2008). Establishing mild, moderate, and severe scores for cancer-related symptoms: How consistent and clinically meaningful are interference-based severity cut-points? *Journal of Pain and Symptom Management, 35*(2), 126–135. Doi:10.1016/j.jpainsymman.2007.03.012.

Given, B. A., Spoelstra, S. L., & Grant, M. (2011, May). The challenges of oral agents as antineoplastic treatments. In *Seminars in Oncology Nursing* (Vol. 27, No. 2, pp. 93–103). WB Saunders.

Grunfeld, E. A., Hunter, M. S., Sikka, P., & Mittal, S. (2005). Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Education and Counseling*, *59*(1), 97–102.

Hess, L. M., Louder, A., Winfree, K., Zhu, Y. E., Oton, A. B., & Nair, R. (2017). Factors associated with adherence to and treatment duration of erlotinib among patients with non-small cell lung cancer. *Journal of Managed Care & Specialty Pharmacy*, *23*(6), 643–652.

Heisig, S. R., Shedden-Mora, M. C., Blanckenburg, P., Rief, W., Witzel, I., Albert, U. S., & Nestoriuc, Y. (2016). What do women with breast cancer expect from their treatment? Correlates of negative treatment expectations about endocrine therapy. *Psycho-Oncology*, *25*(12), 1485–1492.

Hilliard, M. E., Eakin, M. N., Borrelli, B., Green, A., & Riekert, K. A. (2015). Medication beliefs mediate between depressive symptoms and medication adherence in cystic fibrosis. *Health Psychology*, *34*(5), 496–504. Doi: 10.1037/hea0000136.

Horne, R., Chapman, S. C., Parham, R., Freemantle, N., Forbes, A., & Cooper, V. (2013). Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: A meta-analytic review of the Necessity-Concerns Framework. *PLOS One*, *8*(12), 1–24. Doi: http://dx.doi.org/10.1371/journal.pone.0080633.

Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology and Health*, *17*(1), 17–32.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health*, 14(1), 1–24. Doi:10.1080/08870449908407311.

Horne, R. (2003). Treatment perceptions and self-regulation. In The self-regulation of health and illness behavior. In L. D. Cameron, & H. Leventhal (Eds.), *The self-regulation of health and illness behavior* (pp. 138–153). New York, NY: Routledge.

Hung, M. S., Chen, I. C., Lee, C. P., Huang, R. J., Chen, P. C., Tsai, Y. H., & Yang, Y. H. (2017). Incidence and risk factors of depression after diagnosis of lung cancer: A nationwide population-based study. *Medicine*, *96*(19).

Iskandarsyah, A., de Klerk, C., Suardi, D. R., Soemitro, M. P., Sadarjoen, S. S., & Passchier, J. (2014). Psychosocial and cultural reasons for delay in seeking help and nonadherence to treatment in Indonesian women with breast cancer: A qualitative study. *Health Psychology*, *33*(3), 214–221.

Jansen, S. J. T., Otten, W., Baas-Thijssen, M. C. M., van de Velde, C. J. H., Nortier, J. W. R., & Stiggelbout, A. M. (2005). Explaining differences in attitude toward adjuvant chemotherapy between experienced and inexperienced breast cancer patients. *Journal of Clinical Oncology*, *23*(27), 6623–6630.

Jansen, S. J., Otten, W., & Stiggelbout, A. M. (2004). Review of determinants of patients' preferences for adjuvant therapy in cancer. *Journal of Clinical Oncology*, *22*(15), 3181–3190.

Kalichman, S., Kalichman, M. O., & Cherry, C. (2016). Medication beliefs and structural barriers to treatment adherence among people living with HIV infection. *Psychology & Health*, *31*(4), 383–395. Doi:10.1080/08870446.2015.1111371.

Kalichman, S. C., Pellowski, J., Kegler, C., Cherry, C., & Kalichman, M. O. (2015). Medication adherence in people dually treated for HIV infection and mental health conditions: Test of the medications beliefs framework. *Journal of Behavioral Medicine*, *38*(4), 632–641.

Kaplan, S. (1995). The restorative benefits of nature: Toward an integrative framework. *Journal of Environmental Psychology*, *15*(3), 169–182.

Krauskopf, K., Federman, A.D., Kale, M.S., Sigel, K.M., Martynenko, M., O'Conor, R., …Wisnivesky, J.P. (2015). Chronic obstructive pulmonary disease illness and medication beliefs are associated with medication adherence. *COPD: Journal of Chronic Obstructive Pulmonary Disease, 12*(2), 151–164. Doi:10.3109/15412555.2014.922067.

Kung, M., Koschwanez, H. E., Painter, L., Honeyman, V., & Broadbent, E. (2012). Immunosuppressant nonadherence in heart, liver, and lung transplant patients: Associations with medication beliefs and illness perceptions. *Transplantation*, *93*(9), 958–963. Doi:10.1097/TP.0b013e31824b822d.

LaPointe, N. M. A., Ou, F. S., Calvert, S. B., Melloni, C., Stafford, J. A., Harding, T., ... & Peterson, E. D. (2010). Changes in beliefs about medications during long-term care for ischemic heart disease. *American Heart Journal*, *159*(4), 561–569. doi:10.1016/j.ahj.2009.12.025.

Lehto, R. H., & Cimprich, B. (2009). Worry and the formation of cognitive representations of illness in individuals undergoing surgery for suspected lung cancer. *Cancer Nursing*, *32*(1), 2–10.

Lin, C., Clark, R., Tu, P., Bosworth, H. B., & Zullig, L. L. (2017). Breast cancer oral anti-cancer medication adherence: A systematic review of psychosocial motivators and barriers. *Breast Cancer Research and Treatment*, *165*(2), 247–260. Doi: 10.1007/s10549-017-4317-2.

Liu, G., Franssen, E., Fitch, M. I., & Warner, E. (1997). Patient preferences for oral versus intravenous palliative chemotherapy. *Journal of Clinical Oncology*, *15*(1), 110–115.

Llewellyn, C. D., McGurk, M., & Weinman, J. (2006). Head and neck cancer: To what extent can psychological factors explain differences between health-related quality of life and individual quality of life?. *British Journal of Oral and Maxillofacial Surgery*, *44*(5), 351–357.

Llewellyn, C. D., McGurk, M., & Weinman, J. (2007). Illness and treatment beliefs in head and neck cancer: Is Leventhal's common sense model a useful framework for determining changes in outcomes over time?. *Journal of Psychosomatic Research*, *63*(1), 17–26.

Maguire, L. K., Hughes, C. M., & McElnay, J. C. (2008). Exploring the impact of depressive symptoms and medication beliefs on medication adherence in hypertension—a primary care study. *Patient Education and Counseling*, *73*(2), 371–376. Doi:10.1016/j.pec.2008.06.016.

Marshall, V., Lehto, R., Given, C.W., Given, B., Sikorskii, A. (2018). Conceptualization of medication beliefs among advanced cancer patients receiving oral oncolytic agents using a theory derivation approach. *Unpublished doctoral dissertation, Michigan State University, East Lansing Michigan*.

Matsuyama, R., Reddy, S., & Smith, T. J. (2006). Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *Journal of Clinical Oncology*, *24*(21), 3490–3496.

Medicare's new part D prescription drug benefit: A major work in progress. (2005). *Journal of Oncology Practice, 1*(4), 162–166. Doi: 10.1200/jop.2005.1.4.162.

Merriman, J. D., Von Ah, D., Miaskowski, C., & Aouizerat, B. E. (2013, November). Proposed mechanisms for cancer-and treatment-related cognitive changes. In *Seminars in Oncology Nursing* (Vol. 29, No. 4, pp. 260–269).

Mohammed, S., Peter, E., Gastaldo, D., & Howell, D. (2016). The "Conflicted Dying" The Active Search for Life Extension in Advanced Cancer Through Biomedical Treatment. *Qualitative Health Research*, *26*(4), 555–567.

Moon, Z., Moss-Morris, R., Hunter, M. S., Carlisle, S., & Hughes, L. D. (2017). Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: A systematic review. *Patient Preference and Adherence*, *11*, 305–322.

Morgan, C., McBeth, J., Cordingley, L., Watson, K., Hyrich, K. L., Symmons, D. P., & Bruce, I. N. (2015). The influence of behavioural and psychological factors on medication adherence over time in rheumatoid arthritis patients: A study in the biologics era. *Rheumatology*, *54*(9), 1780–1791. Doi: 10.1093/rheumatology/kev105.

National Cancer Institute. (2017). Cancer Statistics. www.cancer.gov/about-cancer/understanding/statistics.

Neame, R., & Hammond, A. (2005). Beliefs about medications: A questionnaire survey of people with rheumatoid arthritis. *Rheumatology*, *44*(6), 762–767. Doi: 10.1093/rheumatology/keh587.

Neuss, M. N., Polovich, M., McNiff, K., Esper, P., Gilmore, T. R., LeFebvre, K. B., ... & Jacobson, J. O. (2013). 2013 updated American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards including standards for the safe administration and management of oral chemotherapy. *Journal of Oncology Practice*, *9*(2S), 5–13. Doi: 10.1200/JOP.2013.000874.

Patients Equal Access Coalition. Oral Chemotherapy Access Legislative Landscape. (2017) www.peac.myeloma.org/oral-chemo-access-map/.

Pennebaker, J. W. (1992). Inhibition as the linchpin of health. In H. S. Friedman (Ed.), *Hostility, Coping, & Health* (pp. 127–139). Washington, DC, US: American Psychological Association.

Phillips, L. A., Diefenbach, M. A., Kronish, I. M., Negron, R. M., & Horowitz, C. R. (2014). The necessity-concerns framework: A multidimensional theory benefits from multidimensional analysis. *Annals of Behavioral Medicine*, *48*(1), 7–16. Doi: 10.1007/s12160-013-9579-2.

Porteous, T., Francis, J., Bond, C., & Hannaford, P. (2010). Temporal stability of beliefs about medicines: Implications for 44ehavior44z adherence. *Patient Education and Counseling*, *79*(2), 225–230.

Radloff LS. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 1*(3): 385–401.

Reynolds, N. R., Testa, M. A., Marc, L. G., Chesney, M. A., Neidig, J. L., Smith, S. R., ... & Robbins, G. K. (2004). Factors influencing medication adherence beliefs and self-efficacy in persons naive to antiretroviral therapy: A multicenter, cross-sectional study. *AIDS and Behavior*, *8*(2), 141–150.

Sarfati, D., Koczwara, B., & Jackson, C. (2016). The impact of comorbidity on cancer and its treatment. *CA: A Cancer Journal for Clinicians*, *66*(4), 337–350.

Salgado, T. M., Davis, E. J., Farris, K. B., Fawaz, S., Batra, P., & Henry, N. L. (2017). Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment*, *163*(2), 311–319. Doi: 10.1007/s10549-017-4177-9.

Saratsiotou, I., Kordoni, M., Bakogiannis, C., Livadarou, E., Skarlos, D., Kosmidis, P. A., & Razis, E. (2010). Treatment adherence of cancer patients to orally administered chemotherapy: Insights from a Greek study using a self-reported questionnaire. *Journal of Oncology Pharmacy Practice*, *17*(4), 303–311.

Shimada, Y., Hamaguchi, T., Mizusawa, J., Saito, N., Kanemitsu, Y., Takiguchi, N., ... & Tomita, N. (2014). Randomised phase III trial of adjuvant chemotherapy with oral uracil

and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. *European Journal of Cancer*, *50*(13), 2231–2240.

Shiyanbola, O. O., Farris, K. B., & Chrischilles, E. (2013). Concern beliefs in medications: Changes over time and medication use factors related to a change in beliefs. *Research in Social and Administrative Pharmacy*, *9*(4), 446–457.

Simchowitz, B., Brouillard, D., & Weingart, S. N. (2010). Perceptions and experiences of patients receiving oral chemotherapy. *Clinical Journal of Oncology Nursing*, *14*(4), 447–453.

Spoelstra, S. L., Given, B. A., Given, C. W., Grant, M., Sikorskii, A., You, M., & Decker, V. (2013). An intervention to improve adherence and management of symptoms for patients prescribed oral chemotherapy agents: An exploratory study. *Cancer Nursing*, *36*(1), 18–28.

Thuné-Boyle, I. C., Myers, L. B., & Newman, S. P. (2006). The role of illness beliefs, treatment beliefs, and perceived severity of symptoms in explaining distress in cancer patients during chemotherapy treatment. *Behavioral Medicine*, *32*(1), 19–29.

Tipton, J. M. (2015). Overview of the challenges related to oral agents for cancer and their impact on adherence. *Clinical Journal of Oncology Nursing*, *19*(3), 37–40.

Treharne, G. J., Lyons, A. C., & Kitas, G. D. (2004). Medication adherence in rheumatoid arthritis: Effects of psychosocial factors. *Psychology, Health & Medicine*, *9*(3), 337–349. Doi:10.1080/13548500410001721909.

Turk, C., Salovey, P. (1985). Cognitive Structures, Cognitive Processes, and Cognitive-Behavior Modification: I. Client Issues. *Cognitive Therapy & Research*. *9*(1), pp. 1–17.

US Department of Health and Human Services. (2009). Common terminology criteria for adverse events (CTCAE) version 4.0. *National Institutes of Health, National Cancer Institute*, *4*(03). www.evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. Accessed October 5, 2017.

Walker, L.O., & Avant, K.C. (2011). Theory derivation, In L.O. Walker & K.C. Avant (5 Eds.), *Strategies for Theory Construction in Nursing*. New Jersey: Prentice Hall.

Weingart, S. N., Brown, E., Bach, P. B., Eng, K., Johnson, S. A., Kuzel, T. M., ... & O'Brien, S. (2008). NCCN Task Force Report: Oral chemotherapy. *Journal of the National Comprehensive Cancer Network: JNCCN*, *6*, S1–14.

CHAPTER 2: CONCEPTUALIZATION OF MEDICATION BELIEFS AMONG ADVANCED CANCER PATIENTS RECEIVING ORAL ONCOLYTIC AGENTS USING A THEORY DERIVATION APPROACH

Introduction

The use of oral oncolytic agents (OAs) is increasing and frequently prescribed for patients with advanced stage cancer who have experienced prior failed cancer treatments (Clarke, Johnston, Corrie, Kuhn, & Barclay, 2015; Mohammed, Peter, Gastaldo, & Howell, 2016). The Food and Drug Administration approves several cancer treatments each year, with an estimated 70% of these treatments currently being offered in oral form (Center Watch, 2017). OAs have presented a paradigm shift in the way cancer care is delivered. Patients and family caregivers are taking on the increased responsibility of cancer care, including OA administration and symptom management, in the home environment (Given, Spoelstra, & Grant, 2011; Hess et al., 2017; Weingart et al., 2008).

OAs differ from medications taken for other chronic conditions as patients are faced with a multitude of treatment challenges. First, OAs have complex dosing regimens involving combined therapy, cycling, or regimens that change over the course of treatment depending on how the patient tolerates the medication. Second, OAs are toxic and often cause adverse events, such as severe symptoms, side effects, and toxicities that may require medication interruptions and/or stoppages (Tipton, 2015; Shimada et al., 2014). Unlike traditional chemotherapies, which are administered in the clinic setting, patients are self-managing adverse events of OA medication at home without the close observation of oncology professionals (Hess et al., 2017). Additionally, OAs may make patients feel more ill than before they started the medication.

For advanced cancer patients, OA medications are often offered as a palliative option, not a curative one. OAs also have strict therapeutic ranges (Neuss et al., 2013), so even small decreases in dosage or interruptions and/or stoppages can result in disease progression or

resistance to the medication (Geynisman & Wickersham, 2013). As patients face challenges of OA medication, including complex dosing regimens, symptoms, adverse events, and potentially an unknown limited benefit of delayed disease progression, their medication beliefs regarding the OA can be affected and change over time. Medication beliefs are defined as an individual's perceptions regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003). Medication beliefs are comprised of two components; the positive component represents beliefs that medication provides some benefit to health, and the negative component represents concern for taking the medication (Horne, Weinman, & Hankins, 1999).

Medication beliefs have been the focus of numerous adherence studies across chronic illnesses, including cancer, but current theories used in the research do not address the full phenomenon of medication beliefs. It is unknown how beliefs may change over the treatment trajectory in response to various treatment-related assaults and factors associated with both the positive and negative components of medication beliefs. This paper will use the theory derivation approach, as outlined by Walker & Avant (2011), to explain and describe medication beliefs over time among advanced stage cancer patients receiving oral oncolytic agents.

Purpose

The purpose of this paper is to describe a derived Extended Common-Sense Model of Self-Regulation (Horne, 2003) that gives rise to medication beliefs among advanced cancer patients receiving oral oncolytic agents. The objective was to expand upon and clarify the present conceptualization of medication beliefs.

Methods

Theory derivation is a method by which analogy is used to explain or predict a phenomenon of interest in one field from explanations or predictions in a different field (Walker

& Avant, 2011). Theory derivation is an iterative process and steps may not follow an ordered sequence (Walker & Avant, 2011). This process of derivation involved modifying concepts and/or structure of an existing theory in the field of cognitive psychology to use in in the field of nursing (Walker & Avant, 2011). Theory derivation allows for creativity by the author in order to select parts or the structure of a parent theory that can be modified or redefined in order to advance the theoretical understanding of a phenomenon of interest (Walker & Avant, 2011). Using the methods set forth by Walker & Avant (2011), the five steps used in this theory derivation are described below.

Step 1. Targeted Phenomenon of Interest

The first step of this theory derivation included targeting a phenomenon of interest (e.g. medication beliefs) and becoming acquainted with theory related to the phenomenon in the field of nursing. The level of nursing theory development surrounding medication beliefs was limited and it was determined that further conceptual understanding was warranted.

Step 2. Exploring the Phenomenon in the Literature across Various Fields

The next step was to complete an extensive literature review involving medication beliefs specific to oral medication among patients with various chronic conditions, including hypertension, asthma, chronic obstructive pulmonary disease (COPD), psychiatric disorders, kidney failure, human immunodeficiency virus (HIV), epilepsy, arthritis, and gastrointestinal disorders. The literature review contained research from several fields, including medicine, nursing, pharmacology, and psychology (Table 2.1). An additional integrative review was completed (Marshall & Given, 2018), focusing specifically on the medication beliefs of patients receiving medication to treat cancer (Table 2.2).

A thorough review of the literature allowed for the discovery of gaps in the current theoretical and empirical understanding of medication beliefs, while also determining concepts that are critical to explain the phenomenon of medication beliefs. The literature review was completed in order to guide the selection of a parent study as described in Step 3.

Table 2.1
Search Strategies and Inclusion Criteria for Literature Search across Disciplines & Chronic Illnesses

Search Indexes
Cumulative Index of Nursing and Allied Health Literature (CINAHL) and PubMed.
Key Words
"Medication beliefs"
Inclusion Criteria
Medication beliefs of adults (18 and older
Published in the English language
Peer reviewed
Articles from CINAHL are included if published between the years of 1986-2016
Articles published in PubMed within last 5 years
Exclusion Criteria
Medication beliefs of healthcare providers or caregivers only
Samples including adolescents, children, or pregnant women due to the possible bias of beliefs during a non-chronic condition of pregnancy

Table 2.2
Specific Search Strategies/Criteria for Medication Beliefs in CINAHL, PubMed, & Psych INFO

Search Strategy One	**Search Strategy Two**
"Medication beliefs" OR "treatment beliefs" OR "medication perceptions" OR "treatment perceptions" OR "medication views" OR "treatment views" OR "medication attitudes" OR "treatment attitudes" AND "chemotherapy" OR "oral agents" OR "antineoplastic agents" OR "targeted agents" OR "cancer".	"Beliefs about Medicine* Questionnaire" AND "chemotherapy" OR "oral agents" OR "antineoplastic agents" OR "targeted agents" OR "oral cancer medication" OR "anticancer" OR "cancer".
Search Inclusion Criteria	**Search Exclusion Criteria**
Articles published between the years of 2000-2017	Articles were excluded if beliefs were not specific to cancer medication treatment
In the English language	Articles specific to medication beliefs of cancer physicians or caregivers.
Included examination of medication beliefs among participants ≥ 18 years of age who were prescribed and/or undergoing medication treatment for cancer	Beliefs about cancer-related pain medication

Marshall, V., & Given, B.A. (2018). Factors associated with medication beliefs in patients with cancer: An integrative review. *In Press*. *Oncology Nursing Forum*.

Step 3. Selecting a Parent Theory for Derivation

The third step of this theory derivation was to select a parent theory that could best explain and describe the phenomenon of medication beliefs over time among advanced cancer patients receiving OAs. Based on the literature review, the theoretical framework most widely associated with medication beliefs that could be utilized to advance the state of the science understanding of medication beliefs in nursing was the Extended Common-Sense Model of Self-Regulation (ECSM), which is depicted in Figure 2.1 below (Horne, 2003). The specific components of the ECSM that were used in the derived model are highlighted in gray in Figure 2.1 (See Appendix for copyright permission).

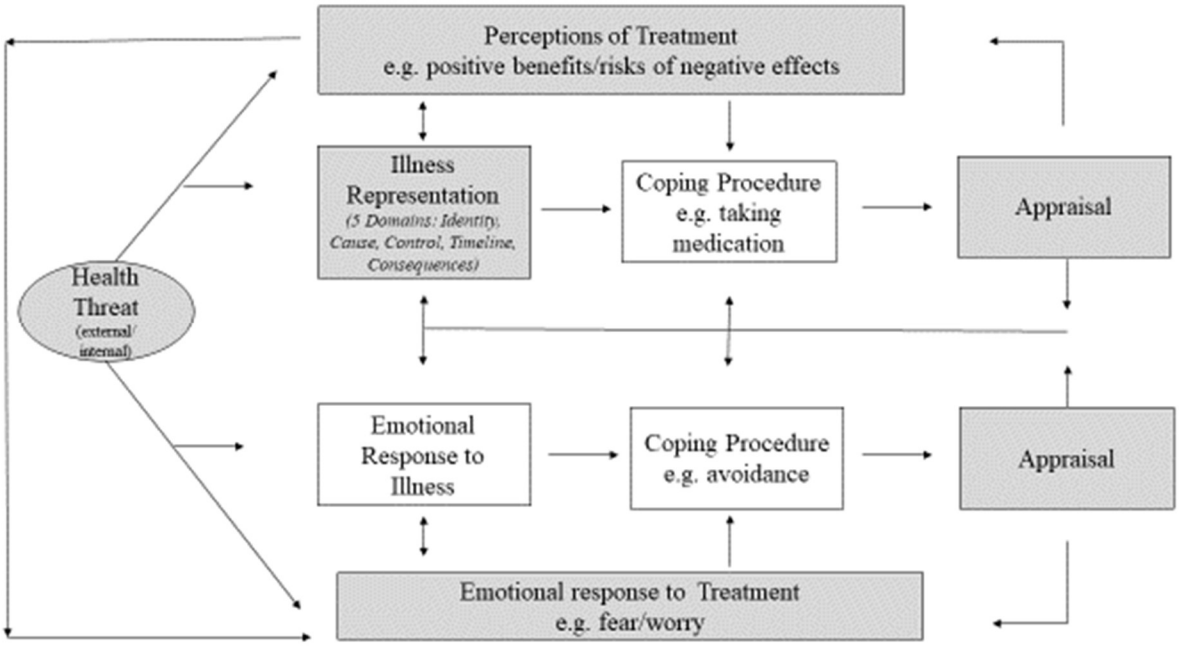

Figure 2.1 The Extended Common-Sense Common of Self-Regulation (Horne, 2003). *Components highlighted in gray are used in the derived conceptual model.*

Step 4. Identifying Concepts/Structure of the Parent Theory to Use in the Derivation

Step 4 of the theory derivation involved selecting concepts and/or structures to be utilized in the derived model from the parent theory (ECSM). Concepts, structures, and statements from the ECSM parent study were evaluated and adapted based on the ability to explain and describe medication beliefs among advanced cancer patients receiving oral oncolytic therapy and derive a nursing conceptual model of the phenomenon of medication beliefs.

Step 5. Redefining Model Concepts/Structure of the Parent Theory to Create a Derived Model

The final step of the theory derivation approach involved modifying and redefining ECSM concepts and creating structural changes to the ECSM. The major contribution of this research is to examine medication beliefs as dependent variables and approaching each of the positive and negative components of medication beliefs as theoretically distinct and not polar opposite constructs (Horne et al., 1999; Kalichman, Kalichman, & Cherry, 2016; Phillips,

Diefenbach, Kronish, Negron, & Horowitz, 2014). This means that patients can hold various strengths of both positive and negative medication beliefs at the same time (Chapman et al., 2015; Iudici, Russo, Mitidieri, Cuomo, & Valentini, 2015; Neame & Hammond, 2005). Holding such seemingly opposite beliefs about medications may develop when an individual understands the need for medication to treat illness, but at the same time has concerns for taking the medication within the context of symptoms or adverse effects of the medications. Positive medication beliefs tend to be more stable as patients have experienced the benefit of medication with other illnesses, whereas negative medication beliefs may fluctuate based on the specific circumstances of the treatment at a specific time point. Therefore, negative medication beliefs would be expected to fluctuate. Medication beliefs can thus be examined to determine how both positive and negative components of medication beliefs may change differently over time, while exploring how treatment-related events along the new OA treatment trajectory influence each of these positive and negative components of medication beliefs separately. The derived conceptual model is shown in Figure 2.2 and provides clarity on how patients can hold opposing beliefs about their medication dialectically. Model components highlighted in gray depict the concepts derived from the ECSM.

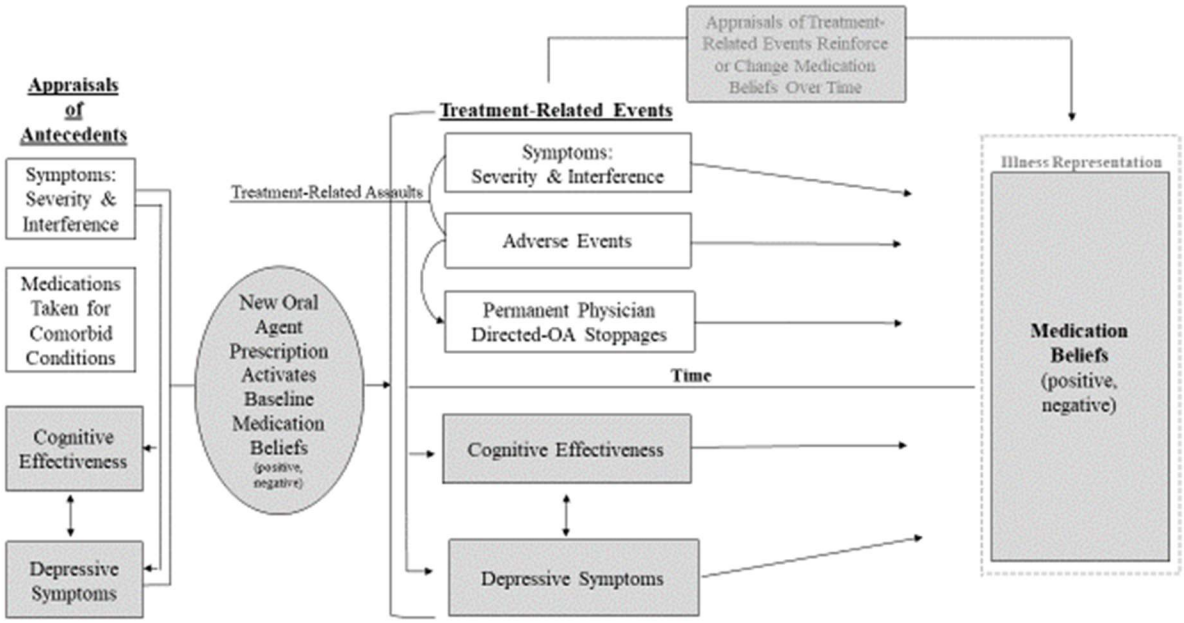

Figure 2.2 The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). *This model is derived from Extended Common-Sense Model of Self-Regulation (Horne, 2003). Derived components from the ECSM that are redefined or modified are shaded in gray.*

Results

Step 1. Targeting a Phenomenon of Interest

Medication beliefs were the targeted phenomenon of interest. Although the literature primarily uses medication beliefs to predict adherence to medications (Chater, Parham, Riley, Hutchison, & Horne, 2014; Kalichman et al., 2016; Lu et al., 2016; McCullough, Tunney, Elborn, Bradley, & Hughes, 2015; Ponieman, Wisnivesky, Leventhal, Musumeci-Szabó, & Halm, 2009), there appeared to be limited studies describing how medication beliefs develop, using medication beliefs as a *dependent* variable, and determining factors that influence medication beliefs. There was also limited research to describe how medication beliefs can change over time. Understanding what influences the positive and negative components of medication beliefs is critical to understanding how each may change differently over time. Nursing theory development, in regard to medication beliefs, is clearly lacking. Advancing the

science regarding medication beliefs should be beneficial to the nursing profession to understand interventions nurses can perform to address medication beliefs in order to improve outcomes, such as adherence.

Step 2. Exploring Phenomenon in the Literature across Various Fields

A literature review, focusing on medication beliefs among various chronic illnesses, allowed for the exploration of current theory among various fields, including medicine, psychology, pharmacology, and nursing, to explain the phenomenon of medication beliefs. An integrative review, specific to medication beliefs among cancer patients receiving cancer medications, facilitated the task of determining concepts critical to explaining the phenomenon of medication beliefs in cancer, understanding relationships between medication beliefs and other variables, and identifying gaps in the literature that served as the basis for developing a derived nursing conceptual model of medication beliefs among cancer patients (Marshall & Given, 2018).

Results of the literature and integrative review are summarized below, as well as the positive and negative components of medication beliefs and their relationship. Key concepts associated with medication beliefs among cancer patients are described, which include prior experiences with health, illness, and medications, treatment-related assaults such adverse events and symptoms, and the goal of cancer treatment.

Positive and negative components of medication beliefs and their relationship.

Medication beliefs arise from illness representations (Horne, 2003). Patients develop positive medication beliefs when they perceive treatment as needed to maintain or improve health and if medication efficacy is supported, hence the reinforcement of positive medication beliefs (Horne, 2003). Negative medication beliefs arise when concern for taking medication is

prompted by either adverse events or symptoms associated with the treatment or when the medication regimen interrupts the daily lives of patients in some way (Horne, 2003). If patients anticipate or experience symptoms, adverse effects or interruptions to daily life, then negative medication beliefs are reinforced (Horne, 2003).

The literature review revealed that individuals hold both positive and negative medication beliefs at the same time (Chapman et al., 2015; Iudici et al., 2015; Neame & Hammond, 2005). However, these positive and negative medication beliefs are not polar opposite constructs (Horne & Weinman, 2002), meaning one can hold any combination of positive and negative medication beliefs at the same time. For example, patients who have strong positive beliefs that their medication is beneficial to maintain or improve health does not necessarily imply they hold weak negative medication beliefs that reflect concern about the medication, and vice versa. A patient may have strong positive beliefs about their medication, but at the same time hold very strong negative medications beliefs.

Positive and negative medication beliefs are independent, theoretically distinct constructs (Phillips et al., 2014). Empirical evidence has repeatedly supported that the negative and positive components of medication beliefs are independent of one another and influenced by different factors (Aikens, Nease, & Klinkman, 2008; Horne et al., 1999; Horne & Weinman, 2002; Kalichman et al., 2016; Neame & Hammond, 2005; Phillips et al., 2014). For example, studies using the Beliefs about Medicine Questionnaire (BMQ) to elicit and quantify medication beliefs among various illness groups in order to test prior theories confirm a distinct two-factor structure that represent the positive and negative medication beliefs (Horne et al., 1999; Horne & Weinman, 2002; Kalichman et al., 2016). Positive and negative medication beliefs have also been linked to different variables (Aikens & Piette, 2009). Additionally, literature supports that

the positive and negative components of medication beliefs have different relationships with outcomes variables, such as adherence (Aikens & Piette, 2009; de Vries et al., 2014; Kalichman et al., 2016; Neame & Hammond, 2005), and with illness representations (Horne & Weinman, 2002).

Prior experiences with health, illness, medications. Prior experiences with physical, cognitive, and emotional health, illness, and medications can influence how medication beliefs are formed and changed, whether these experiences are direct or indirect through experiences of family and friends (Del Castillo, Godoy-Izquierdo,Vázquez, & Godoy, 2011; Iskandarsyah et al., 2014). Experience with medications, whether prescribed for cancer or another comorbid condition, allow an individual to appraise how the medication works to treat their illness, whether or not symptoms or adverse events occur, and, in turn, these appraisals inform future medication beliefs. For example, patients with prior exposure to chemotherapy are reported to have more positive medication beliefs regarding cancer treatment compared to those with no prior exposure to chemotherapy (Bickell et al., 2009; Jansen et al., 2005). Experience with cancer or cancer treatment may provide a more accurate and positive perception about cancer medication (Del Castillo, Godoy-Izquierdo, Vasquez, & Godoy, 2011). Experiences of the positive benefits of cancer treatment such as delayed disease progression can reinforce more positive medication beliefs through a process of cognitive appraisals (Jansen et al., 2005).

Treatment-related assaults: adverse events & symptoms. Treatment-related assaults refer to patient-reported symptoms and adverse events that may include side effects, toxicities, and symptoms associated with the cancer treatment. Cancer medication treatments are distinct in regard to treatment related assaults, often causing more adverse events and symptoms than the cancer illness itself (Thuné-Boyle et al., 2006). Adverse events and symptoms can leave cancer

patients vulnerable to negative cancer medication beliefs (Chen et al., 2014; Jansen et al., 2005; Salgado et al., 2017) as patients appraise these treatment-related assaults and make judgments based on these appraisals. Oncolytic agents produce varying levels of treatment-related assaults over time that could lead to increases in concern for taking the medication and, consequently, changes in negative medication beliefs over time. Positive medication beliefs do not appear to be influenced by treatment-related assaults and were not empirically linked to positive medication beliefs across cancer studies (Heisig et al., 2016; Salgado et al., 2017), thus further supporting that positive and negative medication beliefs are influenced by varying factors.

The goal of cancer treatment. The goal of cancer treatment for patients with advanced cancer is often palliative in nature, which may affect cancer medication beliefs differently than for patients with earlier stage cancers where a cure is attainable (Harrington & Smith, 2008). Patients with advanced cancer may accept cancer treatment that causes an array of adverse events and symptoms, even when the benefit of such treatment is unknown or is minimal (Balmer, Thomas, & Osborne, 2001; Grunfeld, Hunter, Sikka, & Mittal, 2005; Harrington & Smith, 2008; Matsuyama et al., 2006; Silvestri, Pritchard, & Welch, 1998). In contrast, having an earlier-stage cancer has been associated with increased medication concern (Heisig et al., 2016), which can perhaps be explained by a lack of exposure to and experience with cancer treatment.

Patients with advanced cancer have often exhausted other treatment options. Patients may perceive the negative aspects of treatment (adverse events and symptoms) outweigh the choice of no treatment and believe cancer treatment is beneficial or needed until the oncologist informs them all other viable options have been exhausted (Harrington & Smith, 2008). Patients with advanced cancer can perceive that survival gain, no matter how short, is important, especially when they are facing impending death (Koedoot et al., 2003).

In summary, positive and negative medication beliefs are distinctly independent constructs that are influenced by different factors; each of the medication components also influences patient outcomes, such as adherence, differently (Aikens et al., 2008; Horne et al., 1999; Horne & Weinman, 2002; Kalichman et al., 2016; Neame & Hammond, 2005; Phillips et al., 2014). Prior experience with health, illness, and medications, including cancer and cancer treatment, may influence the way patients form positive and negative medication beliefs about newly prescribed cancer medication by way of appraisals that evaluate the illness and/or treatment experience. Those with prior exposure to cancer treatment report more positive medication beliefs via appraisals, such as evaluating the experiences of medication benefit (Del Castillo et al., 2011; Jansen et al., 2005). Those with earlier stage cancers who have little to no exposure to cancer treatment are reported to develop more negative medication beliefs, perhaps as they anticipate concern for adverse effects of the medication (Heisig et al., 2016). Patients experiencing treatment-related assaults, such as symptoms and adverse events, are also vulnerable to develop negative medication beliefs, while positive medication beliefs are not reportedly influenced by symptoms and adverse events (Heisig et al., 2016; Salgado et al., 2017).

Step 3. Selecting a Parent Study for Derivation

The literature review revealed two main conceptual models to describe and explain medication beliefs. Ultimately, the ECSM was selected as the parent study because the model is fundamental in defining medication beliefs. The ECSM explains how a cancer patient's medication beliefs can be formed based on their perceptions of illness representation and how cognitive appraisals may change medication beliefs over time (Horne, 2003). However, the Necessity-Concerns Framework (NCF) will be briefly presented because Horne (2003) proposed a symbiotic relationship between the NCF and the Common-Sense Model of Self-Regulation

during the development of the ECSM. Specifically, Horne (2003) uses both frameworks to explain why patients may vary in their decisions to initiate and adhere to their treatment and explains the importance of illness representations to guide perceptions of treatment necessity. The NCF is also described below because it has been a source of misconception regarding the relationship of positive and negative components of medication beliefs.

Necessity-Concerns Framework. Medication beliefs are most commonly linked to adherence in the literature (Foot, La Caze, Gujral, & Cottrell, 2016; Horne et al., 2013). One of the most common instruments used to quantify medication beliefs is the BMQ (Horne et al., 1999). The BMQ consists of two subscales: *Necessity* represents the patient's belief that medication is needed to improve or maintain health; *Concern* represents misgivings about medications (Horne et al., 1999). The development of the NCF gave rise to the BMQ. Most of the theoretical and conceptual groundwork surrounding the phenomenon of medication beliefs stems from the NCF. The NCF posits the relationship of adherence to medication is based on a patient's assessment regarding whether they perceive a need for medication to treat a condition (*Necessity* beliefs) in relation to their concern (*Concern* beliefs) for taking the medication (Horne & Weinman, 1999). The NCF provides a logical explanation and linkage between the patient's medication beliefs, which postulates if *Necessity* outweighs their *Concern* for taking medication, patients are likely to be adherent (Horne & Weinman, 1999). In contrast, if *Concern* for taking medication is greater than the *Necessity*, patients are likely to be non-adherent (Horne & Weinman, 1999).

The issue with this framework, regarding conceptualizing medication beliefs beyond adherence, is that medication beliefs have positive and negative components that can be independent (Aikens et al., 2008; Aikens & Piette, 2009; Horne et al., 1999; Horne & Weinman,

2002; Kalichman et al., 2016; Neame & Hammond, 2005; Phillips et al., 2014). In addition, the positive and negative components of medication beliefs have different determinants, or factors influencing each component (Aikens et al., 2008; Aikens & Piette, 2009; Horne et al., 1999; Neame & Hammond, 2005; Phillips et al., 2014). The NCF led many researchers to conceptualize medication *Necessity* (positive component) and medication *Concerns* (negative component) have an inverse relationship and that if one increases in strength, the other decreases in strength. This concept is neither empirically nor conceptually supported. Much of this misconception regarding the relationship of the positive and negative components of medication beliefs stems from using the BMQ to collapse the *Necessity* and *Concerns* subscales into one score using a Necessity-Concerns differential (*Necessity* subscale score minus the *Concerns* subscale score) and then arbitrarily grouping patients according to these scales (e.g. high *Necessity*/low *Concerns*). When researchers undertake these approaches, it misrepresents each of the separate components of medication beliefs and fails to adequately investigate their independent contributions to an outcome variable, as well as their combined effects on an outcome (Margolis & Gonzalez, 2014). Although some studies report the use of collapsing the BMQ score is significant to predict adherence, others have found that *Necessity* and *Concerns* do not have an inverse relationship and this non-reciprocal relationship accounted for incremental variance over and above the Necessity-Concerns differential (Margolis & Gonzalez, 2014).

In summary, the NCF has led researchers to conceptualize positive and negative components of medication beliefs as having an inverse relationship and this limits the ability of understanding medication beliefs beyond adherence. The selection of a parent theory from which to develop a derived conceptual model that can explain and describe medication beliefs using a broader framework is the ECSM described below.

Selection of a parent theory: Extended common-sense model of self-regulation. The Extended Common-Sense Model of Self-Regulation (ECSM) identifies that individuals form mental models of their illness (illness representations) and treatment, how to cope with illness and treatment and evaluate their efforts via an appraisal process (Leventhal, Brissette, & Leventhal, 2003). The ECSM integrates both treatment perceptions and illness representations to predict behavior (Horne, 2003) and is depicted in Figure 2.1. The ECSM is fundamental in explaining how a cancer patient's medication beliefs can be formed based on their perceptions of illness representation. Just as patients' perceptions of illness may change over time, their medication beliefs may also change and affect how patients cope and adapt with cancer illness (Horne, 2003). As cancer patients are increasingly responsible for the self-management of cancer treatment regimens and symptoms in the home environment (Given et al., 2011), understanding and addressing medication beliefs that can impact coping with cancer illness is critical. The dynamic interaction between patient beliefs and behavior are highlighted in this model as the patient attempts to achieve a state of health (Horne, 2003).

Self-regulation refers to attempts by an individual to adjust or adapt their cognitions, emotions, and coping behaviors in order to achieve goals of maintaining health and wellness (Cameron & Leventhal, 2003). One key feature of the ECSM is the parallel processing of cognitive and emotional aspects of health threats (Leventhal et al., 2003), which is important to consider among advanced cancer patients who may experience a decline in cognitive effectiveness (Andreotti et al., 2014; Merriman, Von Ah, Miaskowski, & Aouizerat, 2013), anxiety, depressive symptoms, fear of cancer/cancer recurrence (Corter et al., 2013; Salgado et al., 2017), or fear the cancer medication and the treatment regimen itself (Horne, 2003). The parallel processing of cognitive and emotional aspects of a health threat is important when

patients are self-managing their cancer care in the home environment. In order to achieve adherent behaviors and the ability to self-manage aspects of cancer care, patients adapt behavior to reach an ultimate goal of maintaining current health over time (Pennebaker, 1992). This requires individuals to inhibit competing behaviors (e.g. not taking OA medication), thoughts (dialectical beliefs about OA medication), and emotions such as depression, fear, or anxiety (Pennebaker, 1992). The concepts and components of the ECSM model are described below.

Health threat. The ECSM begins with a health threat (Figure 2.1) that activates both illness representations and treatment perceptions, when treatment for the illness is either sought out by the patient or prescribed by a healthcare professional. Health threats can be external or internal (Horne, 20003). External health threats are processed when outside information is evaluated by the patient. Examples of external health threats include the physician's delivery of news regarding an illness diagnosis or prognosis, receiving a prescription for a new medication, or receiving information regarding the potential side effects of a new prescription medication. Internal health threats present in the form of somatic symptoms the patient experiences, which alert them to a potential illness (Horne, 2003). In the derived conceptual model (Figure 2.2), the prescription of a new oral oncolytic agent will activate medication beliefs and may or may not act as a health threat.

Domains of illness representation. There are five domains of illness representation within the ECSM (Figure 2.1): identity, cause, control, timeline, and consequences (Horne, 2003). Each dimension also plays a key role in beliefs about the treatment with medication (Horne, 2003). The five domains of illness representation within the ECSM allow the patient to interpret a health threat and cope with the health threat using common sense actions in order to

maintain health (Horne, 2003). For the purposes of this article, advanced cancer illness and treatment perceptions of OAs will be represented within the domains of illness below.

Identity. The identity domain (Figure 2.1) is described as the characteristics associated with the cancer illness and reflects how the cancer presents itself (Horne, 2003). For example, patients with advanced cancer may experience an onset of severe symptoms indicating the cancer has progressed, while others with advanced cancer may only experience mild symptoms. The identity of an advanced stage cancer illness is important in the formation of medication beliefs regarding OAs. Identity determines whether the patient perceives cancer treatment with medication as benefiting them in some way such as relief of cancer symptoms or delayed disease progression (Horne, 2003). If patients are experiencing *symptoms of cancer*, they are more likely to perceive that medication can be beneficial to treat their cancer illness (Horne, 2003). However, the identity domain could also encompass the adverse events and symptoms experienced by patients as a result of their cancer treatment, which can give rise to negative beliefs about medication. In contrast, symptoms of the cancer medication (e.g. skin rash, hypertension) can actually be a sign of medication efficacy and can be interpreted by the patient in a positive manner that the medication is working (Cai et al., 2013; National Cancer Institute, 2017; Petrelli, Borgonovo, Cabiddu, Lonati, & Barni, 2012), thus increasing positive medication beliefs. Leventhal and colleagues (1986) found similar results among breast cancer patients who interpreted the experience of side effects as a sign the chemotherapy was working, and patients were worried that the absence of such side effects meant the chemotherapy was not beneficial.

Patients who have experienced cancer illness and who have been able to avoid symptom complications of the cancer illness because of the use of OA medication or other cancer treatments may be more accepting of medication (Neuner & Schapira, 2014), which has been

reported among cancer patients previously exposed to chemotherapy (Jansen et al., 2005). Symptom avoidance due to OA medication can facilitate positive medication beliefs as patients experience the benefit of the medication and these benefits of treatment are appraised to inform future beliefs about new medications.

The identity domain depicts characteristics associated with cancer illness and represents what prompts the patient to recognize that they have an illness (Horne, 2003). This recognition of illness is important to the development of medication beliefs.

Cause. Cause of illness (Figure 2.1) describes the individual's impression of how the cancer illness was triggered or the source of their symptoms (Horne, 2003). Cause of an illness can determine how the individual makes common sense out of their treatment with medication (Horne, 2003). Patients with advanced cancer may differ in their interpretation of the cause of their cancer illness compared to other chronic illnesses. Cancer cannot be treated with alternative forms of treatment, such as diet or exercise, and usually entails treatments that are more aggressive. Therefore, advanced cancer patients may perceive treatment with new cancer medications as beneficial. Even when patients have failed prior cancer treatments or may have exhausted all other viable treatment options, they understand that the new medication is their last option for delayed disease progression or relief of cancer symptoms. If patients believe the cause of their illness stems from the cancer treatment in the form of symptoms or adverse events, they may have increasing concern for taking the medication and develop negative medication beliefs.

Control. The control domain of illness (Figure 2.1) of the ECSM refers to the extent to which the individual believes that their illness can be managed or controlled by treatment and/or medication (Horne, 2003). Control relates to the individual's perceptions of the appropriateness of medication to treat the illness, the necessity of the medication to treat the illness, and how

effective they believe the medication will be in treating the illness (Horne, 2003). Patients with advanced stage cancers often have a lack of control over the cancer, however may believe they can delay progression of cancer using a cancer treatment regimen. The OA is often a last resort for advanced cancer patients and therefore an OA may be favorably viewed as appropriate and needed in order to maintain what health the patient does have. If symptoms of cancer are controlled with OAs then a patient experiences a benefit of the medication and appraises these benefits as positive, which reinforces positive medication beliefs.

However, individuals with concerns regarding the risks of negative effects of OAs, such as adverse events, symptoms, or interruption of daily lives, may feel their disease is actually controlling them (Dalbeth, 2011; Tiemensma et al., 2014). This influences the formation of negative medication beliefs as concern for taking the medication mounts.

In summary, a patient's sense of controlling the disease with medication can influence more positive medication beliefs. In contrast, when a patient experiences adverse events, symptoms, or a disruption to their daily schedule because of the medication dosing complexity, this can give rise to negative medication beliefs and growing concern for the medication. This supports that the separate components of medications beliefs are associated with illness representations in different ways.

Timeline. Timeline (Figure 2.1) indicates how long the individual thinks the illness will last, such as an illness that is chronic (terminal) vs. acute/cyclical (Horne, 2003). Individuals with a longer duration of illness and medication treatment, such as patients with advanced cancer, have shown to exhibit more positive medication beliefs, specifically higher perceived benefit of taking medication (Balmer et al., 2001; Jansen et al., 2005; Iudici et al., 2015). This is

perhaps because patients with advanced cancer experience the benefits of treatment, such as a reduction in the symptoms or adverse events caused by cancer or delayed disease progression.

For advanced cancer patients, timeline is viewed differently than for other types of illness, such as diabetes or asthma, because patients have experienced other failed cancer treatments and have typically been given an anticipated timeline of survival by their oncologist. Without cancer treatment, patients may understand their timeline of illness will be terminal sooner than without treatment and thus they may develop positive medication beliefs. Advanced stage cancer patients have already appraised and reappraised their cancer illness and experience with prior treatment. Most patients have recognized the chronic and terminal nature of their illness and the limited options for treatment that remain. In turn, patients with advanced cancer who understand their cancer is terminal, are more willing to accept symptoms and adverse events as a result of treatment (Chan, Lam, Siu, & Yuen, 2016), which can change how negative medication beliefs are formed.

Consequences of Illness and Treatment. The consequences of illness (Figure 2.1) indicate how the individual interprets the illness will affect them (Horne, 2003). Consequences of taking medication refer to the expected outcome of using medication, such as the expectation of the medication to treat symptoms of the illness, delay disease/illness progression, or rather to prevent complications of the illness should no symptoms be present (Horne, 2003). Patients with advanced cancer, who are prescribed an OA, are therefore likely to understand that the OA may serve as a last palliative resort once all other cancer treatment options have been exhausted. Thus, patients with advanced stage cancer prescribed OAs may have more positive medication beliefs because they understand that without the medication, their chance of survival diminishes, and they may have no other alternatives.

However, patients who experience treatment related assaults such as symptoms or adverse events and who consequently have their OA dose altered, interrupted or even stopped may develop more negative medication beliefs and have rising concerns regarding taking their OA medication. Medication stoppages ordered by the oncologists can also negatively influence positive medication beliefs, especially in the event of disease progression when the medication has failed to benefit health.

***Emotional response to illness*.** The emotional response to illness, as described in the ECSM (Figure 2.1), refers to activation of emotions in reaction to illness or treatment (Horne, 2003). Patients diagnosed with cancer develop emotional responses in the form of stress, worry, fear, depression, and anxiety (Darabos & Hoyt, 2017; Fitzgerald et al., 2013; Hendriksen, et al.,2015; Hung et al., 2017). They may fear impending death (Krause, Rydall, Hales, Rodin, & Lo, 2015) and worry if the treatment options available will work to delay disease progression (Darabos & Hoyt, 2017). Cancer patients' emotional responses are not limited to the diagnosis of cancer, but also the aspects of what treatment for the illness will entail.

Emotional and cognitive responses to illness are distinct concepts that occur in parallel, but influence one another (Horne, 2003). For example, as cancer patients experience depressive symptoms as a result their illness or treatment, these emotions may begin to influence cognitive responses to illness and treatment by creating a biased way of interpreting either internal or external information regarding OA medications (Belzung, Willner, & Philippot, 2015; DiMatteo, Lepper, & Croghan, 2000). Such bias can cause the patient to focus on the negative aspects of illness and treatment and the inability to focus on the positive aspects of treatment. In turn, when patients experience the compromised ability to process information because they are dealing with the cancer diagnosis, prognosis and responsibility of self-managing cancer treatment at home,

their cognitive resources are exhausted (Cimprich, 1992). When patients cannot concentrate and focus on their daily tasks because of the cancer or treatment-related realities, they may develop more depressive symptoms and develop negative medication beliefs.

Emotional response to treatment. Just as a health threat activates an emotional response to illness, patients also experience an emotional response to a treatment (Horne, 2003), which is depicted in Figure 2.1. Challenges of the OA medication such as self-managing complex OA dosing regimens, symptoms, and adverse effects of treatment give rise to emotional responses such as depressive symptoms, anxiety, fear, worry and stress (Corter et al., 2013; Salgado et al., 2017). Patients may anticipate negative symptoms and adverse events once the medication is initiated, which can cause an emotional response or worry over how the medication will interrupt their daily life. For patients prescribed an OA, the responsibility of administration of cancer treatment at home without the direct support of oncology professionals may evoke anxiety or worry. Such emotional responses to treatment can affect medication beliefs by inhibiting one's ability to either perceive positive benefits of medication (DiMatteo et al., 2010) or reinforcing negative medication beliefs by focusing attention on the negative aspects of the medication (Salgado et al., 2017).

Perceptions of treatment. Perceptions of treatment include cognitive representations of treatment or medication (e.g. medication beliefs). Horne (2003) describes treatment perceptions in terms of positive benefits and concerns regarding risks of negative effects (Figure 2.1). Patients determine whether or not they need treatment (positive) and can also hold concerns that reflect the medication as a health threat causing adverse effects (negative). Horne (2003) discusses balancing beliefs that medication is needed against concern for taking the medication in relation to coping procedures such as adherence. Horne (2003) hints at the interplay between

perceptions of medication benefit and perceptions of risk regarding negative effects. However, the beliefs that medication is beneficial, and the beliefs of medication concern are theoretically two distinct and separate components of medication beliefs (Horne & Weinman, 2002; Phillips et al., 2014) and prior research indicating an inverse relationship between positive and negative mediation beliefs is not theoretically sound. One can hold both positive and negative medication beliefs at the same time, but one does not necessarily influence the another (Phillips et al., 2014). The major contribution of this derivation is to approach each of the two components of medication beliefs as theoretically distinct constructs (Horne et al., 1999; Kalichman et al., 2016; Phillips et al., 2014) and use these two components as dependent variables.

Coping procedures. When Horne (2003) developed the ECSM, his purpose was to integrate treatment beliefs into the Common-Sense Model of Self-Regulation Theory in order to explain why patients varied in their decisions to initiate treatment and to adhere to a prescribed treatment. The purpose of the ECSM was to focus on adherence as an outcome variable, using treatment perceptions to explain adherence decisions (Horne, 2003). Horne (2003) defined coping procedures (Figure 2.1) as actions or behaviors exhibited by the individual in order to maintain a state of health and he focused specifically on either adhering or not adhering to a treatment regimen. Coping procedures are an essential outcome component of medication beliefs in the ECSM and give rise to the importance of addressing medications beliefs as they can influence patient outcomes.

However, coping will be not be retained in the derived model as the focus of this research is not the outcome of medication beliefs, but medications beliefs as the outcome variable. The goal of the derived conceptual model (Figure 2.2) was to explain how medication beliefs form

and change over time and the factors associated with these changes, using medication beliefs as *dependent* variables.

Appraisals. Appraisal in the ECSM (Figure 2.1) is described by Horne (2003) as the evaluation of coping procedures or outcomes of adherence or non-adherence. Appraisals either reinforce or change illness or treatment representations based on those outcomes (Horne, 2003). For example, if a patient adheres to their medication and as a result they experience a decrease in the illness symptoms, then the benefit of adherence is reinforced and positive medication beliefs that represent the benefit of taking medication are developed or increase in strength. Appraisals in the derived model (Figure 2.2) are based on specific OA treatment-related events that potentiate change of medication beliefs over time.

Summary of the Parent Model & Limitations of the ECSM

Given that medication beliefs are defined within a larger mental model of illness representation for which medication was prescribed, the ECSM is critical to understanding the phenomenon of medication beliefs. Each domain of illness representation influences the positive and negative components of medication beliefs (Horne, 2003). Health threats, whether internal or external, can activate medication beliefs. These health threats also activate emotional and cognitive responses to illness and treatment that can be important to explain how existing illness representations and medication beliefs can be changed. The ECSM coping procedures such as adherence underscore the important relationship between medication beliefs and patient outcomes such as taking medication as prescribed (Horne, 2003). Of all the ECSM model components, appraisals may be the most important to explain how medication beliefs can change over time. However, in the ECSM, appraisals refer to the appraisals of adherence behaviors that can influence future medication beliefs.

The ECSM has limitations in explaining how the positive and negative components of medication beliefs may change separately over time among patients with advanced cancer receiving OAs. In addition, the ECSM does not provide an explanation of factors that influence each of the two components of medication beliefs over time. Much of the literature using the ECSM to guide studies often involves adherence as the outcome variable but fail to fully recognize the factors contributing to an individual's medication beliefs. Medication beliefs are not examined as dependent variables; therefore, the phenomenon of medication beliefs has not been fully explored. Research exploring the factors associated with both positive and negative medication beliefs can give rise to nursing interventions that can facilitate positive medication beliefs, while addressing and intervening to decrease the negative medication beliefs.

There is conceptual clarity to be gained regarding how both the positive and negative components of medication beliefs change over time and what factors are associated with these changes. In order to reconceptualize medication beliefs, a derived conceptual model was developed (Figure 2.2), using the ECSM (Figure 2.1) as a parent study. Figure 2.1 highlights the ECSM concepts that will be used in the derived model. The model components that were not chosen for the derived model included emotional response to illness, as the focus of the derived model is related to medication beliefs and responses to treatment. An additional ECSM model component that was not included in the derived model was coping (e.g. adherence); the purpose of the derived model is to describe the factors influencing medication beliefs and not the outcomes of medication beliefs. The most noteworthy derivations include using positive and negative medication beliefs as dependent variables and describing how treatment-related events along the OA treatment trajectory can influence the two components of medication beliefs

differently. To derive the model specifically to explain medication beliefs among advanced cancer patients taking OAs, additional model components have also been added (Figure 2.2).

The derived model also assumes that patients with advanced cancer have already undergone other cancer treatments that have failed; therefore, patients have gone through the dynamic process of formulating medication beliefs about cancer treatment through a process of appraising their experiences. Perhaps advanced stage cancer patients can understand the positive dimension of medication to benefit them in some way towards the end of life but still have valid concerns regarding the potential adverse effects of treatment. Thus, patients can hold seemingly opposite beliefs at the same time, while these positive and negative beliefs are separate constructs and are influenced by different treatment-related factors across the treatment trajectory. The following section summarizes current gaps in the literature regarding medication beliefs among cancer patients.

Gaps in the Literature

Several gaps exist in research examining the phenomenon of medication beliefs among patients with cancer, including: 1) the majority of studies investigating medication beliefs among cancer patients are cross sectional in nature and there are limited reports of longitudinal studies explaining how medication beliefs change over time; 2) research on medication beliefs among late-stage cancer patients receiving cancer treatment is limited and current studies comprise of earlier stage cancers (Bender et al., 2014; Corter et al., 2013; Grunfeld et al., 2005); 3) there is limited research describing potential changes in the positive and negative components of medication beliefs; 4) factors associated with potential changes in medication beliefs, such as the impact of treatment-related assaults and physician-directed stoppages, is unknown; 5) medication beliefs regarding OAs are not well described in the literature, with the available reports limited to

patients taking adjuvant endocrine or hormone therapy primarily in breast cancer, which may or may not have been used after surgery to prevent cancer recurrence, but not to treat active cancer; and 6) there is a lack of conceptual framework that describes the phenomena of medication beliefs and the factors that can influence changes in medication beliefs over time.

In summary, the science currently lacks both conceptual clarity and empirical evidence regarding how the separate positive and negative components of medication beliefs may change over time among advanced cancer patients receiving OAs, the variables associated with changes in medication beliefs over time, and what effect permanent stoppages of OAs have on medication beliefs.

Steps 4. & 5. Identifying Concepts/Structure of the Parent Theory to Use in the Derivation & Redefining Model Concepts/Structure of the Parent Study to Create a Derived Model

Steps 4 and 5 of the theory derivation involved selecting the concepts and structure to be utilized from the ECSM parent theory (Figure 2.1). Once concepts and structures were chosen for the derived model (Figure 2.2), these concepts and structures were modified, and some redefined. The major contribution to the derived model involves the examination of medication beliefs as dependent variables and approaching each of the positive and negative components of medication beliefs as theoretically distinct constructs (Horne et al., 1999; Kalichman et al., 2016; Phillips et al., 2014) that may change differently over time. Knowledge of the factors associated with each component of medication beliefs can allow a better understanding of why medication beliefs might change over time and why outcomes associated with medication beliefs in turn may change over time (e.g. adherence). A table summarizing author derivations is provided (Table 2.3) and a discussion of the derived model is provided in detail below.

Derivation of the parent model: Introduction of the conceptual model of medication beliefs among advanced cancer patients receiving oral oncolytic agents. Given the limitations of the ECMS, a conceptual model was derived (Figure 2.2) to better explain the factors that influence the positive and negative components of medication beliefs differently over time among advanced cancer patients receiving OAs. The concepts that were modified and derived from the ECSM are highlighted in gray (Figure 2.2). The ECSM parent theory provides the foundation for a definition of medication beliefs and how appraisals may change medication beliefs across the treatment trajectory.

Antecedents. Past experiences with physical, cognitive, and emotional health, illness, and medications are antecedents to positive and negative medication beliefs (Figure 2.2). These past experiences form pre-existing beliefs from which new medication beliefs will be formed when a new medication is prescribed. It is expected that patients with advanced cancer, many who had previously failed cancer treatments, would have symptoms upon being prescribed a new OA. Experiencing symptoms can influence medication beliefs about a new medication. For example, patients experiencing cancer-related symptoms perceive cancer medication as beneficial to relieve the symptoms of cancer because they see a need to improve health. However, patients with an experience of symptoms due to previous treatment for cancer may develop negative medication beliefs because patients may perceive cancer medication as toxic or responsible for causing symptoms and adverse events. Patients can appraise their experiences as either positive or negative, which can influence the development or reinforcement of positive or negative medication beliefs.

Cancer patients are often confronted with comorbid conditions requiring additional medications, especially patients 65 years of age and older (Sarfati, Koczwara, & Jackson, 2016).

Previous experience with illness often involves treatment with medications, which also influence future medication beliefs via the process of appraisal (Figure 2.2). Cancer studies have shown that prior experience with cancer and cancer treatment inform future medication beliefs about treatment (Jansen et al., 2005; Jansen, Otten, & Stiggelbout, 2004). For example, experience with medication used to treat comorbid conditions has been associated with both positive and negative medication beliefs (Aikens & Piette, 2009; Schüz et al., 2011). Patients facing polypharmacy have experienced the benefit of taking medications (Aiken & Piette, 2009), but may also have concern regarding medication interactions and multiple adverse events caused by the medications (Schüz et al., 2011).

Emotional health includes depressive symptoms (Figure 2.2), which are common among patients with advanced cancer (Fitzgerald et al., 2013; Hung et al., 2017). Patients experiencing depressive symptoms can develop altered medication beliefs about a new medication. Patients with depressive symptoms have a decreased ability to perceive the positive benefits of medications (Belzung et al., 2015; DiMatteo et al., 2000), which could weaken positive medication beliefs. Depressive symptoms can also give rise to negative medication beliefs as patients are unable to inhibit negative aspects of treatment (Hilliard, Eakin, Borrelli, Green, & Riekert, 2015; Kalichman et al., 2016; Kalichman, Pellowski, Kegler, Cherry, & Kalichman, 2015; Maguire, Hughes, & McElnay, 2008; Salgado et al., 2017) and are biased to focus on the negative aspects of the cancer treatment, such as symptoms or adverse events. Depression has also been reported to decrease cognitive effectiveness (Asher & Myers, 2015; Belzung et al., 2015; Merriman et al., 2017).

An example of cognitive health is cognitive effectiveness (Figure 2.2), which is the capability to efficiently focus concentration on activities of daily living that necessitate attention

or working memory (Cimprich, 1992). In addition, cognitive effectiveness entails the ability of an individual to inhibit competing behaviors (e.g. not taking OA medication), thoughts (dialectical perceptions of positive and negative medication beliefs), and emotions, such as depression, fear, or anxiety (Pennebaker, 1992). Such inhibitions are important in order to effectively self-regulate and manage cancer care in the home environment by way of decision-making and problem solving.

Cognitive effectiveness among individuals with cancer can be compromised (Asher & Myers, 2015) and influenced by the cancer disease, cancer treatment (Merriman, Von Ah, Miaskowski, & Aouizerat, 2013), or distress of managing the current diagnosis and treatment, to name a few (Andreotti, Root, Ahles, McEwen, & Compas, 2014; Merriman et al., 2013; Cimprich, 1992). Prolonged distress can begin to negatively affect cognitive effectiveness, specifically attention and working memory, which can influence higher-level executive functions, such as decision-making and problem solving, needed to self-regulate and manage care (Berman et al., 2014). As emotional distress increases, cognitive effectiveness decreases, making it difficult for patients to carry out tasks that require concentration (Berman et al., 2014), such as remembering to take medication or inhibiting internal or external information not needed. When prolonged or repeated stressors of cancer and cancer treatment are imposed on patients, their cognitive effectiveness further declines (Andreotti et al., 2014). Cognitive resources eventually become drained as patients manage their cancer care (Cimprich, 1992), including complex dosing regimens, oncology and other related appointments, and, for some patients, managing comorbid conditions and related treatments. The lack of cognitive resources can negatively influence the cognitive reappraisals that are critical in coping with and effectively managing cancer and cancer treatment (Andreotti et al., 2014) in the home environment. Patients

managing additional comorbid condition and treatments are likely to further contribute to a decline in cognitive effectiveness in individuals with cancer (Merriman et al., 2017).

In conclusion, patients with decreased cognitive effectiveness may be vulnerable to developing negative medication beliefs as they lose the ability to inhibit competing thoughts and emotions that may be negative in nature. A decline in cognitive effectiveness can negatively affect a patient's ability to focus and concentrate on self-managing their illness and treatment (Cimprich, 1992). In addition, patients with decreased cognitive effectiveness have an altered ability to perceive the positive benefits of a newly prescribed medication.

New oral oncolytic agent prescription. Just as the health threat in the ECSM activates illness and treatment perceptions, the derived conceptual model denotes a new OA prescription as the stimulus to activate both positive and negative components of medication beliefs (Figure 2.2). When a cancer patient receives a prescription for a new OA, medication beliefs are activated in one of two ways. First, medication beliefs are cognitive structures, which indicates a patient's memory or prior *experiences with health, illness and medications* can influence future medication beliefs. Secondly, medication beliefs can also be activated by way of processing information (Anderson, 2015; Turk & Salovey, 1985), such as interpreting external information regarding the medication that is given to the cancer patient (e.g., education delivered by the oncologist, oncology nurse, or via informative printed materials).

A patient's prior experience with medication and prior medication beliefs can influence and even bias the way external information is processed. For example, patients who have been treated with chemotherapy previously and had a positive experience, such as cancer symptom relief or delayed disease progression, are likely to hold positive medication beliefs and be attentive to new information regarding the benefits of treatment. However, if a cancer patient had

a negative experience with prior cancer treatments such as symptoms and adverse events, negative medication beliefs may have developed, and they are likely focus on the negative aspects of treatment.

Positive medication beliefs. Medication beliefs are defined within a larger domain of illness representation for the cancer illness in which the OA was prescribed (Figure 2.2). The positive medication beliefs are dependent variables in the derived model. The positive component of medication beliefs represents the perception that medication is beneficial to improving or maintaining health, such as improvement of disease symptoms or delayed disease progression (Jansen et al., 2005; Jansen et al., 2004). Positive medication beliefs are based on and grow out of larger long-standing beliefs and past experiences with the positive benefit of medication. These medication beliefs are less vulnerable to change in response to treatment-related assaults experienced over the treatment trajectory and thus may be more stable compared to negative medication beliefs. However, positive medication beliefs may increase in strength if the medication efficacy is supported or, in contrast, weaken if the medication is deemed as unable to benefit health in some manner.

Negative medication beliefs. The negative component of medication beliefs represent concern for taking medication (Horne et al., 1999) and is represented as a dependent variable in the derived model (Figure 2.2). Negative medication beliefs are vulnerable to change over time as patients experience and appraise various treatment-related assaults, such as symptoms and adverse events, that cause interruptions in a patient's routine or daily schedule (Bhattacharya et al., 2012; Corter et al., 2013; Chen et al., 2014; Salgado et al., 2017). Experiencing treatment-related assaults can strengthen negative medication beliefs (Salgado et al., 2017).

Oral oncolytic agent treatment trajectory (Time). The OA trajectory is placed in the derived model to denote time during active oral oncolytic treatment (Figure 2.2). Patients are taking OAs long term and medication beliefs may change over time.

Treatment-related events. There are various treatment-related events that occur across the OA treatment trajectory that can influence medication beliefs, including treatment-related assaults that include symptoms and adverse events, permanent physician-directed OA stoppages, depressive symptoms, and a decrease in cognitive effectiveness (Figure 2.2). These events are described below.

Treatment-related assaults (symptoms & adverse events). Over the course of the cancer treatment trajectory, patients may experience a number of treatment-related assaults, including symptoms and adverse events (Figure 2.2). Symptoms are defined as a perceived physical or psychological disturbance experienced by the patient (National Cancer Institute, n.d.). Adverse events involve unanticipated medical problems that occur during treatment (National Cancer Institute, n.d.) and can include symptoms, side effects, and toxicities. The latter, if confirmed by oncologists, could further reinforce negative beliefs about medications. Treatment-related assaults influence the way in which medication beliefs are formed or change the strength of a belief. For example, if a patient experiences many severe symptoms of the medication, these symptoms are appraised, and this is expected to increase the strength of negative medication beliefs. However, if the patient's symptoms of the cancer are relieved by the OA medication or patients do not experience symptoms of the OA medication or the cancer illness, the strength of the negative medication beliefs would be expected to weaken. Based on a review of the cancer literature concerning medication beliefs among cancer patients, the positive component of

medication beliefs is not influenced by cancer treatment-related assaults (Heisig et al., 2017; Salgado et al., 2017).

Permanent physician-directed oral agent stoppage. A permanent physician-directed OA stoppage is defined as the discontinuation of an oral agent without the intent to restart the medication (Figure 2.2). Such stoppages may be due to lack of response to the medication, disease progression, deteriorating physical function (Clarke, Johnston, Corrie, Kuhn, & Barclay, 2015), adverse events (Atkinson et al., 2017; Di Maio, Basch, Bryce, & Perrone, 2016), or when treatment-related assaults have outweighed the benefit of treatment (Chan et al., 2016). If the OA is permanently stopped by the physician, it is conceptualized that positive medication beliefs will weaken because the medication is no longer benefiting the patient and negative medication beliefs could be influenced if adverse events were the reason for the OA stoppage.

Cognitive effectiveness & depressive symptoms. In the ECSM, the cognitive response was the perception of illness or treatment (Figure 2.1). In the derived model, cognitive effectiveness was added and describes the cognitive response to treatment in addition to the impact of a decline of cognitive effectiveness on medication beliefs (Figure 2.2). Cognitive effectiveness is defined as the ability to efficiently attend to activities of daily living requiring attention or working memory (Cimprich, 1992). Advanced cancer patients can face many challenges with cancer and cancer treatment. The multiple treatment-related assaults and demands of self-managing cancer treatment can begin to negatively affect cognitive processing and effectiveness (Cimprich, 1992). The self-management of OA medication and treatment-related assaults can drain cognitive resources and lead to decreased cognitive effectiveness, also known as cognitive fatigue. Decreased cognitive effectiveness can influence medication beliefs as the ability to concentrate and focus attention is reduced and patients lose the ability to inhibit negative

behaviors, thoughts, and emotions required for effective self-regulation (Kaplan, 1995; Pennebaker, 1992). When patients cannot focus on incoming information, they cannot properly formulate beliefs, or their perceptions may be altered to focus on the negative aspects of treatment. In addition, depressive symptoms are associated with decreased cognitive effectiveness, which can give rise to the development of negative medication beliefs and the inability to perceive the positive benefits of medication (Belzung et al., 2015; DiMatteo et al., 2000).

Just as patients can have cognitive responses to treatment, emotional responses also occur in parallel (Figure 2.2). In the derived model, depressive symptoms have been chosen to represent the emotional response to treatment. Patients with advanced cancer often experience depression (Fitzgerald et al., 2013; Hung et al., 2017). Patients develop depressive symptoms in response to treatment needed to sustain life and are also associated with various treatment-related assaults (Fitzgerald et al., 2013; Hung et al., 2017).

Depressive symptoms can decrease cognitive effectiveness and bias medication beliefs, such as the ability to perceive positive benefits of medications (Belzung et al., 2015; DiMatteo et al., 2000). Depressive symptoms can also impact the development of negative medication beliefs and increase medication concerns (Hilliard et al., 2015; Kalichman et al., 2016; Kalichman et al., 2015; Maguire et al., 2008; Salgado et al., 2017) as patients are biased and focus on the negative aspects of treatment, such as symptoms or adverse events. Depressive symptoms can also bias external information received from oncology health professionals and they may only focus their attention on the negative aspects of the information received, which can give rise to negative medication beliefs and heightened concerns, such as symptoms or adverse events associated with the medication.

Appraisals. Cancer patients experience various events along the treatment trajectory (Figure 2.2). These treatment-related events are appraised and evaluated either positively or negatively. The appraisals that patients make about the treatment-related events explain how medication beliefs are reinforced or can change over time. For example, patients experiencing treatment-related assaults appraise associated symptoms and adverse events, which either results in the development of and/or reinforcement of negative medication beliefs. Therefore, patients with unresolved treatment-related assaults may see increases in the strength of negative medication beliefs (concerns) over time. Whereas patients whom experience relief of treatment-related assaults may have weakened negative medication beliefs (concerns) over time.

Positive appraisals that reinforce the beliefs that medication is benefiting the patient's health can arise from cancer illness symptom relief once initiating a new oral OA or diagnostic confirmation that disease progression has been delayed. In some cases, the development of symptoms, such as skin rash, may be interpreted that the medication is actually working (Petrelli et al., 2012) and be appraised positively, increasing the strength of the positive medication beliefs. There are instances when appraisals can lead to a decrease in positive medication beliefs. For example, when a patient is told by their oncologist that their OA medication is being stopped because is not delaying disease progression, they have not responded to treatment, or adverse events outweigh the benefit of treatment, this information can change beliefs that the medication is beneficial to maintain or improve health.

Depressive mood and cognitive effectiveness play a unique role in appraisals. Experiencing depressive symptoms can affect cognitive effectiveness and vice versa. Patients who have depressive symptoms and decreased cognitive effectiveness may have biased appraisals of treatment-related events. Patients with depressive symptoms have difficulty

perceiving the positive benefit of medication and may focus on the negative aspects of treatment (Belzung et al., 2015; DiMatteo et al., 2000). Patients with decreased cognitive effectiveness have an altered ability to process new information. When appraisals are made, patients are required to take in new information, evaluate the information and make judgements. This process can bias the way treatment-related events are processed.

Summary Relationship of Model Components

Medication beliefs are influenced by previous experiences with cognitive, emotional, and physical health, illness, and medications. Medication beliefs are defined within a larger mental model of illness representation for which the medication was prescribed. Once advanced cancer patients receive a prescription for OA medication, medication beliefs are activated, both positive and negative components. The two components of medication beliefs are independent of one another, indicating one can hold both positive and negative medication beliefs at the same time. This distinction is critical to understanding how the different components of medication beliefs can change differently over time as they can be influenced by different treatment-related factors.

The separate components of medication beliefs are influenced by different factors. Positive medication beliefs represent the beliefs that the patient will benefit from medication. Positive medication beliefs among cancer patients are not associated with treatment-related assaults (Heisig et al., 2017; Salgado et al., 2017). Thus, it is hypothesized that the positive medication beliefs are more stable over the cancer treatment trajectory in response to treatment-related assaults. However, positive medication beliefs can change. They can strengthen as patients confirm medication efficacy or weaken if a patient experiences a permanent physician-directed OA stoppage. Once the oncologist stops the medication, the medication can be appraised as having no further benefit for the patient's health. It is not known how physician-

directed stoppages influence negative medication beliefs and therefore an exploratory analysis will be completed. Evidence of medication efficacy can also increase the strength of the positive medication beliefs.

Negative medication beliefs represent concern for taking OAs. Among cancer patients, negative medication beliefs appear to be impacted by treatment-related assaults, such as symptoms and adverse events (Bhattacharya et al., 2012; Salgado et al., 2017), which are common among patients receiving OAs (Tipton, 2015). Because of the experience of treatment-related events along the OA treatment trajectory, it is hypothesized that the negative medication beliefs are more vulnerable to change over time. In contrast, the positive medication beliefs are not impacted by OA treatment-related assaults, such as symptoms and adverse events, and therefore remain more stable until a permanent physician-directed OA stoppage occurs or medication efficacy is confirmed.

Discussion

The Conceptual Model of Medication Beliefs among Advanced Stage Cancer Patients Receiving Oral Oncolytic Agents gives conceptual clarity to the phenomenon of medication beliefs by explaining the two separate components of medication beliefs, how these separate components are influenced by different factors over the OA treatment trajectory, and how the two components of medication beliefs change differently over time. Knowledge gained from the development of the derived conceptual model can help inform oncology-based interventions for advanced cancer patients receiving OAs. Depression and declining cognitive effectiveness should be monitored regularly to prevent a negative impact on medication beliefs and allow patients to understand the benefits of the OA medication, while also discussing the potential concerns with patients. Specifically, negative medication beliefs must be evaluated and addressed by oncology professionals, especially in response to ongoing treatment-related

assaults. Oncology professionals should focus on interventions to assist with the observation and reporting of symptoms and adverse events in the home. Oncology professionals monitoring and grading the severity of adverse events can counsel patients and address medication beliefs once more objectively obtained information regarding the OA treatment-related assaults are known (e.g. diagnostic or laboratory findings). It is important that oncologists discuss and address patients' medication beliefs in response to weighing the negative impact of treatment with the cancer treatment that may offer no further benefit. Oncologists who share the belief that the threats to health are worse with treatment and outweigh the medical benefit intended in the last months of life may be able to help patients transition to end of life care (Chan et al., 2016). Patients may continue to believe that their OA medication is beneficial until their oncologist shares the benefit of treatment no longer exists (Harrington & Smith, 2008).

Table 2.3

Description of ECSM and Derived Model Concepts

ECSM Concepts/Components	**Theory/Concept Derivations**	**Derived Model Concepts/Components**
Health Threat	Health threat in the ECSM activates perceptions of treatment. In the derived conceptual model, the new oral oncolytic agent prescription activates treatment perceptions in the form of medication beliefs.	*New Oral OA Prescription* activates medication beliefs and may or may not act as a health threat.
Perceptions of Treatments (needs and concerns)	In the ECSM. Treatment perceptions including need for treatment and concern for treatment are activated from the health threat.	*Medication Beliefs* are activated when a patient receives a new oral oncolytic agent. Medication beliefs have both a positive component (represents benefit of taking medication to improve or maintain health) and a negative component (representing concern for taking medication).
Illness Representations	Illness Representations in the ECSM are a main focus of the model in relation to treatment perceptions. Illness Representation in the derived model are displayed only to define medication beliefs within the domain of cancer illness representation for which the oral oncolytic agent was prescribed.	*Illness Representations* in the derived model are displayed to explain that medication beliefs are defined within a larger domain of illness representation for which the medication was prescribed to treat.
Emotional Response to Illness	Emotional Response to Illness is not represented in the derived model as illness representations are not the focus of the derived model.	Emotional Response to Illness is not represented in the derived model. It is assumed these emotional responses are ongoing and influence medication beliefs, which are encompassed within a larger domain of illness representation that are depicted in the model.
Emotional Response to Treatment	Emotional Response to Treatment in the ECSM acts in parallel with Cognitive Representations of Treatment in the form of Treatment Perceptions.	The derived conceptual model also displays parallel processing of emotional response to the oral oncolytic agent via *Depressive Symptoms* and cognitive response to the oral oncolytic agent via *Cognitive Effectiveness*, both affecting medication beliefs over time and interfering with the patient's ability to inhibit behaviors, thoughts, and emotions. Both components inhibit the capacity to view positive aspects of medication beliefs and introduce cognitive bias towards negative aspects of medication.
Coping Procedures	Coping procedures in the ECSM were removed in the new conceptual model.	Coping procedures in the ECSM were removed in the new conceptual model as the focus is to explain and predict medication beliefs, not outcomes of medication beliefs.
Appraisals	The appraisal is described in the ECSM as "the outcome of adherence or non-adherence is appraised with subsequent reinforcement or change in treatment representations" (Horne, 2003, pg. 147).	The derived model describes the *Appraisals* as evaluating treatment-related events (e.g. symptom severity & interference/adverse events) experienced along the oral oncolytic agent treatment trajectory that can reinforce and/or change medication beliefs over time.

Table 2.3 (cont'd)

Newly Added Model Concepts		
ECSM Concepts/Components	**Theory/Concept Derivations**	**Derived Model Concepts/Components**
N/A	Past experiences with health, illness and medications act as antecedents to medication belief structure.	*Past Experiences with Health, Illness and Medications* are important in the development of medication beliefs and are fundamental in the experiences that formulate beliefs of new medications; thus are added *antecedents* and appear at the beginning of the model.
N/A	Oral Oncolytic Treatment Trajectory *(Time)* was added to the derived conceptual model to depict the concept of time across he treatment trajectory.	*Oral Oncolytic Treatment Trajectory (Time)* was added to the derived conceptual model to represent how medication beliefs change over time as patients appraise treatment-related events that either reinforce or change existing medication beliefs.
N/A	Treatment-Related Assaults were added to the derived conceptual model to signify the influence of symptom severity and adverse events on medication beliefs across the oral oncolytic agent treatment trajectory.	*Treatment-Related Assaults* were added to the derived conceptual model to signify the effect of *Symptom Severity & Interference* (patient-reported) and *Adverse Events* (documented in the medical record audit) on medication beliefs across the oral oncolytic agent treatment trajectory.
N/A	Physician-Directed Stoppages are specific to oral oncolytic agent treatment and were added to conceptualize how such medication stoppages can influence medication beliefs.	*Physician-Directed Stoppages,* which are experienced by patients with advanced cancer along the OA treatment trajectory, affect medication beliefs after patients appraise and evaluate oral oncolytic agents after the medication is no longer beneficial to improving or maintaining health.
N/A	Cognitive Effectiveness was added to the derived model to represent the cognitive response to treatment as described in the ECSM as occurring in parallel with emotional response to treatment. In the ECSM, cognitive response to treatment is depicted in treatment perceptions.	*Cognitive Effectiveness* is important for cognitive processing and the formation of medication beliefs. As patients face treatment-related events along the OA treatment trajectory, cognitive effectiveness is challenged, decreasing the ability to inhibit stimuli and, therefore, affecting medication beliefs. Specifically, declining cognitive effectiveness can alter one's ability to inhibit behaviors, thoughts, and emotions, and can interrupt the ability to self-regulate cancer care and medication taking in the home environment.

APPENDIX

APPENDIX

Routledge Copyright Permission: Extended Common-Sense Model of Self-Regulation

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REFERENCES

REFERENCES

Aikens, J. E., Nease, D. E., & Klinkman, M. S. (2008). Explaining patients' beliefs about the necessity and harmfulness of antidepressants. *The Annals of Family Medicine*, *6*(1), 23–29.

Aikens, J. E., & Piette, J. D. (2009). Diabetic patients' medication underuse, illness outcomes, and beliefs about antihyperglycemic and antihypertensive treatments. *Diabetes Care*, *32*(1), 19–24. Doi:10.2337/dc08-1533.

Anderson, J. R. (2015). *Cognitive Psychology and Its Implications*. New York, NY: Worth Publishers.

Andreotti, C., Root, J. C., Ahles, T. A., McEwen, B. S., & Compas, B. E. (2015). Cancer, coping, and cognition: A model for the role of stress reactivity in cancer-related cognitive decline. *Psycho-Oncology*, *24*(6), 617–623.

Asher, A., & Myers, J. S. (2015). The effect of cancer treatment on cognitive function. *Clinical Advances in Hematology Oncology*, *13*(7), 441–450.

Atkinson, T. M., Hay, J. L., Shoushtari, A., Li, Y., Paucar, D. J., Smith, S. C., ... & Milhem, M. M. (2017). Relationship between physician-adjudicated adverse events and patient-reported health-related quality of life in a phase II clinical trial (NCT01143402) of patients with metastatic uveal melanoma. *Journal of Cancer Research and Clinical Oncology*, *143*(3), 439–445.

Balmer, C. E., Thomas, P., & Osborne, R. J. (2001). Who wants second-line, palliative chemotherapy?. *Psycho-Oncology*, *10*(5), 410–418. Doi: 10.1002/pon.538.

Belzung, C., Willner, P., & Philippot, P. (2015). Depression: from psychopathology to pathophysiology. *Current Opinion in Neurobiology*, *30*, 24–30. Doi: http://dx.doi.org/10.1016/j.conb.2014.08.013.

Bhattacharya, D., Easthall, C., Willoughby, K. A., Small, M., & Watson, S. (2012). Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. *Journal of Oncology Pharmacy Practice*, *18*(3), 333–342.

Bickell, N. A., Weidmann, J., Fei, K., Lin, J. J., & Leventhal, H. (2009). Underuse of breast cancer adjuvant treatment: Patient knowledge, beliefs, and medical mistrust. *Journal of Clinical Oncology*, *27*(31), 5160–5167.

Cai, J., Ma, H., Huang, F., Zhu, D., Bi, J., Ke, Y., & Zhang, T. (2013). Correlation of bevacizumab-induced hypertension and outcomes of metastatic colorectal cancer patients

treated with bevacizumab: A systematic review and meta-analysis. *World Journal of Surgical Oncology*, *11*(1), 306.

Cameron, L. D., & Leventhal, H. (Eds.). (2003). *The self-regulation of health and illness 92ehavior*. Psychology Press. London: Routledge.

Center Watch. (2017). FDA Approved Drugs for Oncology. Retrieved from https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology.

Chan, W. L., Lam, K. O., Siu, W. K., & Yuen, K. K. (2016). Chemotherapy at end-of-life: An integration of oncology and palliative team. *Supportive Care in Cancer*, *24*(3), 1421–1427.

Chapman, S. C., Horne, R., Eade, R., Balestrini, S., Rush, J., & Sisodiya, S. M. (2015). Applying a perceptions and practicalities approach to understanding nonadherence to antiepileptic drugs. *Epilepsia*, *56*(9), 1398–1407. Doi:10.1111/epi.13097.

Chater, A. M., Parham, R., Riley, S., Hutchison, A. J., & Horne, R. (2014). Profiling patient attitudes to phosphate binding medication: A route to 92ehavior92zing treatment and adherence support. *Psychology & Health*, *29*(12), 1407–1420. Doi:10.1080/08870446.2014.942663.

Chen, L. C., Chen, T. C., Huang, Y. B., & Chang, C. S. (2014). Disease acceptance and adherence to imatinib in Taiwanese chronic myeloid leukaemia outpatients. *International Journal of Clinical Pharmacy*, *36*(1), 120–127.

Cimprich B. (1992). Attentional fatigue following breast cancer surgery. *Research in Nursing & Health*, *15*:199–207. Doi: 10.1002/nur.4770150306.

Clarke, G., Johnston, S., Corrie, P., Kuhn, I., & Barclay, S. (2015). Withdrawal of anticancer therapy in advanced disease: A systematic literature review. *BMC Cancer*, *15*(1), 892–900.

Corter, A. L., Findlay, M., Broom, R., Porter, D., & Petrie, K. J. (2013). Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology*, *18*(1), 168–181.

Dalbeth, N., Petrie, K. J., House, M., Chong, J., Leung, W., Chegudi, R., ... & Taylor, W. J. (2011). Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. *Arthritis Care & Research*, *63*(11), 1605–1612. Doi: 10.1002/acr.20570.

Darabos, K., & Hoyt, M. A. (2017). Cancer-related worry and physical well-being in the context of perceived stress in young adults with testicular cancer. *Journal of Adolescent and Young Adult Oncology*, *6*(2), 363–366.

De Vries, S. T., Keers, J. C., Visser, R., de Zeeuw, D., Haaijer-Ruskamp, F. M., Voorham, J., & Denig, P. (2014). Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes. *Journal of Psychosomatic Research*, *76*(2), 134–138.

Del Castillo, A., Godoy-Izquierdo, D., Vázquez, M. L., & Godoy, J. F. (2011). Illness beliefs about cancer among healthy adults who have and have not lived with cancer patients. *International Journal of Behavioral Medicine*, *18*(4), 342–351.

Di Maio, M., Basch, E., Bryce, J., & Perrone, F. (2016). Patient-reported outcomes in the evaluation of toxicity of anticancer treatments. *Nature Reviews Clinical Oncology*, *13*(5), 319–325.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, *160*(14), 2101-2107. Doi:10.1001/archinte.160.14.2101.

Fitzgerald, P., Lo, C., Li, M., Gagliese, L., Zimmermann, C., & Rodin, G. (2013). The relationship between depression and physical symptom burden in advanced cancer. *BMJ Supportive & Palliative Care*, *5*, 381–388.

Foot, H., La Caze, A., Gujral, G., & Cottrell, N. (2016). The necessity–concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Education and Counseling*, *99*(5), 706–717. doi:10.1016/j.pec.2015.11.004.

Geynisman, D. M., & Wickersham, K. E. (2013). Adherence to targeted oral anticancer medications. *Discovery Medicine*, *15*(83), 231–241.

Given, B. A., Spoelstra, S. L., & Grant, M. (2011). The challenges of oral agents as antineoplastic treatments. *Seminars in Oncology Nursing, 27*(2), 93–103. Doi: 10.1016/j.soncn.2011.02.003

Grunfeld, E. A., Hunter, M. S., Sikka, P., & Mittal, S. (2005). Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Education and Counseling*, *59*(1), 97–102.

Harrington, S. E., & Smith, T. J. (2008). The role of chemotherapy at the end of life: "When is enough, enough?". *Journal of the American Medical Association*, *299*(22), 2667–2678.

Heisig, S. R., Shedden-Mora, M. C., Blanckenburg, P., Rief, W., Witzel, I., Albert, U. S., & Nestoriuc, Y. (2016). What do women with breast cancer expect from their treatment? Correlates of negative treatment expectations about endocrine therapy. *Psycho-Oncology*, *25*(12), 1485–1492.

Hendriksen, E., Williams, E., Sporn, N., Greer, J., DeGrange, A., & Koopman, C. (2015). Worried together: A qualitative study of shared anxiety in patients with metastatic non-small cell lung cancer and their family caregivers. *Supportive Care in Cancer*, *23*(4), 1035–1041.

Hess, L. M., Louder, A., Winfree, K., Zhu, Y. E., Oton, A. B., & Nair, R. (2017). Factors associated with adherence to and treatment duration of erlotinib among patients with non-small cell lung cancer. *Journal of Managed Care & Specialty Pharmacy*, *23*(6), 643–652.

Hilliard, M. E., Eakin, M. N., Borrelli, B., Green, A., & Riekert, K. A. (2015). Medication beliefs mediate between depressive symptoms and medication adherence in cystic fibrosis. *Health Psychology*, *34*(5), 496–504. Doi: 10.1037/hea0000136.

Horne, R. (2003). Treatment perceptions and self-regulation. In The self-regulation of health and illness behavior. In L. D. Cameron, & H. Leventhal (Eds.), *The self-regulation of health and illness behavior* (pp. 138–153). New York, NY: Routledge.

Horne, R., Chapman, S. C., Parham, R., Freemantle, N., Forbes, A., & Cooper, V. (2013). Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: A meta-analytic review of the Necessity-Concerns Framework. *PLOS One*, *8*(12), 1–24. Doi: http://dx.doi.org/10.1371/journal.pone.0080633.

Horne, R., & Weinman, J. (2002). Self-regulation and self-management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology and Health*, *17*(1), 17–32.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. Psychology & Health, 14(1), 1–24. Doi:10.1080/08870449908407311.

Hung, M. S., Chen, I. C., Lee, C. P., Huang, R. J., Chen, P. C., Tsai, Y. H., & Yang, Y. H. (2017). Incidence and risk factors of depression after diagnosis of lung cancer: A nationwide population-based study. *Medicine*, *96*(19).

Iskandarsyah, A., de Klerk, C., Suardi, D. R., Soemitro, M. P., Sadarjoen, S. S., & Passchier, J. (2014). Psychosocial and cultural reasons for delay in seeking help and nonadherence to treatment in Indonesian women with breast cancer: A qualitative study. *Health Psychology*, *33*(3), 214–221.

Iudici, M., Russo, B., Mitidieri, M., Cuomo, G., & Valentini, G. (2015). Glucocorticoids in systemic sclerosis: Patients' beliefs and treatment adherence. *Scandinavian Journal of Rheumatology*, *44*(3), 229–237. Doi:10.3109/03009742.2014.957239.

Jansen, S. J. T., Otten, W., Baas-Thijssen, M. C. M., van de Velde, C. J. H., Nortier, J. W. R., & Stiggelbout, A. M. (2005). Explaining differences in attitude toward adjuvant

chemotherapy between experienced and inexperienced breast cancer patients. *Journal of Clinical Oncology*, *23*(27), 6623–6630.

Jansen, S. J., Otten, W., & Stiggelbout, A. M. (2004). Review of determinants of patients' preferences for adjuvant therapy in cancer. *Journal of Clinical Oncology*, *22*(15), 3181–3190.

Kalichman, S., Kalichman, M. O., & Cherry, C. (2016). Medication beliefs and structural barriers to treatment adherence among people living with HIV infection. *Psychology & Health*, *31*(4), 383–395. Doi:10.1080/08870446.2015.1111371.

Kalichman, S. C., Pellowski, J., Kegler, C., Cherry, C., & Kalichman, M. O. (2015). Medication adherence in people dually treated for HIV infection and mental health conditions: Test of the medications beliefs framework. *Journal of Behavioral Medicine*, *38*(4), 632–641.

Kaplan, S. (1995). The restorative benefits of nature: Toward an integrative framework. *Journal of Environmental Psychology*, *15*(3), 169–182.

Koedoot, C. G., De Haan, R. J., Stiggelbout, A. M., Stalmeier, P. F. M., De Graeff, A., Bakker, P. J. M., & de Haes, J. C. J. M. (2003). Palliative chemotherapy or best supportive care? A prospective study explaining patients' treatment preference and choice. *British Journal of Cancer*, *89*(12), 2219–2226.

Krause, S., Rydall, A., Hales, S., Rodin, G., & Lo, C. (2015). Initial validation of the Death and Dying Distress Scale for the assessment of death anxiety in patients with advanced cancer. *Journal of Pain and Symptom Management*, *49*(1), 126–134.

Leventhal, H., Brissette, I., & Leventhal, E. A. (2003). The common-sense model of self-regulation of health and illness. *The self-regulation of health and illness 95ehavior* (pp. 42–65). London: Routledge.

Leventhal, H., Easterling, D.V., Coons H.L., Luchterhand, C.M, & Love, R.R. (1986). Adaption to chemotherapy treatments. In B.L. Anderson (Ed.), *Women with cancer: psychological perspectives* (pp. 172–203). New York: Springer.

Lu, Y., Arthur, D., Hu, L., Cheng, G., An, F., & Li, Z. (2016). Beliefs about antidepressant medication and associated adherence among older Chinese patients with major depression: A cross-sectional survey. *International Journal of Mental Health Nursing*, *25*(1), 71–79. Doi:10.1111/inm.12181.

Maguire, L. K., Hughes, C. M., & McElnay, J. C. (2008). Exploring the impact of depressive symptoms and medication beliefs on medication adherence in hypertension—a primary care study. *Patient Education and Counseling*, *73*(2), 371–376.

Margolis, S. A., & Gonzalez, J. S. (2014). Beliefs about Medicines in 3D: A Comment on Phillips et al. *Annals of Behavioral Medicine: A publication of the Society of Behavioral Medicine*, *48*(1), 1–3.

Marshall, V., & Given, B. (*In Press*). Factors associated with medication beliefs in patients with cancer: An integrative review. *Oncology Nursing Forum.*

Marshall, V., Lehto, R., Given, C.W., Given, B., Sikorskii, A. (2018). Conceptualization of medication beliefs among advanced cancer patients receiving oral oncolytic agents using a theory derivation approach. *Unpublished doctoral dissertation, Michigan State University, East Lansing Michigan*.

Matsuyama, R., Reddy, S., & Smith, T. J. (2006). Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *Journal of Clinical Oncology*, *24*(21), 3490–3496.

McCullough, A. R., Tunney, M. M., Elborn, J. S., Bradley, J. M., & Hughes, C. M. (2015). Predictors of adherence to treatment in bronchiectasis. *Respiratory Medicine*, *109*(7), 838–845. Doi: http://dx.doi.org/10.1016/j.rmed.2015.04.011.

Merriman, J. D., Von Ah, D., Miaskowski, C., & Aouizerat, B. E. (2013, November). Proposed mechanisms for cancer-and treatment-related cognitive changes. In *Seminars in Oncology Nursing* (Vol. 29, No. 4, pp. 260–269).

Mohammed, S., Peter, E., Gastaldo, D., & Howell, D. (2016). The "Conflicted Dying": The active search for life extension in advanced cancer through biomedical treatment. *Qualitative Health Research*, *26*(4), 555–567.

National Cancer Institute. (n.d.). NCI Dictionary of Cancer Terms. Adverse Events. Retrieved from: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid = 444960. Accessed January 29, 2017.

National Cancer Institute. (n.d.). NCI Dictionary of Cancer Terms. Symptoms. Retrieved from: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid = 45022. Accessed January 29, 2017.

National Cancer Institute. (n.d.). NCI Dictionary of Cancer Terms. Toxicity. Retrieved from: https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid = 445093. Accessed September 28, 2017.

National Cancer Institute. (2017). *Targeted Cancer Therapies: What are the side effects of targeted cancer therapies?* Retrieved from: https://www.cancer.gov/aboutcancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet#q7. Accessed November 20, 2017.

Neame, R., & Hammond, A. (2005). Beliefs about medications: A questionnaire survey of people with rheumatoid arthritis. *Rheumatology*, *44*(6), 762–767. Doi: 10.1093/rheumatology/keh587.

Neuner, J. M., & Schapira, M. M. (2014). Patient perceptions of osteoporosis treatment thresholds. *The Journal of Rheumatology*, *41*(3), 516–522. Doi:10.3899/jrheum.130548.

Neuss, M. N., Polovich, M., McNiff, K., Esper, P., Gilmore, T. R., LeFebvre, K. B., ... & Jacobson, J. O. (2013). 2013 updated American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards including standards for the safe administration and management of oral chemotherapy. *Journal of Oncology Practice*, *9*(2S), 5–13. Doi: 10.1200/JOP.2013.000874.

Pennebaker, J. W. (1992). Inhibition as the linchpin of health. In H. S. Friedman (Ed.), *Hostility, Coping, & Health* (pp. 127–139). Washington, DC, US: American Psychological Association.

Petrelli, F., Borgonovo, K., Cabiddu, M., Lonati, V., & Barni, S. (2012). Relationship between skin rash and outcome in non-small-cell lung cancer patients treated with anti-EGFR tyrosine kinase inhibitors: A literature-based meta-analysis of 24 trials. *Lung Cancer*, *78*(1), 8–15.

Phillips, L. A., Diefenbach, M. A., Kronish, I. M., Negron, R. M., & Horowitz, C. R. (2014). The necessity-concerns framework: A multidimensional theory benefits from multidimensional analysis. *Annals of Behavioral Medicine*, *48*(1), 7–16. Doi: 10.1007/s12160-013-9579-2.

Ponieman, D., Wisnivesky, J. P., Leventhal, H., Musumeci-Szabó, T. J., & Halm, E. A. (2009). Impact of positive and negative beliefs about inhaled corticosteroids on adherence in inner-city asthmatic patients. *Annals of Allergy, Asthma & Immunology*, *103*(1), 38–42. doi:10.1016/S1081-1206(10)60141-X.

Salgado, T. M., Davis, E. J., Farris, K. B., Fawaz, S., Batra, P., & Henry, N. L. (2017). Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment*, *163*(2), 311–319. Doi: 10.1007/s10549-017-4177-9.

Sarfati, D., Koczwara, B., & Jackson, C. (2016). The impact of comorbidity on cancer and its treatment. *CA: A Cancer Journal for Clinicians*, *66*(4), 337–350.

Schüz, B., Wurm, S., Ziegelmann, J. P., Warner, L. M., Tesch-Römer, C., & Schwarzer, R. (2011). Changes in functional health, changes in medication beliefs, and medication adherence. *Health Psychology*, *30*(1), 31–39. Doi:10.1037/a0021881.

Shimada, Y., Hamaguchi, T., Mizusawa, J., Saito, N., Kanemitsu, Y., Takiguchi, N., ... & Tomita, N. (2014). Randomised phase III trial of adjuvant chemotherapy with oral uracil and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. *European Journal of Cancer*, *50*(13), 2231–2240.

Silvestri, G., Pritchard, R., & Welch, H. G. (1998). Preferences for chemotherapy in patients with advanced non-small cell lung cancer: Descriptive study based on scripted interviews. *British Medical Journal*, *317*(7161), 771–775.

Thuné-Boyle, I. C., Myers, L. B., & Newman, S. P. (2006). The role of illness beliefs, treatment beliefs, and perceived severity of symptoms in explaining distress in cancer patients during chemotherapy treatment. *Behavioral Medicine*, *32*(1), 19–29.

Tiemensma, J., Andela, C. D., Pereira, A. M., Romijn, J. A., Biermasz, N. R., & Kaptein, A. A. (2014). Patients with adrenal insufficiency hate their medication: Concerns and stronger beliefs about the necessity of hydrocortisone intake are associated with more negative illness perceptions. *The Journal of Clinical Endocrinology & Metabolism*, *99*(10), 3668–3676. Doi: http://dx.doi.org/10.1210/jc.2014-1527.

Tipton, J. M. (2015). Overview of the challenges related to oral agents for cancer and their impact on adherence. *Clinical Journal of Oncology Nursing*, *19*(3), 37–40.

Turk, C. & Salovey, P. (1985). Cognitive structures, cognitive processes, and cognitive-behavior modification: I. client issues. *Cognitive Therapy & Research*. *9*(1), 1–17.

Walker, L.O., & Avant, K.C. (2005). Theory derivation. In L.O. Walker & K.C. Avant (5 Eds.). *Strategies for Theory Construction in Nursing*. New Jersey: Prentice Hall.

Weingart, S. N., Brown, E., Bach, P. B., Eng, K., Johnson, S. A., Kuzel, T. M., ... & O'Brien, S. (2008). NCCN Task Force Report: Oral chemotherapy. *Journal of the National Comprehensive Cancer Network: JNCCN*, *6*, S1–14.

CHAPTER 3: TESTING CHANGE OF MEDICATION BELIEFS AMONG ADVANCED CANCER PATIENTS RECEIVING ORAL ONCOLYTIC AGENTS

Background

Oral oncolytic agents (OAs) account for over half of the new cancer treatments approved by the Food and Drug Administration (Center Watch, 2017). The development of new OAs has broadened the treatment options for patients with various solid tumors who have not responded to other anti-cancer treatment options (Matsuyama, Reddy, & Smith, 2006; Mohammed, Peter, Gastaldo, & Howell, 2016). Patients and their caregivers are required to self-manage complex OA dosage regimens and symptoms in the home environment without the close supervision of oncology personnel. OA medications often have narrow therapeutic ranges and safety margins (Neuss et al., 2013), making patients vulnerable to uncontrolled symptoms (Given, Spoelstra, & Grant, 2011; Shimada et al., 2014; Spoelstra et al., 2013; Tipton, 2015).

The challenges of OA medication complexity and symptoms negatively influence patients' medication beliefs (Salgado et al., 2017), increase depressive symptoms (Salgado et al., 2017) and decrease cognitive effectiveness (Cimprich, 1992). Medication beliefs are defined as the perception regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003). Medication beliefs have a positive component representing the benefit of treatment and a negative component representing concern for taking the medication (Horne, Weinman, & Hankins, 1999). Medication beliefs have been examined as independent, explanatory variables and linked to outcomes, such as adherence, among cancer patients (Arriola et al., 2014; Moon et al., 2017; Saratsiotou et al., 2010). Less is known about the factors influencing medication beliefs that could influence change of these beliefs over time. Understanding the factors associated with medication beliefs could give rise to nursing interventions that can address these beliefs and improve patient outcomes such as adherence.

Research examining factors influencing medication beliefs in cancer patients receiving OAs over time is limited, with the available reports restricted to cross-sectional studies involving patients taking adjuvant endocrine or hormone therapy primarily in breast cancer patients (Arriola et al., 2014; Corter, Findlay, Broom, Porter, & Petrie, 2013; Heisig et al., 2016). This study will examine whether medication beliefs of patients with advanced cancer change over the first 12 weeks since initiating a new OA and explore the influence that patient-reported symptoms (severity and interference), depressive symptoms and cognitive effectiveness have on medication beliefs over time. A review of the literature is provided to describe what is currently known regarding medication beliefs and associated correlates.

Review of the Literature

Medication beliefs have been linked to previous experiences with health, illness, medications, symptoms, and depression. The number, type, and severity of symptoms as a result of cancer or cancer treatment varies (Thuné-Boyle, Myers, & Newman, 2006) and multiple debilitating symptoms are common among patients with advanced cancer (Mercadante et al., 2015; Moens, Higginson, & Harding, 2014; Teunissen et al., 2007). Patients also experience an array of symptoms, side effects, and toxicities associated with OA medication (Given et al., 2011; Spoelstra et al., 2013; Tipton, 2015). Often cancer medication can result in more symptoms than the cancer illness itself (Thuné-Boyle et al., 2006). The experience of symptoms leaves patients vulnerable to the development of negative medication beliefs about their cancer treatment (Bhattacharya, Easthall, Willoughby, Small, & Watson, 2012; Salgado et al., 2017) over time and threatens the stability of existing medication beliefs. Research has not shown the same effect of symptom experience on the positive component of medication beliefs (Heisig et al., 2016; Salgado et al., 2017).

Symptoms associated with cancer illness and cancer treatment have shown to fluctuate over time, especially in patients with advanced cancer (Mercadante et al., 2016; Seow et al., 2011). As symptoms change, so do appraisals of the symptom experience, which can cause change in medication beliefs across the treatment trajectory (Dong, Butow, Costa, Lovell, & Agar, 2014). Increasing concern for taking cancer medication negatively impacts patient outcomes such as medication taking behavior (Bhattacharya et al., 2012; Iskandarsyah et al., 2014).

Medication beliefs are formed as a result of experiences with illness and medications used to treat illness (Horne, 2003). Cancer patients, especially those 65 or older, often encounter comorbid conditions, which require additional medications beyond cancer treatment (Sarfati, Koczwara, & Jackson, 2016; Smith, 2008). Patients with comorbidities requiring multiple medications influence the way medication beliefs are formed, and influence both positive and negative components of medication beliefs (Aikens & Piette, 2009; Schüz et al., 2011). For example, patients receiving multiple medications for numerous chronic conditions can influence more positive medication beliefs as patients experience the benefits of medication, which reinforce that the medication is useful in treating their illness (Aiken & Piette, 2009). Schüz et al. (2011) found that patients taking multiple medication for comorbid conditions had both an increased perception of the need for medications, but at the same time had increased concerns about taking multiple medications. Past experiences with adverse side effects and concern of medication interactions among patients taking multiple medications has also been reported to influence more negative perceptions of medication (Barsky, Saintfort, Rogers, & Borus, 2002; Cassell et al., 2015; Krummenacher et al., 2014; Schüz et al., 2011; Shiyanbola, Farris, &

Chrischilles, 2013). There is limited research examining how taking medications for comorbid conditions influences cancer medications beliefs (Heisig et al., 2016; Salgado et al., 2017).

In contrast, patients experiencing the symptoms of cancer illness may have symptom relief once starting OA treatment and therefore develop more positive medication beliefs (Chen, Chen, Huang, & Chang, 2014). Prior exposure to adjuvant chemotherapy has been reported to positively influence patients' perceptions towards current chemotherapy treatments, perhaps due to experiencing the positive benefits of medication (Blinman, King, Norman, Vine, & Stockler, 2012; Jansen, Otten, & Stiggelbout, 2004; Jansen et al., 2005; Kunneman et al., 2014). More positive perceptions of medication for patients with other chronic conditions taking multiple oral medications for non-cancer related illnesses have been reported (Schüz et al., 2011; Verhoef et al., 2014).

Depression is common among patients with advanced cancer, especially those dealing with the burden of symptoms (Fitzgerald et al., 2013; Hung et al., 2017). Depressive symptoms among patients with various chronic illnesses, including cancer, are reported to influence the development of negative beliefs about treatment efficacy and heighten medication concerns (Hilliard, Eakin, Borrelli, Green, & Riekert, 2015; Kalichman, Kalichman, & Cherry, 2016; Kalichman, Pellowski, Kegler, Cherry, & Kalichman, 2015; Maguire, Hughes, & McElnay, 2008; Reynolds et al., 2004; Salgado et al., 2017). Depressive symptoms can bias a patient's perceptions of medication by focusing on the negative aspects of treatment, such as the risk of adverse events discussed with oncology professionals, concentrating on symptoms, or the disruption that the medication regimen causes in their daily routine (Belzung, Willner, & Philippot, 2015). Such negative perceptions give rise to negative medication beliefs (Heisig et al., 2016). Patients attempting to self-manage their OA medication regimen and related

symptoms, can exhibit more depressive symptoms as well as a decrease in cognitive effectiveness. Depressive symptoms have also been reported to decrease cognitive effectiveness (Merriman et al., 2017) and the ability to perceive positive benefits of medications (Belzung et al., 2015; DiMatteo, Lepper, & Croghan, 2000).

Cognitive effectiveness is the ability to efficiently attend to activities of daily living that necessitate attention or working memory (Cimprich, 1992). Specific to self-regulation and managing care in the home environment, cognitive effectiveness also entails the ability of an individuals to inhibit competing behaviors (e.g. not taking medication), thoughts (dialectical perceptions of medication) and emotions such as depression, fear or anxiety (Kaplan 1995; Pennebaker, 1992). When cognitive effectiveness is compromised, patients may not be able to take their medications as prescribed because they cannot inhibit other distractions and forget (Pennebaker, 1992; Cimprich, 1992; Cimprich et al., 2011). Patients with a decline in cognitive effectiveness may not be able to process incoming information from their oncologist or nurse regarding their medication because they cannot concentrate on the information or are unable to inhibit competing stimuli. Lastly, patients can lose the ability to inhibit negative perceptions about their medication or experience depressive symptoms that compromise effective self-management of cancer care in the home.

During the OA treatment trajectory, patients are required to process information regarding their diagnosis and treatment. In addition, patients must manage complex OA regimens and symptoms in the home environment without being consistently monitored by oncology professionals. Directed attention to the day-to-day self-management responsibilities of cancer treatment can begin to deplete cognitive resources (Cimprich, 1992; Cimprich, Visovatti, & Ronis, 2011), leaving patients vulnerable to developing negative medication beliefs.

In summary, the fluctuation in physical, emotional, and cognitive health is appraised by the patient throughout the cancer treatment trajectory. As patients experience increasing symptom severity and symptom interference, negative medication beliefs develop and strengthen through a process of appraisal. If symptoms are relieved, the strength of the negative medication beliefs can weaken. As symptoms worsen and increase in severity and interference, patients also develop more depressive symptoms and decreased cognitive effectiveness because they are exhausting their cognitive resources on managing the symptoms. Patients with depressive symptoms and decreased cognitive effectiveness tend to develop more negative medication beliefs and increased concern for their medication. Appraisals of treatment-related events that compromise a patient's physical, emotional, and cognitive health over the OA treatment trajectory can change medication beliefs over time.

In previous research the dynamic process of evaluating medication beliefs over time has not been performed. Studies have only provided a cross-sectional snapshot of medication beliefs and have typically done so by linking medication beliefs with adherence and not describing how such beliefs can be influenced over time. During treatment with OAs, there are several factors that can influence an individual's perception of their medication as patients appraise their illness and treatment over time. These factors are described in the conceptual model provided below.

Conceptual Framework

The Conceptual Model of Medication Beliefs among Advanced Stage Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018) is used to guide the study (Figure 3.1). The conceptual model was derived from the Extended Common-Sense Model of Self-Regulation (Horne, 2003) to explain and describe medication beliefs among patients with advanced cancers receiving treatment with a new OA medication over the first 12

weeks. The model begins with antecedents that influence new medication beliefs such as past experiences with physical, emotional, and cognitive health, illness, and medications. Patients have both positive and negative components of medication beliefs activated when they receive a prescription for a new OA. Patients use past experiences when developing new medication beliefs and therefore, baseline medication beliefs are adjusted for in this study.

The positive component of medication beliefs depicts the belief that medication is beneficial to improve or maintain current health (Horne et al., 1999; Horne, 2003). The negative component of medication beliefs represents the patient's concern for taking the OA medication (Horne, 2003). The model denotes that patients encounter a variety of treatment-related events along the first 12 weeks of the OA treatment trajectory including symptoms (severity and interference), adverse events, permanent physician-directed stoppages, depressive symptoms and decreased cognitive effectiveness. Treatment-related events are then appraised by patients, which reinforces and/or changes their existing medication beliefs over time.

Negative medication beliefs are more vulnerable to change than positive medication beliefs over the 12-week treatment trajectory as challenges with OA medication are met (e.g. symptoms). For example, when patients are experiencing high levels of symptom severity or symptom interference, they also tend to experience an increase in depressive symptoms and decreased cognitive effectiveness. These treatment-related events are appraised and reinforce and/or strengthen negative medication beliefs or concern for taking the medication. If symptom severity or interference consequently subsides, the patient's appraisal of the symptom can then change by weakening the negative medication belief.

Positive and negative components of medication beliefs are independent of one another. One holds both positive and negative components of medication beliefs at the same time and these beliefs are influenced differently by illness and treatment-related events over time.

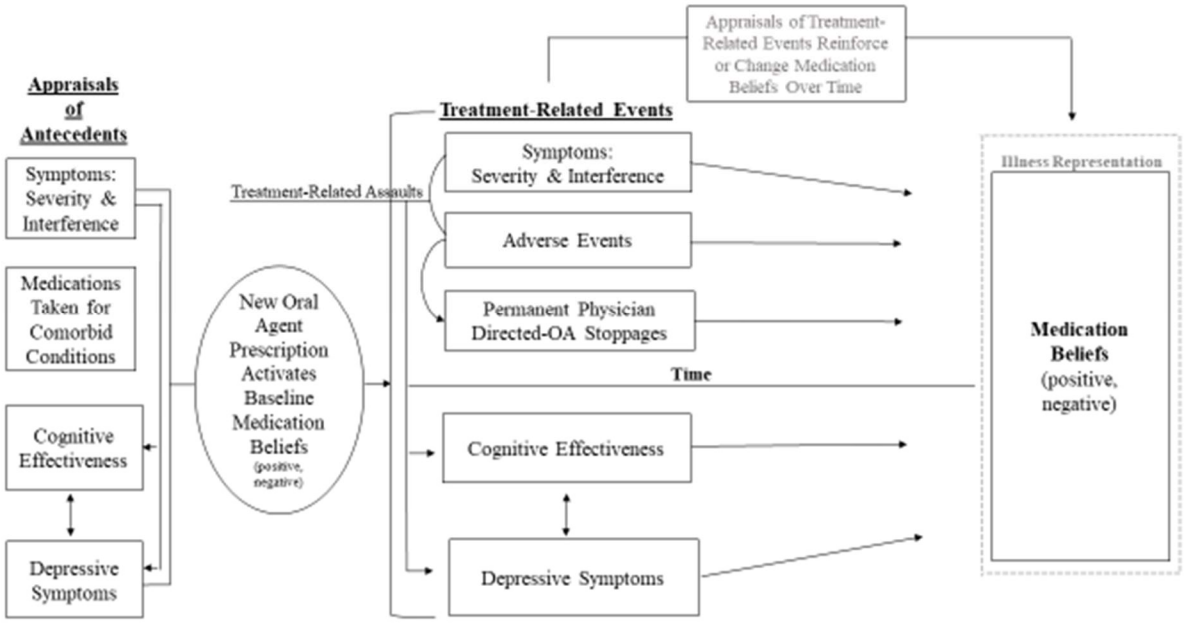

Figure 3.1 The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). *This model is derived from Extended Common-Sense Model of Self-Regulation. Horne, R. (2003). Derived components from the ECSM that are redefined or modified are highlighted in gray.*

Purpose & Aims

The purpose of this study is to examine relationships among variables of a derived model, The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). Each study aim will include the longitudinal examination of medication beliefs over 12 weeks since initiation of a new oral oncolytic agent by adjusting for baseline medication beliefs and using three repeated measures of beliefs at 4 weeks, 8 weeks and 12 weeks and include: 1) to examine whether positive and negative components of medication beliefs change over time; 2) to examine the effects of summed symptom severity and interference indices on the positive and negative

components of medication beliefs in independent models over time; 3) if effects in aim two are found, explore whether specific symptoms are driving this effect, using the five most prevalent patient-reported symptoms to guide the exploratory analysis and; 4) to explore the distinct influence of depression and cognitive effectiveness on the positive and negative dimensions of medication beliefs over time and over and above the summed symptom severity and interference indices.

Methods

Design

The design is a secondary analysis using data derived from a National Cancer Institute, randomized controlled trial, *Improving Adherence to Oral Cancer Agents and Self Care of Symptoms Using an IVR (1R01CA162401-O1A1*), which tests an intervention to promote symptom management and OA adherence over 12 weeks since initiating an OA by using four data collection points of baseline, 4 weeks, 8 weeks and 12 weeks (Given & Given, 2013-2017). Patients were randomized to either the experimental or control group after the baseline interview using a minimization approach. Patient allocations to the experimental or control group were equalized with respect to recruitment location, cancer site, continuous versus intermittent OA dosing, and depressive symptomatology.

Both the control group and experimental group received weekly interactive voice response calls monitoring adherence and symptom management for 8 weeks. The experimental group also received daily OA adherence reminders specific to the prescribed dosing regimen for 4 weeks and were referred to symptom self-management strategy recommendations provided in a symptom management toolkit for an 8-week duration if symptoms were reported as ≥4 on a 1-9 rating sale, with higher ratings indicating more severe symptoms. The Symptom Management

Toolkit provides evidence-based self-management strategies for commonly experienced symptoms of cancer and cancer treatment (Given, Given, & Majeske, 2013). The toolkit provides patients with a description of symptoms, common causes of symptoms, strategies to prevent or manage symptoms, and tips to guide communication with healthcare providers regarding symptoms and when to seek medical attention (Given et al., 2013).

Setting/Sample

Institutional Review Board (IRB) approval for ethical treatment and protection of human subjects was obtained from the affiliated university for both the parent study and secondary analyses as well as all respective recruitment locations. Site recruiters, trained on the parent study's protocol, identified patients from eight different Midwestern United States cancer centers who received a new prescription for one of 28 Food and Drug Administration (FDA) approved OAs (see Appendix A). Patient eligibility criteria included: 1) 21 years of age or older; 2) received a new prescription for an OA; 3) cognitively intact; 4) English speaking; 5) able/willing to complete phone calls and; 6) obtained an Eastern Cooperative Oncology Group performance score of 0–2 (Oken et al., 1982) or a Karnofsky score ≥50 (Karnofsky, 1949), both measures are presented in Appendix B.

An attrition analysis was completed in the parent study. An abbreviated table describing the number of patients in each the experimental and control group who completed each of the 4 interviews over the 12-week study period is provided in Appendix C. Of the 272 patients completing the baseline interview, 58 attrited over the 12-week study period, resulting in a 21% attrition rate. Reasons for attrition included being too ill, death, oral agent stopped, changed their mind, lost to follow-up, and entered hospice.

Data Collection

Data were collected by trained interviewers via telephone. The initial interview was completed within one week of patients initiating a new oral oncolytic agent and established the baseline interview, followed by interviews at 4, 8, and 12 weeks. Additional data using an interactive voice response call monitored adherence and symptom management for 8 weeks and then both trial arms were evaluated for sustainability for the following 4 weeks of the study.

Measures

Patient demographic and cancer/treatment characteristics. Patient demographic characteristics including age, sex, race, ethnicity, and education were obtained during enrollment and at the baseline interview (see Appendix D) of the parent study and results are presented in Table 3.1. In addition, cancer type, cancer stage, whether cancer was recurrent, OA dosage as continuous or intermittent, drug classification, and whether the patient was receiving concurrent intravenous chemotherapy or radiation, and study group assignment were collected (see Appendix D) and used to describe the sample (Table 3.1). Patients who had intermittent dosing schedules had planned rest periods in which the medication was stopped and then reintroduced after a pre-specified time (e.g. cycling). Continuous dosing refers to constant dosing patterns without rest periods. Drug classification was organized into four categories including cytotoxics, kinase inhibitors, sex hormone inhibitors, and other. Study group assignment indicated whether patients were in the control group or intervention group as previously described.

Beliefs about medicine questionnaire-specific. Medication beliefs are defined as an individual's perception regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003). Medication beliefs were measured using the Beliefs about Medicines Questionnaire-Specific (BMQ), a 10-item questionnaire

evaluating cognitive representations reflecting common perceptions about medication (Horne et al., 1999). Patients rate medication beliefs on a 5-point Likert scale (1 = *strongly disagree* to 5 = *strongly agree*). The BMQ scale in the parent study was adapted to reflect beliefs specific to OA medication and an additional item was added for this study to indicate beliefs about unpleasant side effects (See Appendix F), which are common among patients receiving OA medication (Tipton, 2015). The BMQ has two subscales; *Necessity* represents positive medication beliefs that indicate some benefit from taking medication and *Concern* represents negative risks or consequences of taking the medication (Horne et al., 1999).

Responses in this study consist of a five-point Likert scale and were reversed in the parent study to present more positive responses first. Responses range from 1 (*strongly agree)* to 5 (*strongly disagree)*. Item scores of each *Necessity* and *Concerns* subscales were summed, with scores ranging from 5 to 25 for the *Necessity* subscale and 6-30 for the *Concern* subscale. Item responses were reverse coded during analysis, to indicate that higher BMQ scores signify stronger beliefs on a continuous scale. There is currently no validated cut-off score indicating specifically what constitutes a weak versus strong belief on the BMQ and current measures attempting to categorize beliefs in such a manner are arbitrary and not validated. This study used each of the subscale scores calculated at each data collection point including baseline, 4, 8, and 12 weeks by averaging the subscales' corresponding BMQ item scores. Each of the BMQ subscale scores were used as dependent variables to evaluate the relationship that patient-reported symptom severity and interference, depressive symptoms and cognitive effectiveness have on medication beliefs over the first 12 weeks after initiating a new oral oncolytic agent and determine potential changes of medication beliefs over time.

Reliability and validity of the BMQ have been reported among various chronic conditions in the literature. Initial instrument internal consistency reliability testing was completed by obtaining Cronbach alpha values (α) for the two BMQ subscales among six different illness groups, yielding acceptable limits ranging from 0.74-0.86 on the *Necessity* subscale and 0.73-0.80 on the *Concerns* subscale among asthmatic, diabetic, and cardiac patients (Horne et al., 1999). The renal sample, which had the lowest sample size (n = 47) yielded an internal consistency reliability of 0.55 for the *Necessity* subscale and 0.73 for the *Concerns* subscale. The general/medical sample revealed an internal consistency reliability of 0.86 for *Necessity* and 0.65 for the *Concerns* subscale and for the psychiatric group 0.74 for *Necessity* and 0.63 for *Concerns*. Original instrument test-retest reliability revealed significant correlations for *Necessity* (0.77) and *Concerns* (0.76). Internal consistency reliabilities of the *Necessity* subscale were respectable and exceeded 0.76 at each of the four data collection points. *Concerns* subscale internal consistency reliabilities were acceptable between 0.68-0.70 at each data collection point.

Initial criterion validity during instrument development was evaluated by assessing correlations among the BMQ-Specific *Necessity* and *Concerns* subscales and other valid measures such as the Illness Perception Questionnaire (Weinman, Petrie, Moss-Morris, & Horne, 1996) and the Sensitive-Soma Scale (Diefenbach, Leventhal, &Leventhal, 1996). Original discriminant validity was established by assessing the ability of the instrument to discriminate between patients in different illness groups (Horne et al., 1999). Construct validity was confirmed with use of Principal Component Analysis and Confirmatory Factor Analysis to validate the factor structures (Horne et al., 1999). Additional literature completing validity testing on the BMQ-Specific show similar results, upholding the validity of the instrument

among various illnesses (Brown et al., 2005; LaPointe et al., 2010; Mahler et al., 2010; Verhoef et al., 2014).

Cancer symptom experience inventory. Symptom severity and symptom interference were assessed using the Cancer Symptom Experience Inventory (CSEI), an index used in previous cancer research studies measuring the symptom experience (Given et al., 2008). The CSEI is a checklist of 18 patient-reported symptoms commonly associated with OA including: fatigue, sleep disturbance, anxiety, weakness, pain, headaches, skin rash/skin sores, numbness or tingling, redness/peeling/pain in hands or feet, swelling of hands or feet, joint pain, mouth sores, lack of appetite, nausea or vomiting, diarrhea, constipation, cough or shortness of breath (Appendix G). Patients were first asked to answer whether they experienced symptoms and if the patients answered yes, they were asked to rate symptoms due to the cancer or its treatment at their worst within the past seven days. When symptom was present, severity was rated on a 1–9 scale (1 = *very little* to 9 = *worst possible*). Patients were then asked how much the symptom interfered with their daily activities on a scale of 0-9 (0 = *did not interfere* to 9 = *interfered completely*). For analysis, severity was coded from 0 when symptom was not present. The interference of each symptom with daily activities was coded from 0 (did not interfere) to 9 (interfered completely) based on patient's rating. Summed severity and interference indices across the 18 symptoms were used for analysis to determine their relationship with the positive and negative components of medication beliefs over the first 12 weeks since initiating a new OA. The CSEI is an index, not a scale, and thus internal consistency reliability is not applicable.

Center for epidemiologic studies-depression scale. Depressive symptoms were measured using the Center for Epidemiologic Studies-Depression (CES-D) scale (Appendix H), a well-established reliable and valid measure of depressive symptoms (Radloff, 1977; Devins et

al., 1998; Lewinsohn, Seeley, Roberts, & Allen, 1997). Patients rated 20 depressive symptoms experienced in the past seven days on a 4-point Likert scale (1 = *rarely or none of the time* [less than 1 day] to 4 = *most/all of the time* [5–7 days]). Total CES-D scale scores range from 0-60, with lower scores indicating lower risk for clinical depression and higher scores indicate greater risk for clinical depression on a continuous scale. A CES-D score of ≥ 16 is used as a recognized cut-off for value for patients at risk for clinical depression, while those below 16 are not at risk of clinical depression (Krebber et al., 2014; Lewinsohn et al., 1997). However, for this study the continuous CES-D scores were used to determine their influence on the positive and negative medication beliefs over the first 12 weeks since initiating a new oral oncolytic agent.

Original scale development revealed an internal consistency coefficient alpha value exceeding 0.85 and acceptable test-retest reliability. An internal consistency reliability of the CES-D across four data collection points in this study exceeded 0.83. Construct validity was evaluated using principal component factor analysis. Discriminant validity was supported by the ability of the CES-D to discriminate between psychiatric inpatients and the general population, and convergent validity was supported by high correlations between the CES-D and other scales of depression (Radloff, 1977).

Attentional function index. Perceived cognitive effectiveness is the patients' perceived ability to efficiently attend to activities of daily living that necessitate attention or working memory (Cimprich, 1992). A 13-item Attentional Function Index (Appendix I) measured perceived cognitive effectiveness (Cimprich et al., 2011). The Attentional Function Index (AFI) was developed to assess cancer patient-reported effectiveness in activities that necessitate attention and working memory in order to function in everyday circumstances. The AFI has three subscales including effective action, attentional lapses and interpersonal effectiveness (Cimprich

et al., 2011). Patients rated item responses from 0 (*not at all*) to 10 (*extremely well*) with scores ranging from 0-130 on the 13-item scale (Cimprich et al., 2011). These scores are adapted from the original AFI scale, which used a 100-point visual analog scale. An exploratory factor analysis revealed one main construct was being measured and thus the total index across all 13 items was used in this study, with higher scores indicating greater cognitive effectiveness and lower scores representing compromised cognitive effectiveness (Cimprich, 1992). Cut-off points indicating high (AFI scores > 75), moderate (AFI scores between 50-75) and low (AFI scores < 50) cognitive functioning have been published for the original 16-item AFI scale (Cimprich, So, Ronis, Trask, 2005), however, no such values have been established for the 13-item scale.

During original scale development, Cronbach's alpha was 0.89 for the entire 13-item instrument, with alpha for each subscale ranging from 0.80 to 0.92 (Cimprich et al., 2011). Internal consistency reliability for the entire 13-item instrument utilized in this study was 0.94 at each of the four data collection points.

Construct validity was established during original instrument development using exploratory principal component factor analysis (Cimprich et al., 2011). Additional validity testing indicated that the scores on the AFI showed expected correlations with established measures of ability to concentrate, cognitive failures, states of confusion, and mental fatigue, and could distinguish differences in perceived cognitive functioning between younger and older age groups (Cimprich et al., 2011).

Medical record audit: number of comorbid conditions requiring medication. Medical record audits (Appendix J) were used in this study to confirm documented medications prescribed for comorbid conditions including but not limited to heart disease, hypertension, emphysema/chronic lung disease, asthma, kidney disease, diabetes, depression, arthritis, and

anemia. Medical record audits were completed at the end of the study period by trained personnel. Total number comorbid conditions requiring medication were computed and used as a continuous variable for analyses to examine the relationship that number of comorbid conditions requiring medication have on the development of positive and negative OA medication beliefs at baseline.

Data Management

Data a from the parent study were acquired by trained interviewers, entered into a secure database and stripped of all identifiers prior to any secondary data analyses. No outliers were present and therefore patients cannot be identified based on outlying values.

Scales were scored per established instrument manual guidelines. Data for the secondary data analyses were stored in electronic format on a password protected database maintained by the College of Nursing at Michigan State University and archived according to university policy.

Statistical Analyses

Statistical analyses were be performed in SPSS. Descriptive statistics summarized age, sex, race, ethnicity, level of education, site of cancer, cancer medication characteristics including dosage as continuous versus intermittent, drug class, and study group assignment (Table 3.1). Distribution of the BMQ subscales scores (outcome variable) and explanatory variables including patient-reported symptom severity and interference, depressive symptoms, cognitive effectiveness, and medications used to treat comorbid conditions were evaluated.

The study group (experimental vs. control) was controlled for in all analyses. The analyses that included symptom severity and interference were repeated with and without study group variable to avoid potential collinearity.

Aim 1 Analyses

Linear mixed effects models (LME) were used to relate each BMQ subscale at the three data collection points (4, 8, & 12 week) to the fixed explanatory covariates (age, sex, race, ethnicity, level of education, site of cancer, cancer medication drug category, cancer medication as continuous or intermittent, and study group assignment). Baseline medication beliefs were adjusted for as a fixed covariate. LME models allow data missing at random, time-varying covariates, and modeling of the covariance matrix over the repeated measures (Bernal-Rusiel, Greve, Reuter, Fischl, & Sabuncu, 2013). Time was entered as a categorical value in reference to the three data collection points (4, 8, & 12 weeks) to capture potential non-linear change patterns among study participants over the course of the 12-week study. Least squares means of each BMQ subscale at 4, 8, and 12 weeks were output from the LME and differences among them were tested to evaluate if positive and negative dimensions of medication beliefs change over time (Table 3.2).

Aim 2 Analyses

Building upon the model in the Aim 1 analyses, patient-reported summed symptom severity and interference indices were added to the LME one at a time as time varying-covariates. We explored which specific symptoms from the array of 18 have the most influence on the BMQ, using the five most prevalent symptoms reported to guide this exploratory analysis (Table 3.4). Each symptom severity and interference scores from the most prevalent symptoms were entered one at a time instead of the summed severity and interference.

Aim 3 Analyses

Aim 3 analyses built upon the LME model in Aims 1 & 2 by adding time-varying covariates of depressive symptoms and cognitive effectiveness one at a time in addition to fixed

covariates of the number of medications used to treat comorbid conditions. Symptom severity and interference were then added back into the model one at a time to determine the influence of depression and cognitive effectiveness on medication beliefs above and beyond symptom severity and interference.

Results

A total of 272 patients completed the baseline interview. Descriptive statistics for the study sample, cancer, and cancer treatment characteristics are provided in Table 3.1. There was the same proportion of males and females in the sample. The mean age was 61.39 years (SD 12.22). The sample was predominantly Caucasian (91%, N = 247) and non-Hispanic/Latino ethnicity (98%, N = 267). Patients had a mean of 3.39 (SD 1.99) comorbid conditions for which they were taking medications.

Gastrointestinal cancers (32%, N = 88) were the most prevalent cancers followed by breast cancer (21%, N = 57). Patients were largely diagnosed with Stage 4 cancer (71%, N = 193). Kinase inhibitors (47%, N = 127) and cytotoxics (35%, N = 95) were the prevalent forms of OA treatment. Twenty-two percent of patients (N = 61) were receiving concurrent intravenous chemotherapy and only 7% (N = 19) were receiving concurrent radiation therapy.

A model for Aim 1 using fixed variables and time as a categorical variable is presented in Table 3.2. Least square means of each BMQ subscale at 4, 8, and 12 weeks are presented in Table 3.3. Baseline Necessity beliefs were significantly associated with Necessity beliefs at 4, 8, and 12 weeks (Table 3.2). Results revealed a significant increase in Necessity beliefs between week 4 and week 12 with a mean difference of 0.112, standard error, SE=0.055, p = .04 (Table 6). Concern beliefs did not change over time. Baseline Concern beliefs were significantly associated with Concern beliefs at 4, 8, and 12 weeks (Table 3.2). Higher Concern beliefs were

significantly associated with being male and having more chronic conditions requiring medications (Table 3.2). Those with stage four cancers had significantly lower Concern beliefs compared to those with stage 1-3 cancers or those whose cancers were not staged (Table 3.2).

Symptom severity and interference indices were added one at a time to the LME model. Neither symptom severity (B = -0.003, standard error (SE) = 0.002, p = .09) nor interference (B = -0.002, SE = 0.002, p = .16) were significant in the Necessity LME model. In contrast, both severity and interference indices were statistically significant in the Concerns LME model. As symptom severity (B = 0.009, SE = 0.001, p = <.01) and interference indices (B = 0.009, SE = 0.001, p = <.01) increased, Concern beliefs also increased. Significant associations between Concern beliefs and variables as described above remained significant when severity and interference were added to the LME.

An exploratory analysis was completed to determine what specific symptoms may be driving the effect found on Concern beliefs using the six most prevalent symptoms from the CSEI. The six most prevalent symptoms were fatigue, weakness, pain, loss of appetite, numbness and tingling, and sleep disturbance (Table 3.4). Originally, we planned to include the five most prevalent symptoms, however, there were six symptoms that were predominantly prevalent and then the frequencies of the remaining 12 symptoms included in the CSEI began to level off. Each of the six most prevalent symptom severity scores were entered into the LME separately and each were significantly associated with Concern beliefs (data not shown). The analysis was repeated using symptom interference scores of the most prevalent symptoms and only fatigue (B = 0.092, SE = 0.042, p = .03), weakness (B = 0.139, SE = 0.050, p = .01), and loss of appetite (B = 0.172, SE = 0.052, p = <.01) remained significant in this LME model.

For Aim three depression and cognitive effectiveness were added to the LME model one at a time. Depressive symptoms were associated with decreased Necessity (B = -0.012, SE = 0.004, p =< .01) and increased Concerns (B = 0.021, SE = 0.003, p = <.01). Cognitive effectiveness was not significantly associated with Necessity beliefs (B = 0.001, SE = 0.001, p = .29). Higher levels of cognitive effectiveness were significantly associated with lower levels of Concern beliefs (B = 0.006, SE = 0.001, p = <.01). To explore the influence that depression and cognitive effectiveness had on medication beliefs over and above summed symptom severity and interference, four separate models were created. Depression remained significantly associated with Necessity beliefs over and above symptom severity (B = -0.010, SE = 0.005, p = .02) and interference (B = -0.011, SE = 0.005, p = .02), while symptom severity and interference remained insignificant in relation to Necessity beliefs. The association between depression and Concern beliefs remained significant over and above symptom severity (B = 0.013, SE = 0.004, p = <.01) and symptom interference (B = 0.013, SE = 0.004, p = <.01), while both symptom severity and interference also remained significant in each of the models. Cognitive effectiveness (B = 0.000, SE = 0.001, p = .87) and symptom severity (B = -0.003, SE = 0.002, p = .07) were added to the Necessity beliefs LME model and both remained insignificant and the same results were shown when cognitive effectiveness (B = 0.003, SE = 0.001, p = .80) and symptom interference (B = -0.003, SE = 0.002, p = .12) were modeled. When cognitive effectiveness (B = -0.003, SE = 0.001, p = <.01) and severity (B = 0.007, SE = 0.001, p = <.01) were added to the Concern beliefs LME model, both remained significant. Similar results were shown when cognitive effectiveness (B = -0.003, SE = 0.001, p = <.01) and symptom interference (B = 0.008, SE = 0.002, p = <.01) were added to the Concern beliefs LME.

All analyses were completed with and without the group assignment to ensure the symptom intervention in the parent study did not influence results. No differences were seen in results with and without the group assignment variable.

Discussion

Results of this study revealed a significant increase in positive beliefs over time. An increase in positive beliefs could have stemmed from either a reduction of cancer-related symptoms the patients experienced before initiating the new OA or perhaps diagnostic/laboratory testing that revealed the medication was working to slow disease progression. Unfortunately, no data was collected to be able to associate positive beliefs with diagnostic/laboratory testing that could have confirmed efficacy of the medication. It is also not feasible to expect that laboratory/diagnostic testing would be completed as often as medication beliefs were elicited during the 12-week study. Therefore, increases in positive beliefs could be a result of cognitive reappraisals of the benefit of medication, which has been previously supported in the cancer literature (Jansen et al., 2005).

Patients with stage four cancers accounted for the majority of the sample and prior exposure to previous cancer therapies could have given them a more realistic expectation of their treatment, increasing positive medication beliefs over time. Those with prior experience with cancer treatment have been reported to have more positive views of their cancer medication (Del Castillo, Godoy-Izquierdo, Vasquez, & Godoy, 2011). An increase in positive medication beliefs among advanced stage cancer patients could also be a result of knowing that the new OA medication may be their last resort as they have exhausted other treatment options.

Negative beliefs did not change over time. Changes in negative medication beliefs only became evident when the symptom experience was accounted for. Increased levels of symptom

severity and interference were associated with increases in negative medication beliefs. Patients make appraisals about the symptom experience and if the symptom experience is contributed to the new OA medication, then this reinforces negative medication beliefs. This means that changes in negative medication beliefs are dependent on and vulnerable to the symptom experiences in this study sample. The symptoms can interfere with an individual's daily life and if these symptoms are attributed to the OA medication, negative medication beliefs are reinforced via an appraisal process. The negative component of medication beliefs is therefore contextual and likely to fluctuate as patients experience symptoms, whereas positive medication beliefs are more stable over time.

Baseline Necessity (positive) and Concern (negative) beliefs were significantly associated with medication beliefs at 4, 8, and 12 weeks, which support the conceptual model (Table 3.2). Medication beliefs originate from experiences with health and illness and past beliefs with other medications, which informs future beliefs. Men had significantly higher negative medication beliefs compared to women and this could have been largely due to the type of OA medication prescribed to the males in our study, which may have caused a distinct set of symptoms that drove these negative medication beliefs (Table 3.2). An integrative review of literature involving cancer medication beliefs and associations with sex are inconclusive (Marshall & Given, 2018). Patients with stage four cancers had significantly lower negative medication beliefs compared to those with stage one to stage three cancers or those whose cancers were not staged (Table 3.2), which is consistent with prior research (Heisig et al., 2016). Patients with stage four cancers may be more focused on survival at any cost and be more accepting of the negative impact of OA medications resulting in lower negative medication beliefs (Balmer, Thomas, & Osborne, 2001; Hirose et al., 2009; Stiggelbout, De Haes, Kiebert,

Kievit, & Leer, 1996). Patients with stage four cancers may have also experienced treatment related assaults with other cancer therapies and learned how to self-manage such negative effects of medication, therefore negative medication beliefs are lower because they have a sense of what to expect and how to manage symptoms.

Patients in our study had a mean of 3.39 (SD 1.99) comorbid conditions that required medication in addition to their OA. Those with more chronic conditions requiring medications had significantly higher negative medication beliefs (Table 3.2). Schüz et al. (2011) found similar results for patients taking multiple medications for comorbid conditions who reported an increase in concerns for taking multiple medications. Increases in negative medication beliefs could be a result of worry over drug interactions, increased risk of symptoms and side effects, cost, remembering to take medications as prescribed, and managing multiple medication regimens at once. Patients attempting to manage multiple medications may have concern regarding how to structure their schedule around taking medications, especially in accordance to special instructions for each regimen such as taking medication with or without food or to avoid certain foods.

Positive medication beliefs were not associated with symptom severity or symptom interference. Positive medication beliefs represent the benefit of taking medication such as slowed disease progression. Positive medication beliefs would not be expected to be associated with the adverse effects of medication such as symptom severity and interference because patients could experience symptoms, while still having an improved outcome with the OA medication. However, negative medication beliefs were significantly associated with both symptom severity and interference. As patients' symptom severity and interference increased, negative medication beliefs also increased. Symptoms have been associated with negative

medication beliefs in multiple studies, including those investigating symptoms of cancer (Chen et al., 2014; Salgado et al., 2017). As symptoms change, so do a patient's appraisals of the symptom experience, which can cause changes in negative medication beliefs across the 12-week treatment trajectory. Patients are likely attributing symptoms to the new OA medication and develop negative perceptions that may include how the medication interrupts their life, worry about long term effects of the OA, or unpleasant side effects. Therefore, in line with previous research, the experience of symptoms leaves patients vulnerable to the development of negative medication beliefs about their cancer treatment (Bhattacharya, Easthall, Willoughby, Small, & Watson, 2012; Salgado et al., 2017) over time and threatens the stability of existing medication beliefs.

Higher levels of depressive symptoms were associated with a decrease in positive medication beliefs and increased negative medication beliefs. Depressive symptoms impact an individual's perceptions and may inhibit the positive aspects of the OA medication. Patients with depressive symptoms can also be biased to focus on the negative components of medications. It is important to note that the mean depressive symptoms in this study was surprisingly low at each data collection point considering the population. According to the conceptual model, depressive symptoms and cognitive effectiveness are associated. However, cognitive effectiveness was not associated with positive medication beliefs but was associated with negative medication beliefs. Patients with higher cognitive effectiveness had significantly less negative medication beliefs and this is what would be expected based on the conceptual model. Patients in our study who experienced both depressive symptoms and declines in cognitive effectiveness had increased negative medication beliefs and this may be because patients were

unable to inhibit negative perceptions about the medication and were bias to focus on the negative aspects of OA treatment.

In summary, this study contributes to advancing the science by filling several gaps in the literature. This study is one of the first to report longitudinal data on medication beliefs. Secondly, there is a lack of conceptual clarity regarding how medication beliefs may change over time and what factors influence changes in those beliefs across the treatment trajectory among advanced cancer patients receiving OAs. This study used a derived conceptual model to guide specific aims to answer these questions over the first 12 weeks after initiating a new OA. We have preliminary evidence that patients hold both positive and negative components of medication beliefs and each component is influenced by different factors and change differently over time. Understanding the factors associated with medication beliefs could give rise to nursing interventions that can address these beliefs and improve patient outcomes such as adherence.

Study Limitations

This study evaluated medication beliefs over the first 12 weeks of the cancer treatment trajectory for patients prescribed a new oral oncolytic agent. The study is one of the first to report longitudinal data examining medication beliefs over time in individuals with cancer. However, 12 weeks is a relatively short period of time compared to the chronic nature of treatment that patients with cancer face. The sample was mostly Caucasian and a limited number of patients from diverse ethnic and racial background were represented, thus limiting the generalizability of the findings. Previous research has shown that individuals of diverse racial and ethnic backgrounds have different medication beliefs (Horne et al., 2004; Jin & Acharya, 2016). For example, patients of Chinese descent reportedly believe Western medicine is more harmful than

traditional Chinese medicine (Jin & Acharya, 2016). Higher medication Concerns have been reported among Hispanic and African Americans compared to their White counterparts in a study examining patients with various chronic conditions (Burnett-Zeigler et al., 2014; Piette, Heisler, Harand, & Juip, 2010).

Nursing Implications

Nurses are at the forefront of oncology care for patients receiving oral oncolytic agents. Patients on oral therapies are not seen in the clinical setting as often as patients receiving other traditional treatment modalities, yet they still experience symptoms and other treatment related events that can influence medication beliefs. Understanding the factors associated with medication beliefs could give rise to nursing interventions that can address these beliefs and improve patient outcomes such as adherence.

Medication beliefs were negatively influenced by symptom severity and interference in this study. Oral oncolytic agents offer convenience to patients and their families, but at the same time oral agents may interfere with their daily activates due to complex dosing strategies and symptoms experienced as a result of the medication. Nurses can assess symptoms in the clinical setting and provide patients with education and trusted resources regarding symptom management. Patients should be instructed on symptoms to expect, what symptoms to report promptly, and potential interventions patients can try at home to reduce the burden of symptoms. In addition, patients with chronic conditions requiring medication have more negative medication beliefs and nurses should address medication lists, potential medication interactions, and questions surrounding these concerns at each clinical visit. Depression can negatively impact positive medication beliefs and increase negative medication beliefs. Nurses should screen patients for depressive symptoms and be aware of the impact such symptoms can have on medication beliefs that can lead to potential nonadherence of the medication. Cognitive

effectiveness is also associated with negative medication beliefs. Nurses can screen patients for signs of cognitive decline and intervene to discuss specific concerns the patient has regarding their OA medication.

Medication beliefs should be elicited at each clinic visit. Nurses need to recognize that patients with symptoms, depressive symptoms, declining cognitive effectiveness, and comorbid conditions requiring medication are more vulnerable to developing negative medication beliefs in the form of Concerns. Symptoms, depression, and declines in cognitive effectiveness must be assessed and managed on a continuous basis. Medication beliefs can be conveniently and reliably measured using the BMQ in the clinical setting.

Future research is needed to examine interventions that can improve positive medication beliefs and lower negative beliefs among patients receiving OA. Additional research is needed to examine medication beliefs among broader ethnic and racial backgrounds. As patients are receiving and self-managing their OA medication, interventions that can be carried out in the home environment are warranted. Factors identified to increase negative medication beliefs including symptoms, depressive symptoms, declines in cognitive effectiveness, and polypharmacy should be targeted in interventions to improve medication beliefs.

Conclusions

Positive medication beliefs changed and increased over time, while negative medication beliefs changed and increased only when symptom severity and symptom interference were entered into the LME model. Medication beliefs differ among patients with advanced stage cancer compared to those with lower staged cancers or those whose cancer have not been staged. Patients with advanced cancers have less negative medication beliefs for their OA medication. Those experiencing symptoms, depressive symptoms, declines in cognitive effectiveness, or who

have comorbid conditions requiring medication have higher negative medication beliefs. Baseline Necessity and Concern beliefs are significantly associated with future medication beliefs. An increase in negative medication beliefs has been associated nonadherence and therefore addressing medication concerns for patients self-managing their medication in home environment is imperative.

Table 3.1
Descriptive Statistics of Sample Demographic, Cancer and Cancer Treatment
N = 272

Characteristic	**N (%)**
Sex	
Male	136 (50)
Female	136 (50)
Race	
Caucasian	247 (91)
Other	25 (9)
Ethnicity	
Hispanic or Latino	5 (2)
Not Hispanic or Latino	267 (98)
Education Level Completed	
High school or less	71 (26)
Some college or completed college	150 (55)
Graduate or professional degree	49 (18)
Group Assignment	
Experimental	137 (50)
Control	135 (50)
	Mean (SD)
Age	61.39 (12.22)
Number of comorbid conditions treated with medications	3.39 (1.99)
Cancer/Cancer Treatment Characteristic	**N (%)**
Site of cancer	
Breast	57 (21)
GI (Colorectal, Esophageal, Pancreatic)	88 (32)
Leukemia/Lymphoma	19 (7)
Liver	12 (4)
Lung	10 (4)
Melanoma	8 (3)
Myeloma	7 (3)
Prostate	26 (10)
Renal	24 (9)
Sarcoma	15 (5)
Brain	2 (1)
Other	4 (1)
Stage of Cancer	
I-II	22 (8)
III	22 (8)
IV	193 (71)
Other	33 (12)
Missing	2 (1)
Recurrent Cancer	
Yes	112 (41)
No	144 (53)
Unknown/Missing	16 (6)
Cancer Treatment Dosing	
Continuous	127 (47)
Intermittent	144 (53)

Table 3.1 (cont'd)

Drug Category	
Cytotoxics	95 (35)
Kinase Inhibitors	127 (47)
Sex Hormone Inhibitors	27 (10)
Other	23 (8)
Concurrent Treatment	
Intravenous Chemotherapy	61 (22)
Radiation	19 (7)

Table 3.2

Linear Mixed Model Relating BMQ Scores to Covariates

	BMQ Necessity		BMQ Concerns	
	Estimate (SE)	**P**	**Estimate (SE)**	**P**
Time				
4 week	-0.112 (0.055)	0.04	-0.014 (0.049)	0.78
8 week	-0.087 (0.046)	0.06	0.038 (0.041)	0.36
12 week (ref)				
Baseline BMQ	0.701 (0.049)	<0.01	0.624 (0.042)	<0.01
Sex				
Male	-0.013 (0.072)	0.85	0.157 (0.059)	<0.01
Female (ref)				
Education Level Completed				
High school or less	-0.156 (0.108)	0.15	0.076 (0.090)	0.40
Some college or completed college	-0.168 (0.094)	0.08	0.081 (0.079)	0.31
Graduate or professional degree (ref)				
Stage				
Stage 4	0.103 (0.079)	0.20	-0.197 (0.066)	< 0.01
Stages1-3/Unstaged (ref)				
Age	0.002 (0.003)	0.64	-0.005 (0.003)	0.09
Number of Conditions Treated with Medications	-0.011 (0.018)	0.52	0.048 (0.014)	< 0.01

*BMQ = Beliefs about Medicines Questionnaire

*LME = Linear Mixed Model

* (ref) = reference value

Table 3.3

Least Square Means of each BMQ subscale at 4, 8, and 12 weeks

	BMQ Necessity			**BMQ Concerns**		
		95% Confidence Interval			95% Confidence Interval	
week	Mean (SE)	Lower Bound	Upper Bound	Mean (SE)	Lower Bound	Upper Bound
4	3.651 (.050)	3.552	3.750	2.570 (.042)	2.486	2.653
8	3.676 (.051)	3.576	3.776	2.621 (.043)	2.537	2.706
12	3.763 (.053)	3.658	3.867	2.583 (.045)	2.495	2.672

Table 3.4

Description of Most Prevalent Symptoms at Each Data Collection Point Using the Cancer Symptom Experience Inventory

Data Collection Point	Symptom (in order of most prevalent)	Prevalence N (%)
Baseline		
Symptom 1	Fatigue	174 (64)
Symptom 2	Weakness	120 (44)
Symptom 3	Pain	117 (43)
Symptom 4	Sleep disturbance	102 (38)
Symptom 5	Loss of appetite	100 (36.8)
4 weeks		
Symptom 1	Fatigue	153 (56)
Symptom 2	Weakness	98 (36)
Symptom 3	Pain	90(33.1)
Symptom 4	Numbness & tingling	89 (32.7)
Symptom 5	Loss of appetite	77 (28.3)
8 weeks		
Symptom 1	Fatigue	128 (47.1)
Symptom 2	Weakness	83 (31)
Symptom 3	Numbness & tingling	78 (29)
Symptom 4	Pain	75 (28)
Symptom 5	Sleep disturbance	62 (23)
12 weeks		
Symptom 1	Fatigue	119 (44)
Symptom 2	Numbness & tingling	78 (29)
Symptom 3	Weakness	75 (28)
Symptom 4	Pain	73 (27)
Symptom 5	Loss of appetite	56 (21)

**The most prevalent symptom across the 12-week study were Fatigue, Weakness, Pain, Loss of Appetite, Numbness and Tingling, and Sleep Disturbance.*

APPENDICES

APPENDIX A: FDA Approved Oral Agents Included in the Parent Study

Table 3.5

FDA Approved Oral Agents Included in the Parent Study

Oral Oncolytic Agents Organized Alphabetically by Trade Name	
Afinitor (Everolimus)	Stivarga (Regorafenib)
Bosulif (Bosutinib)	Sutent (Sunitinib)
Gilotrif (Afatinib)	Tafinlar (Dabrafenib)
Gleevec (Imatinib)	Tarceva (Erlotinib)
Ibrance (Palbociclib)	Tasigna (Nilotinib)
Imbruvica (Ibrutinib)	Temodar (Temozolomide)
Inlyta (Axitinib)	Tykerb (Lapatinib)
Lenvima (Lenvatinib)	Votrient (Pazopanib)
Lonsurf (Tipiracil & Trifluridine)	Xalkori (Crizotinib)
Lynparza (Olaparib)	Xeloda (Capecitabine)
Nexavar (Sorafenib)	Xtandi (Enzalutamide)
Pomalyst (Pomalidomide)	Zydelig (Idelalisib)
Revlimid (Lenalidomide)	Zykadia (Ceritinib)
Sprycel (Dasatinib)	Zytiga (Abiraterone acetate)

APPENDIX B: Eastern Cooperative Oncology Group Scale of Performance Status & Karnofsky Status Performance Scale

Table 3.6

Eastern Cooperative Oncology Group Scale of Performance Status & Karnofsky Status Performance Scale

WHO/ECOG Grade	WHO/ECOG Activity	Karnofsky Grade	Karnofsky Activity
0	Fully active, able to carry on all normal activities without restriction	100%	Normal no complaints; no evidence of disease
		90%	Able to carry on normal activity; minor signs or symptoms of disease
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80%	Normal activity with effort; some sign or symptoms of disease
		70%	Cares for self; unable to carry on normal activity or do active work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours	60%	Requires occasional assistance, but is able to care for most personal needs
		50%	Requires considerable assistance and frequent medical care
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours	40%	Disabled; requires special care and assistance
		30%	Severely disabled; hospitalization admission is indicated, although death not imminent
4	Completely disabled. Cannot carry on any self-care, totally confined to bed or chair.	20%	Very sick; hospital admission necessary; active support treatment is necessary
		10%	Moribund; fatal processes progressing rapidly
5	Dead	0%	Dead

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T., & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology*, *5*(6), 649-656.

Karnofsky, D. A. (1949). The clinical evaluation of chemotherapeutic agents in cancer. *Evaluation of Chemotherapeutic Agents*. In MacLeod CM (Ed), Evaluation of Chemotherapeutic Agents, Columbia University Press, New York.

APPENDIX C: Abbreviated Parent Study CONSORT

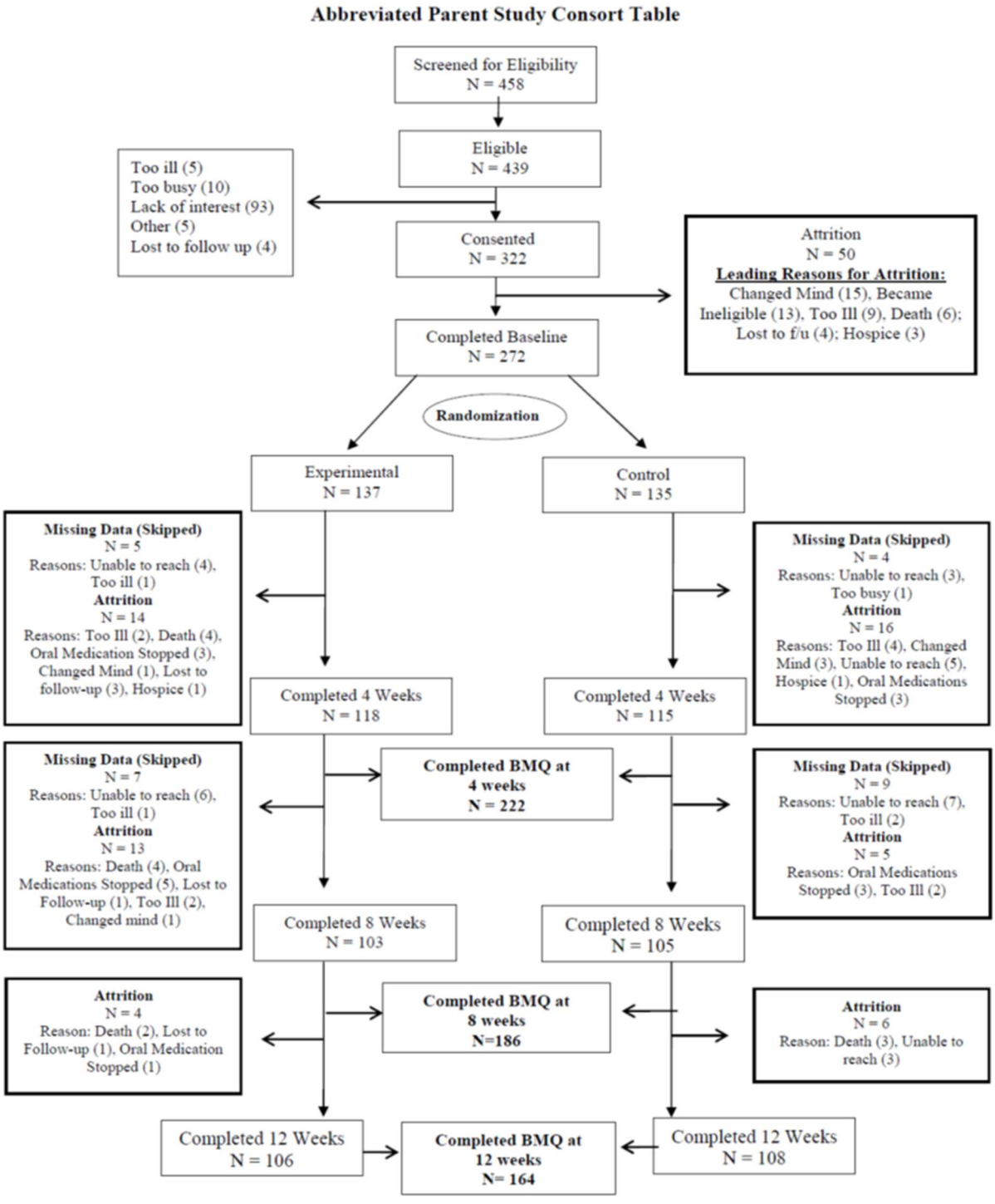

Figure 3.2 Abbreviated Parent Study CONSORT. Given, B.A., & Given, C.W. (2013–2017). *Improving adherence to oral cancer agents and self care of symptoms using an IVR (1R01CA162401-O1A1)*. [National Cancer Institute clinical trial]. Retrieved from https://clinicaltrials.gov/ct2/show/NCT02043184.

APPENDIX D: Screening/Baseline Data Collection Tools for Cancer/Cancer Demographic and Treatment Characteristics

What is your highest level of education completed?

- o No formal education
- o Completed grade school
- o Completed some high school
- o Completed high school
- o Completed some college or technical college or associate degree
- o Completed college
- o Completed graduate/professional degree (post baccalaureate degree)
- o Refused

What is your current marital status?

- o Never married
- o Married
- o Divorced/Separated
- o Widowed
- o Living together
- o Refused

What is your ethnic background?

- o Hispanic or Latino
- o Not Hispanic or Latino
- o Unknown
- o Refused

What is your race or ethnic background?

- o American Indian or Alaskan Native
- o African American or Black
- o Asian
- o Native Hawaiian or Pacific Islander
- o White
- o More than one race
- o Unknown
- o Refused

Screening Eligibility Form from Parent Study
(Collecting patient and disease characteristics)

Gender:

- o Male
- o Female

Ethnicity:

- o Hispanic/Latino
- o Not Hispanic/Latino

Race (check all that apply):

- American Indian/Alaska Native
- Asian
- Native Hawaiian/Pacific Islander
- Black/African American
- White

Cancer Site:

- Breast
- Colorectal
- Gastrointestinal
- Leukemia
- Liver
- Lung
- Lymphoma
- Melanoma
- Myeloma
- Pancreatic
- Prostate
- Renal
- Sarcoma

Stage:

- I
- II
- III
- IV
- Other

If 'Other' write in stage: _____

On Concurrent IV chemotherapy?:

- Yes
- No
- If yes, medication and frequency:_____
-

On Concurrent Radiation?

- Yes
- No
- If yes, treatment name and frequency: _____

Patient Eligibility:

- Yes
- No
-

(If NO to ANY of the questions below, patient is NOT eligible)

Can hear on telephone?

- Yes
- No

Can read and understand English?

- Yes
- No

21 or older?

- Yes
- No
- Age:_____

ECOG Performance status within 0-2 or Karnofsky performance status within 50-100?

- Yes
- No
- Score:_____

Has a land line/cell phone with touch pad numbers?

- Yes
- No

Is on an eligible oral cancer medications?

- Yes
- No

Date Screened: _____

Recruiter Initials: _____

Eligibility:

- Eligible
- Ineligible

Enrollment Status:

- Consented
- Refused
- Lost to follow-up

Reason, if refused:

- Too ill
- Too busy
- Lack of interest
- Other

APPENDIX E: Adapted Beliefs about Medicine Questionnaire

Table 3.7

Adapted Beliefs about Medicine Questionnaire

	Strongly Agree 1	Agree 2	Uncertain 3	Disagree 4	Strongly Disagree 5	Refused 6
My health, at present, depends on my oral cancer medications.						
Having to take my oral cancer medications worries me.						
My life would be impossible without my oral cancer medications.						
Without my oral cancer medications I would be very ill.						
I sometimes worry about the long-term effects of my oral cancer medication.						
My oral cancer medications are a mystery to me.						
My oral cancer medications give me unpleasant side effects.						
My health in the future will depend on my oral cancer medications.						
My oral cancer medications disrupt my life.						
I sometimes worry about becoming too dependent on my oral cancer medications.						
My oral cancer medications protect me from becoming worse.						

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, *14*(1), 1-24.

APPENDIX F: Cancer Symptom Experience Inventory

Table 3.8

Cancer Symptom Experience Inventory

1. In the past 7 days have you experienced **fatigue** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your fatigue at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did fatigue interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
2. In the past 7 days have you experienced **sleep disturbance** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your sleep disturbance at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did sleep disturbance interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
3. In the past 7 days have you experienced **anxiety** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your anxiety at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did anxiety interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
4. In the past 7 days have you experienced **weakness** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		

Table 3.8 (cont'd)

a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your weakness at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did weakness interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
5. In the past 7 days have you experienced **pain** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your pain at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did pain interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
6. In the past 7 days have you experienced **headaches** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your headaches at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did headaches interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
7. In the past 7 days have you experienced **skin rash or skin sores** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your skin rash or skin sores at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did skin rash or skin sores **fatigue** interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10

Table 3.8 (cont'd)

Did not interfere ---------- Interfered completely										Refused
8. In the past 7 days have you experienced **numbness or tingling, especially in hands or feet** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your numbness or tingling, especially in hands or feet at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did numbness or tingling, especially in hands or feet interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
9. In the past 7 days have you experienced **redness, peeling or pain in hands or feet** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your redness, peeling or pain in hands or feet at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did redness, peeling or pain in hands or feet interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
10. In the past 7 days have you experienced **swelling of hands or feet** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your swelling of hands or feet at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did swelling of hands or feet interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
11. In the past 7 days have you experienced **joint pain** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		

Table 3.8 (cont'd)

a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your joint pain at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did joint pain interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
12. In the past 7 days have you experienced **sores in mouth** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your sores in mouth at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did sores in mouth interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
13. In the past 7 days have you experienced **lack of appetite** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your lack of appetite at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did lack of appetite interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
14. In the past 7 days have you experienced **nausea or vomiting** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your nausea or vomiting at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did nausea or vomiting interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10

Table 3.8 (cont'd)

Did not interfere ---------- Interfered completely										Refused
15. In the past 7 days have you experienced **diarrhea** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your diarrhea at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did diarrhea interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
16. In the past 7 days have you experienced **constipation** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your constipation at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did constipation interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
17. In the past 7 days have you experienced **cough** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your cough at its WORST in the past 7 days. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	
Very little ---------- Worst possible									Refused	
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did cough interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
18. In the past 7 days have you experienced **shortness of breath** related to your cancer or its treatment? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Please rate on a scale from 1-9, with 1 being very little, to 9 being worst possible, your shortness of breath at its WORST in the past 7 days. *(Circle one response)*										

Table 3.8 (cont'd)

1	2	3	4	5	6	7	8	9	10
Very little ---------- Worst possible									Refused
b. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did shortness of breath interfere in your daily activities in the last 7 days? *(Circle one response)*									
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
19. In the past 7 days did you or anyone else including your doctor take your temperature? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
a. **If Yes:** Was your temperature above 101 degrees Fahrenheit? *(Circle one response)*										
1				2				3		
Yes				No				Refused		
i. **If Yes:** On a scale of 0 – did not interfere, to 9 – interfered completely, overall how much did your fever interfere in your daily activities in the last 7 days? *(Circle one response)*										
0	1	2	3	4	5	6	7	8	9	10
Did not interfere ---------- Interfered completely										Refused
ii. **If Yes:** Did you report your fever to your oncologist? *(Circle one response)*										
1				2				3		
Yes				No				Refused		

Given, B., Given, C. W., Sikorskii, A., Jeon, S., McCorkle, R., Champion, V., & Decker, D. (2008). Establishing mild, moderate, and severe scores for cancer-related symptoms: How consistent and clinically meaningful are interference-based severity cut-points? *Journal of Pain and Symptom Management,35*(2), 126–135. Doi:10.1016/j.jpainsymman.2007.03.01

APPENDIX G: Center for Epidemiologic Studies-Depression Scale

Table 3.9

Center for Epidemiologic Studies-Depression Scale

	Rarely or none of the time (less than 1 day) 1	Some or little of the time (1-2 days) 2	Moderate amount of the time (3-4 days) 3	Most of all the time (5-7 days) 4	Refused 5
I was bothered by things that usually don't bother me.					
I did not feel like eating, my appetite was poor.					
I felt that I could not shake off the blues even with help from my family and friends.					
I felt that I was just as good as other people.					
I had trouble keeping my mind on what I was doing.					
I felt depressed.					
I felt that everything I did as an effort.					
I felt hopeful about the future.					
I thought my life had been a failure.					
I felt fearful.					
My sleep was restless.					
I was happy.					
I talked less than usual.					
I felt lonely.					
People were unfriendly.					
I enjoyed life.					
I had crying spells.					
I enjoyed life.					
I had crying spells.					
I felt sad.					
I felt that people dislike me.					
I could not get "going."					

Radloff LS. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 1* (3): 385-401.

APPENDIX H: Attentional Function Index

Table 3.10

Attentional Function Index

1. Getting started on activities (task, jobs) you intend to do. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all ----------Extremely Well										Refused
2. Following through on your plans. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all ----------Extremely Well										Refused
3. Doing things that take time and effort *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- Extremely Well										Refused
4. Making your mind up about things *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all ----------Extremely Well										Refused
5. Keeping you mind on what you are doing *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all ----------Extremely Well										Refused
6. Remembering to do all the things you started out to do *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- Extremely Well										Refused
7. Keeping your mind on what others are saying or doing. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- Extremely Well										Refused
8. Keeping yourself from saying or doing things you did not want to say or do. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all ----------Extremely Well										Refused
9. Being patient with others. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- Extremely Well										Refused

For the next questions, rate your response on a scale of 0-10, with 0 being Not at all, and 10 being a Great Deal.

10. How hard you find it to concentrate on details. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- A Great Deal										Refused
11. How often you make mistakes on what you are doing. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- A Great Deal										Refused
12. Forgetting to do important things. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- A Great Deal										Refused
13. Getting easily annoyed or irritated. *(Circle one response)*										
1	2	3	4	5	6	7	8	9	10	11
Not at all---------- A Great Deal										Refused

Cimprich, B., Visovatti, M., & Ronis, D. L. (2011). The Attentional Function Index—a self-report cognitive measure. *Psycho-Oncology*, *20*(2), 194-202.

APPENDIX I: Comorbid Conditions Requiring Medication: Medical Record Audit

Please list all medications (other than chemotherapy agents listed in Table 1) that were prescribed during the audit period, as well as medications that the patient was on for comorbid conditions during the audit period.

Table 3.11
Comorbid Conditions Requiring Medication: Medical Record Audit

NAME OF DRUG	**DATE PRESCRIBED** ***IF DURING THE AUDIT PERIOD***

REFERENCES

REFERENCES

Aikens, J. E., & Piette, J. D. (2009). Diabetic patients' medication underuse, illness outcomes, and beliefs about antihyperglycemic and antihypertensive treatments. *Diabetes Care*, *32*(1), 19-24. Doi:10.2337/dc08-1533.

Arriola, K. R. J., Mason, T. A., Bannon, K. A., Holmes, C., Powell, C. L., Horne, K., & O'Regan, R. (2014). Modifiable risk factors for adherence to adjuvant endocrine therapy among breast cancer patients. *Patient Education and Counseling*, *95*(1), 98-103.

Balmer, C. E., Thomas, P., & Osborne, R. J. (2001). Who wants second-line, palliative chemotherapy?. *Psycho-Oncology*, *10*(5), 410–418.

Barsky, A. J., Saintfort, R., Rogers, M. P., & Borus, J. F. (2002). Nonspecific medication side effects and the nocebo phenomenon. *Journal of the American Medical Association*, *287*(5), 622-627.

Belzung, C., Willner, P., & Philippot, P. (2015). Depression: From psychopathology to pathophysiology. *Current Opinion in Neurobiology*, *30*, 24-30. Doi: http://dx.doi.org/10.1016/j.conb.2014.08.013.

Bernal-Rusiel, J. L., Greve, D. N., Reuter, M., Fischl, B., & Sabuncu, M. R. (2013). Statistical Analysis of Longitudinal Neuroimage Data with Linear Mixed Effects Models. *NeuroImage*, *0*, 249–260. http://doi.org/10.1016/j.neuroimage.2012.10.065.

Bhattacharya, D., Easthall, C., Willoughby, K. A., Small, M., & Watson, S. (2012). Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. *Journal of Oncology Pharmacy Practice*, *18*(3), 333-342.

Blinman, P., King, M., Norman, R., Viney, R., & Stockler, M. R. (2012). Preferences for cancer treatments: An overview of methods and applications in oncology. *Annals of Oncology*, *23*(5), 1104-1110. Doi: 10.1093/annonc/mdr559.

Brown, C., Battista, D. R., Bruehlman, R., Sereika, S. S., Thase, M. E., & Dunbar-Jacob, J. (2005). Beliefs about antidepressant medications in primary care patients: Relationship to self-reported adherence. *Medical Care*, *43*(12), 1203-1207.

Burnett-Zeigler, I., Kim, H. M., Chiang, C., Kavanagh, J., Zivin, K., Rockefeller, K., ... & Kales, H. C. (2014). The association between race and gender, treatment attitudes, and antidepressant treatment adherence. *International Journal of Geriatric Psychiatry*, *29*(2), 169-177. Doi:10.1002/gps.3984.

Cassell, B., Gyawali, C. P., Kushnir, V. M., Gott, B. M., Nix, B. D., & Sayuk, G. S. (2015). Beliefs about GI medications and adherence to pharmacotherapy in functional GI

disorder outpatients. *The American Journal of Gastroenterology*, *110*(10), 1382-1387. Doi:10.1038/ajg.2015.132.

Center Watch. FDA Approved Drugs for Oncology. (2017). www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology. Accessed July 2017.

Chen, L. C., Chen, T. C., Huang, Y. B., & Chang, C. S. (2014). Disease acceptance and adherence to imatinib in Taiwanese chronic myeloid leukaemia outpatients. *International Journal of Clinical Pharmacy*, *36*(1), 120-127.

Cimprich B. (1992). Attentional fatigue following breast cancer surgery. *Research in Nursing & Health*, *15*:199–207. Doi: 10.1002/nur.4770150306.

Cimprich, B., So, H., Ronis, D., Trask, C. (2005). Pretreatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psycho-Oncology*, 14,70–78. Doi: 10.1002/pon.821.

Cimprich, B., Visovatti, M., & Ronis, D. L. (2011). The Attentional Function Index—a self-report cognitive measure. *Psycho-Oncology*, *20*(2), 194-202.

Corter, A. L., Findlay, M., Broom, R., Porter, D., & Petrie, K. J. (2013). Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology*, *18*(1), 168-181.

Del Castillo, A., Godoy-Izquierdo, D., Vázquez, M. L., & Godoy, J. F. (2011). Illness beliefs about cancer among healthy adults who have and have not lived with cancer patients. *International Journal of Behavioral Medicine*, *18*(4), 342–351.

Devins, G. M., Orme, C. M., Costello, C. G., Binik, Y. M., Frizzell, B., Stam, H. J., & Pullin, W. M. (1988). Measuring depressive symptoms in illness populations: Psychometric properties of the Center for Epidemiologic Studies Depression (CES-D) scale. *Psychology & Health, 2*(2), 139–156. doi:10.1080/08870448808400349.

Diefenbach, M., Leventhal, H., and Leventhal, E.A. (1996). The Sensitive Soma Scale. Unpublished.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, *160*(14), 2101-2107. Doi:10.1001/archinte.160.14.2101.

Dong, S. T., Butow, P. N., Costa, D. S., Lovell, M. R., & Agar, M. (2014). Symptom clusters in patients with advanced cancer: A systematic review of observational studies. *Journal of Pain and Symptom Management*, *48*(3), 411-450.

Fitzgerald, P., Lo, C., Li, M., Gagliese, L., Zimmermann, C., & Rodin, G. (2013). The relationship between depression and physical symptom burden in advanced cancer. *BMJ Supportive & Palliative Care*, *5*, 381-388.

Given, B.A., & Given, C.W. (2013–2017). *Improving adherence to oral cancer agents and self care of symptoms using an IVR (1R01CA162401-O1A1)*. [National Cancer Institute clinical trial]. Retrieved from https://clinicaltrials.gov/ct2/show/NCT02043184.

Given, B.A., Given, C.W., Majeske, C. (2013). Medication Management & Symptom Management Toolkit. East Lansing, MI. Michigan State University.

Given, B., Given, C. W., Sikorskii, A., Jeon, S., McCorkle, R., Champion, V., & Decker, D. (2008). Establishing mild, moderate, and severe scores for cancer-related symptoms: How consistent and clinically meaningful are interference-based severity cut-points? *Journal of Pain and Symptom Management,35*(2), 126–135. Doi:10.1016/j.jpainsymman.2007.03.012.

Given, B. A., Spoelstra, S. L., & Grant, M. (2011, May). The challenges of oral agents as antineoplastic treatments. In *Seminars in Oncology Nursing* (Vol. 27, No. 2, pp. 93-103). WB Saunders.

Heisig, S. R., Shedden-Mora, M. C., Blanckenburg, P., Rief, W., Witzel, I., Albert, U. S., & Nestoriuc, Y. (2016). What do women with breast cancer expect from their treatment? Correlates of negative treatment expectations about endocrine therapy. *Psycho-Oncology*, *25*(12), 1485-1492.

Hilliard, M. E., Eakin, M. N., Borrelli, B., Green, A., & Riekert, K. A. (2015). Medication beliefs mediate between depressive symptoms and medication adherence in cystic fibrosis. *Health Psychology*, *34*(5), 496-504. Doi: 10.1037/hea0000136.

Hirose, T., Yamaoka, T., Ohnishi, T., Sugiyama, T., Kusumoto, S., Shirai, T., ... & Adachi, M. (2009). Patient willingness to undergo chemotherapy and thoracic radiotherapy for locally advanced non-small cell lung cancer. *Psycho-Oncology*, *18*(5), 483–489.

Horne, R. (2003). Treatment perceptions and self-regulation. In The self-regulation of health and illness behavior. In L. D. Cameron, & H. Leventhal (Eds.), *The self-regulation of health and illness behavior* (pp. 138–153). New York, NY: Routledge.

Horne, R., Graupner, L., Frost, S., Weinman, J., Wright, S. M., & Hankins, M. (2004). Medicine in a multi-cultural society: The effect of cultural background on beliefs about medications. Social Science & Medicine, 59(6), 1307-1313. doi:10.1016/j.socscimed.2004.01.009.

Horne, R., & Weinman, J. (1999). Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal of Psychosomatic Research*, *47*(6), 555-567. doi:10.1016/S0022-3999(99)00057-4.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health, 14*(1), 1–24. doi:10.1080/08870449908407311.

Hung, M. S., Chen, I. C., Lee, C. P., Huang, R. J., Chen, P. C., Tsai, Y. H., & Yang, Y. H. (2017). Incidence and risk factors of depression after diagnosis of lung cancer: A nationwide population-based study. *Medicine*, *96*(19).

Iskandarsyah, A., de Klerk, C., Suardi, D. R., Soemitro, M. P., Sadarjoen, S. S., & Passchier, J. (2014). Psychosocial and cultural reasons for delay in seeking help and nonadherence to treatment in Indonesian women with breast cancer: A qualitative study. *Health Psychology*, *33*(3), 214-221.

Jansen, S. J. T., Otten, W., Baas-Thijssen, M. C. M., van de Velde, C. J. H., Nortier, J. W. R., & Stiggelbout, A. M. (2005). Explaining differences in attitude toward adjuvant chemotherapy between experienced and inexperienced breast cancer patients. *Journal of Clinical Oncology*, *23*(27), 6623-6630. Doi: 10.1200/JCO.2005.07.171.

Jansen, S. J., Otten, W., & Stiggelbout, A. M. (2004). Review of determinants of patients' preferences for adjuvant therapy in cancer. *Journal of Clinical Oncology*, *22*(15), 3181-3190. Doi: 10.1200/JCO.2004.06.109.

Jin, L., & Acharya, L. (2016). Cultural Beliefs Underlying Medication Adherence in People of Chinese Descent in the United States. *Health Communication*, *31*(5), 513-521. Doi:10.1080/10410236.2014.974121.

Kalichman, S., Kalichman, M. O., & Cherry, C. (2016). Medication beliefs and structural barriers to treatment adherence among people living with HIV infection. *Psychology & Health*, *31*(4), 383-395. Doi:10.1080/08870446.2015.1111371.

Kalichman, S. C., Pellowski, J., Kegler, C., Cherry, C., & Kalichman, M. O. (2015). Medication adherence in people dually treated for HIV infection and mental health conditions: Test of the medications beliefs framework. *Journal of Behavioral Medicine*, *38*(4), 632-641. Doi:10.1007/s10865-015-9633-6.

Karnofsky, D. A. (1949). The clinical evaluation of chemotherapeutic agents in cancer. Evaluation of Chemotherapeutic Agents. In C. M. MacLeod (Ed.), *Evaluation of Chemotherapeutic Agents*. New York, NY: Columbia University Press.

Krebber, A. M. H., Buffart, L. M., Kleijn, G., Riepma, I. C., de Bree, R., Leemans, C. R., Becker, A., Brug, J., van Straten, A., Cuijpers, P. and Verdonck-de Leeuw, I. M. (2014), Prevalence of depression in cancer patients: A meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology*, 23: 121–130. Doi:10.1002/pon.3409.

Krummenacher, I., Spencer, B., Du Pasquier, S., Bugnon, O., Cavassini, M., & Schneider, M. P. (2014). Qualitative analysis of barriers and facilitators encountered by HIV patients in an

ART adherence programme. *International Journal of Clinical Pharmacy*, *36*(4), 716-724. Doi: 10.1007/s11096-014-9930-0.

Kunneman, M., Pieterse, A. H., Stiggelbout, A. M., Nout, R. A., Kamps, M., Lutgens, L. C. H. W., ... & Creutzberg, C. L. (2014). Treatment preferences and involvement in treatment decision making of patients with endometrial cancer and clinicians. *British Journal of Cancer*, *111*(4), 674-679. Doi:10.1038/bjc.2014.322.

LaPointe, N. M. A., Ou, F. S., Calvert, S. B., Melloni, C., Stafford, J. A., Harding, T., ... & Peterson, E. D. (2010). Changes in beliefs about medications during long-term care for ischemic heart disease. *American Heart Journal*, *159*(4), 561-569. doi:10.1016/j.ahj.2009.12.025.

Lewinsohn P.M., Seeley J.R., Roberts R.E., Allen N.B. (1997). Center for epidemiologic studies depression scale (CES-D) as a screening instrument for depression among community-residing older adults. *Psychology and Aging, 12***,** 277-287.

Maguire, L. K., Hughes, C. M., & McElnay, J. C. (2008). Exploring the impact of depressive symptoms and medication beliefs on medication adherence in hypertension—a primary care study. *Patient Education and Counseling*, *73*(2), 371-376. Doi:10.1016/j.pec.2008.06.016.

Mahler, C., Hermann, K., Horne, R., Jank, S., Haefeli, W. E., & Szecsenyi, J. (2012). Patients' beliefs about medicines in a primary care setting in Germany. *Journal of Evaluation in Clinical Practice*, *18*(2), 409-413. Doi: 10.1111/j.1365-2753.2010.01589.x.

Marshall, V. & Given, B. (*In Press*). Factors Associated with Medication Beliefs in Patients with Cancer: An Integrative Review. *Oncology Nursing Forum*.

Marshall, V., Lehto, R., Given, C.W., Given, B., Sikorskii, A. (2018). Conceptualization of medication beliefs among advanced cancer patients receiving oral oncolytic agents using a theory derivation approach. *Unpublished doctoral dissertation, Michigan State University, East Lansing Michigan*.

Matsuyama, R., Reddy, S., & Smith, T. J. (2006). Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *Journal of Clinical Oncology*, *24*(21), 3490-3496.

Mercadante, S., Aielli, F., Adile, C., Ferrera, P., Valle, A., Fusco, F., ... & Valenti, M. (2015). Prevalence of oral mucositis, dry mouth, and dysphagia in advanced cancer patients. *Supportive Care in Cancer*, *23*(11), 3249-3255.

Mercadante, S., Aielli, F., Masedu, F., Valenti, M., Verna, L., Mercadante, A., & Porzio, G. (2016). Pattern of symptoms and symptomatic treatment in adults and the aged population: A retrospective analysis of advanced cancer patients followed at home. *Current Medical Research and Opinion*, *32*(5), 893-898.

Moens, K., Higginson, I. J., & Harding, R. (2014). Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review. *Journal of Pain and Symptom Management*, *48*(4), 660-677.

Mohammed, S., Peter, E., Gastaldo, D., & Howell, D. (2016). The "Conflicted Dying": The active search for life extension in advanced cancer through biomedical treatment. *Qualitative Health Research*, *26*(4), 555-567.

Moon, Z., Moss-Morris, R., Hunter, M. S., Carlisle, S., & Hughes, L. D. (2017). Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: A systematic review. *Patient Preference and Adherence*, *11*, 305-322.

Neuss, M. N., Polovich, M., McNiff, K., Esper, P., Gilmore, T. R., LeFebvre, K. B., ... & Jacobson, J. O. (2013). 2013 updated American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards including standards for the safe administration and management of oral chemotherapy. *Journal of Oncology Practice*, *9*(2S), 5-13. Doi: 10.1200/JOP.2013.000874.

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T., & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology, 5*(6), 649–655. Doi:10.1097/00000421-198212000-00014.

Piette, J. D., Heisler, M., Harand, A., & Juip, M. (2010). Beliefs about prescription medications among patients with diabetes: Variation across racial groups and influences on cost-related medication underuse. *Journal of Health Care for the Poor and Underserved*, *21*(1), 349-361. Doi: 10.1353/hpu.0.0247.

Radloff LS. (1977). The CES-D Scale: A self report depression scale for research in the generalpopulation. *Applied Psychological Measurement, 1* (3): 385-401.

Reynolds, N. R., Testa, M. A., Marc, L. G., Chesney, M. A., Neidig, J. L., Smith, S. R., ... & Robbins, G. K. (2004). Factors influencing medication adherence beliefs and self-efficacy in persons naive to antiretroviral therapy: A multicenter, cross-sectional study. *AIDS and Behavior*, *8*(2), 141-150.

Salgado, T. M., Davis, E. J., Farris, K. B., Fawaz, S., Batra, P., & Henry, N. L. (2017). Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment*, *163*(2), 311-319. Doi: 10.1007/s10549-017-4177-9.

Saratsiotou, I., Kordoni, M., Bakogiannis, C., Livadarou, E., Skarlos, D., Kosmidis, P. A., & Razis, E. (2010). Treatment adherence of cancer patients to orally administered

chemotherapy: Insights from a Greek study using a self-reported questionnaire. *Journal of Oncology Pharmacy Practice*, *17*(4), 303-311.

Sarfati, D., Koczwara, B., & Jackson, C. (2016). The impact of comorbidity on cancer and its treatment. *CA: A Cancer Journal for Clinicians*, *66*(4), 337-350.

Schüz, B., Wurm, S., Ziegelmann, J. P., Warner, L. M., Tesch-Römer, C., & Schwarzer, R. (2011). Changes in functional health, changes in medication beliefs, and medication adherence. *Health Psychology*, *30*(1), 31-39. Doi:10.1037/a0021881.

Seow, H., Barbera, L., Sutradhar, R., Howell, D., Dudgeon, D., Atzema, C., ... & Earle, C. (2011). Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. *Journal of Clinical Oncology*, *29*(9), 1151-1158.

Shimada, Y., Hamaguchi, T., Mizusawa, J., Saito, N., Kanemitsu, Y., Takiguchi, N., ... & Tomita, N. (2014). Randomised phase III trial of adjuvant chemotherapy with oral uracil and tegafur plus leucovorin versus intravenous fluorouracil and levofolinate in patients with stage III colorectal cancer who have undergone Japanese D2/D3 lymph node dissection: final results of JCOG0205. *European Journal of Cancer*, *50*(13), 2231-2240.

Shiyanbola, O. O., Farris, K. B., & Chrischilles, E. (2013). Concern beliefs in medications: Changes over time and medication use factors related to a change in beliefs. *Research in Social and Administrative Pharmacy*, *9*(4), 446-457. doi:10.1016/j.sapharm.2012.07.003.

Smith, A. W., Reeve, B. B., Bellizzi, K. M., Harlan, L. C., Klabunde, C. N., Amsellem, M., ... & Hays, R. D. (2008). Cancer, comorbidities, and health-related quality of life of older adults. *Health Care Financing Review*, *29*(4), 41-56.

Spoelstra, S. L., Given, B. A., Given, C. W., Grant, M., Sikorskii, A., You, M., & Decker, V. (2013). An intervention to improve adherence and management of symptoms for patients prescribed oral chemotherapy agents: An exploratory study. *Cancer Nursing*, *36*(1), 18-28.

Stiggelbout, A. M., De Haes, J. C. J. M., Kiebert, G. M., Kievit, J., & Leer, J. W. H. (1996). Tradeoffs between quality and quantity of Life: Development of the QQ Questionnaire for cancer patient attitudes. *Medical Decision Making*, *16*(2), 184–192.

Teunissen, S. C., Wesker, W., Kruitwagen, C., de Haes, H. C., Voest, E. E., & de Graeff, A. (2007). Symptom prevalence in patients with incurable cancer: A systematic review. *Journal of Pain and Symptom Management*, *34*(1), 94-104.

Thuné-Boyle, I. C., Myers, L. B., & Newman, S. P. (2006). The role of illness beliefs, treatment beliefs, and perceived severity of symptoms in explaining distress in cancer patients during chemotherapy treatment. *Behavioral Medicine*, *32*(1), 19-29.

Tipton, J. M. (2015). Overview of the challenges related to oral agents for cancer and their impact on adherence. *Clinical Journal of Oncology Nursing*, *19*(3), 37-40.

Verhoef, T. I., Redekop, W. K., Bouvy, M. L., Dorenbos, B., Karwar, Z., Schie, R. M., ... & Maitland-van der Zee, A. H. (2014). Beliefs about medicines in Dutch Acenocoumarol and Phenprocoumon users. *British Journal of Clinical Pharmacology*, *78*(2), 422-429. Doi: 10.1111/bcp.12346.

Weinman, J., Petrie, K. J., Moss-Morris, R., & Horne, R. (1996). The illness perception questionnaire: A new method for assessing the cognitive representation of illness. *Psychology and Health*, *11*(3), 431-445. Doi:10.1080/08870449608400270.

CHAPTER 4: EXPLORING THE IMPACT OF ADVERSE EVENTS AND PERMANENT PHYSICIAN-DIRECTED ORAL ONCOLYTIC AGENT STOPPAGES ON MEDICATION BELIEFS AMONG ADVANCED CANCER PATIENTS

Introduction

Patients with advanced cancer are living longer, in part due to the new developments of cancer treatments and broadened treatment options (Matsuyama, Reddy, & Smith, 2006; Mohammed, Peter, Gastaldo, & Howell, 2016). The use of oral oncolytic agents (OAs) among patients who have experienced previously failed cancer treatments is increasing, allowing patients and their caregivers to receive cancer care in the comfort of their own home (Mohammed et al., 2016). Chemotherapy prescribed as a last line of treatment serves to prolong life by delaying disease progression, manage symptoms of cancer, delay the onset of new cancer symptoms, maintain patient function, and give patients a sense of hope that something is being done to treat their cancer (Grunfeld et al., 2006; Koedoot et al., 2003). However, patients with advanced cancer who have previously failed treatments are at risk for experiencing adverse events related to the oral cancer medication and permanent physician-directed OA stoppages (Ding et al., 2017). It is not known how adverse events and permanent physician-directed OA stoppages impact medication beliefs about cancer treatment. Medication beliefs are defined as the perceptions regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003).

This research examines the relationship of documented adverse events and physician-directed stoppages on OA medication beliefs. Results of this study can assist oncology professionals to initiate timely end of life planning among advanced cancer patients.

Background & Significance

Adverse events are defined by the National Cancer Institute as "any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure" (US Department of Health and Human Services, 2009, pg. 2). This definition of adverse events encompasses different domains including analytic diagnostic testing (e.g. laboratory testing and computed tomography), objective clinical assessment (e.g. physical examination), and subjective data that includes the patient's accounts of symptoms (Trotti et al., 2007).

Tracking adverse events is an important assessment tool for oncologists in order to make treatment-related decisions (Atkinson et al., 2017; Di Maio, Basch, Bryce, & Perrone, 2016; Trotti, Colevas, Setser, & Basch, 2007). For example, when caring for patients with advanced cancer receiving OAs for palliative benefit, assessment and evaluation of adverse events is critical for making decisions regarding the continued course of cancer treatment. Adverse events influence physicians' decisions to stop OA treatment (Atkinson et al., 2017; Di Maio et al., 2016) when it is acknowledged that the beneficial nature of palliative cancer treatment has ended (Chan et al., 2016). Such decisions to stop OA medication in these circumstances is in line with the American Society of Clinical Oncology's recommendations to discontinue cancer treatment when there is no further benefit of treatment or when potential harm outweighs treatment benefit (Schnipper et al., 2013). Adverse events are not the only reason for physician-directed OA stoppages, however. Other reasons for discontinuing cancer treatment among patients with advanced stage cancer include disease progression and deteriorating functional status (Clarke, Johnston, Corrie, Kuhn, & Barclay, 2015). However, both adverse events and physician-directed

stoppages may impact medication beliefs (Salgado et al., 2017) and the examination of these relationships can have important implications for oncology intervention research.

A widely accepted measure of adverse events among cancer patients receiving anticancer treatment is the Common Terminology Criteria for Adverse Events (CTCAE), which defines each adverse event and offers a grading scale to measure the severity of each adverse event (US Department of Health and Human Services, 2009). However, there has been criticism over the use of the CTCAE to appropriately measure a patient's symptomatic toxicities, specifically the potential for physicians to underreport or fail to report these events (Di Maio et al., 2016).

In contrast with adverse events, a symptom is defined as the patient's perception of a physical or psychological disturbance and is best reported by the patient (Di Maio et al., 2016). Although a physician may assess patient symptoms, they can fail to correctly interpret the patient's symptoms or consider the symptoms related to the cancer and not the cancer medication (Di Maio et al., 2016). Patients also may not report their symptoms to the doctor (Krebber et al., 2014; Müller-Schwefe et al., 2014). Such criticisms have directed research towards the inclusion of patient-reported outcome (PRO) measures in the CTCAE (Atkinson et al., 2017; Basch, 2010; Basch et al., 2014; Di Maio et al., 2016; Trotti et al., 2007). In addition, reporting of adverse events is at the physician's discretion. Physicians' attempts to screen and report patient symptoms and grade symptom severity using the CTCAE can be inconsistent, biased, and even misinterpret the patient's account of their symptoms (Trotti et al., 2007). This can lead to underreporting of patient symptoms that can characterize oncology treatment medication as less toxic than they actually are (Trotti et al., 2007).

However, the CTCAE's analytic data such as diagnostic testing (e.g. laboratory values or computerized tomography) and objective data that uses the physician's clinical expertise such as

physical examination findings are more accurately reported by the physician (Trotti et al., 2007). In a longitudinal study, Basch et al. (2009) reported that adverse events measured by the CTCAE and documented by oncology professionals better predicted unfavorable clinical events such as death and emergency room visits than patient-reported symptoms. Although patient-reported symptoms are extremely meaningful because they offer self-perceptions of physical or emotional disturbance and are a better indicator of the patient's overall health status, the CTCAE indicate adverse events can influence discontinuation of oral agents (Chan et al., 2016) and impact patients' perceptions of treatment.

Permanent physician-directed OA stoppages, whether a result of disease progression or documented adverse events that outweigh palliative benefit of continued treatment, require difficult discussions with patients (Chan et al., 2016). Information that the cancer medication is more harmful than beneficial must be processed by the patient, which can change positive beliefs that reflect the OA medication is beneficial for improving or maintaining health. Receiving and processing this information can not only influence medication beliefs, but potentially the acceptance of impending death and end of life care such as hospice (Chan et al., 2016).

Adverse events may be accepted by cancer patients who are striving for survival (Chan et al., 2016), but when these adverse events place the patient at risk for a permanent-physician directed OA stoppage, this can increase their negative medication beliefs about their OA medication. Adverse events are linked to negative medication beliefs (Salgado et al., 2017), but have not been directly linked to positive medication beliefs in the literature (Heisig et al., 2016; Salgado et al., 2017). However, when oncologists share that the medication must be stopped because it is more harmful than beneficial (Chen et al., 2016), this may weaken positive medication beliefs and further increase the strength of negative medication beliefs.

Patients with advanced cancers also have different beliefs about their cancer medication compared to patients with earlier stage cancers (Harrington & Smith, 2008; Heisig et al., 2016). Patients who are facing impending death may find it important to strive for survival, even if this survival is short such as weeks or months (Koedoot et al., 2003). Patients with advanced cancer may endure cancer treatment that results in an array of adverse events even for a small chance of benefit, such as extending survival by only weeks to months (Balmer, Thomas, & Osborne, 2001; Chan, Lam, Siu, & Yuen, 2016; Grunfeld et al., 2006; Harrington & Smith, 2008; Matsuyama et al., 2006; Silvestri, Pritchard, & Welch, 1998). Patients with advanced cancer, who are striving for survival, may be accepting of adverse events (Chan et al., 2016; Matsuyama et al., 2006). However, adverse events related to the cancer treatment may cause more harm than benefit and result in medication stoppage under the oncologist's order (Chan et al., 2016).

Importantly, cancer patients are starting new cancer regimens closer to end of life (Earle et al., 2004; Harrington & Smith, 2008; Matsuyama et al., 2006; National Cancer Institute, 2017). Studies have reported that patients on oral chemotherapy continue receiving their treatment closer to death than those receiving intravenous chemotherapy (Pirl et al., 2015). Patients receiving oral agents near the end of life are also not as likely to enter hospice (Chan et al., 2016). Patients' choice to accept cancer treatment, especially those with previous experience with cancer and cancer treatment, may result from having exhausted other treatment options or the belief that the negative effects of treatment are better than choosing no treatment at all (Chan et al., 2016; Koedoot et al., 2003). Many patients believe they need cancer treatment until they are told no other viable options are available (Harrington & Smith, 2008). This is a critical point given that patients may continue with cancer treatment that offers no benefit and causes more adverse effects than the cancer itself near the end of life (Chan et al., 2016).

Patients striving for survival rely on their past experiences with medication (Koedoot et al., 2003) to guide their beliefs about newly prescribed medications. Patients may believe their cancer medication is beneficial and purposeful to delay disease progression or relieve symptoms caused by cancer illness because they have experienced the advantages of other cancer treatments. However, OAs are frequently associated with adverse events (Spoelstra et al., 2013; Tipton, 2015), which necessitates dosing modifications including cancer medication stoppages (Chan et al., 2016). For example, in both OA clinical trials and oncology settings, treatment-related adverse events often result in discontinuing the cancer medication (Clarke et al., 2015; Rizvi et al., 2015; Rosenberg et al., 2016).

Research examining medication beliefs among patients with advanced cancer receiving OAs is not well described. The current research is limited to earlier stage breast cancer patients receiving adjuvant endocrine or hormone therapy (Arriola et al., 2014; Bender et a., 2014; Corter et al., 2013; Heisig et al., 2017; Salgado et al., 2017). Patients with advanced cancer are willing to accept adverse events in exchange for even small benefits of cancer treatment (Balmer et al., 2001; Grunfeld et al., 2006; Harrington & Smith, 2008; Matsuyama et al., 2006; Silvestri, et al., 1998). However, when adverse events are determined to be a greater risk to health and therefore outweigh the benefit of palliative treatment, oncologists often order a permanent stoppage of the cancer medication (Chen et al., 2016). Such decisions to permanently stop cancer medication can initiate end of life care, including hospice (Chen et al., 2016). It is not known how patients' medication beliefs are affected by physician-directed stoppages once they are told the medication, often ordered as a last treatment resort, is no longer effective or is causing more harm than benefit in the case of adverse events. Such knowledge could assist oncology

professionals to discuss medication beliefs among patients with advanced cancer and support timely end of life planning.

Conceptual Framework

This study is guided by the Conceptual Model of Medication Beliefs among Advanced Stage Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018) (see Figure 4.1). The derived conceptual model was developed to explain and describe medication beliefs among patients with advanced cancers receiving OAs. The model highlights antecedents to medication beliefs, including past experiences with physical, cognitive and emotional health, illness, and medications. Once the new oral agent is prescribed, medication beliefs are activated. Medication beliefs are comprised of both positive and negative components. Positive and negative components of medication beliefs are independent of one another, but individuals can hold both beliefs at the same time.

Positive medication beliefs represent that medication provides the benefit of improved health or the ability to maintain health. Negative medication beliefs represent concern for taking the OA medication, such as adverse events. Patients experience various treatment-related events along the OA treatment trajectory including symptoms (severity and interference), adverse events, permanent physician-directed stoppages, depressive symptoms, and decreased cognitive effectiveness. Several model relationships are depicted. Adverse events often result in permanent physician-directed stoppages (Atkinson et al., 2017; Clarke et al., 2015; Di Maio et al., 2016). Such treatment-related events are appraised by the patient and either reinforce and/or change medication beliefs over time. For example, when a patient experiences adverse events and then consequently has their OA medication permanently stopped, they are likely to develop more negative medications beliefs. Positive medication beliefs can weaken if the stoppage of OA

medication indicates the treatment is no longer benefiting their health. Negative medication beliefs are conceptualized as more vulnerable to change in response to treatment-related events across the OA treatment trajectory. Whereas, the positive component of medication beliefs is not as vulnerable to change associated with treatment related assaults (symptoms, adverse events). However, the positive component of medication beliefs can be influenced if the OA is found to no longer be of benefit to improve or maintain health.

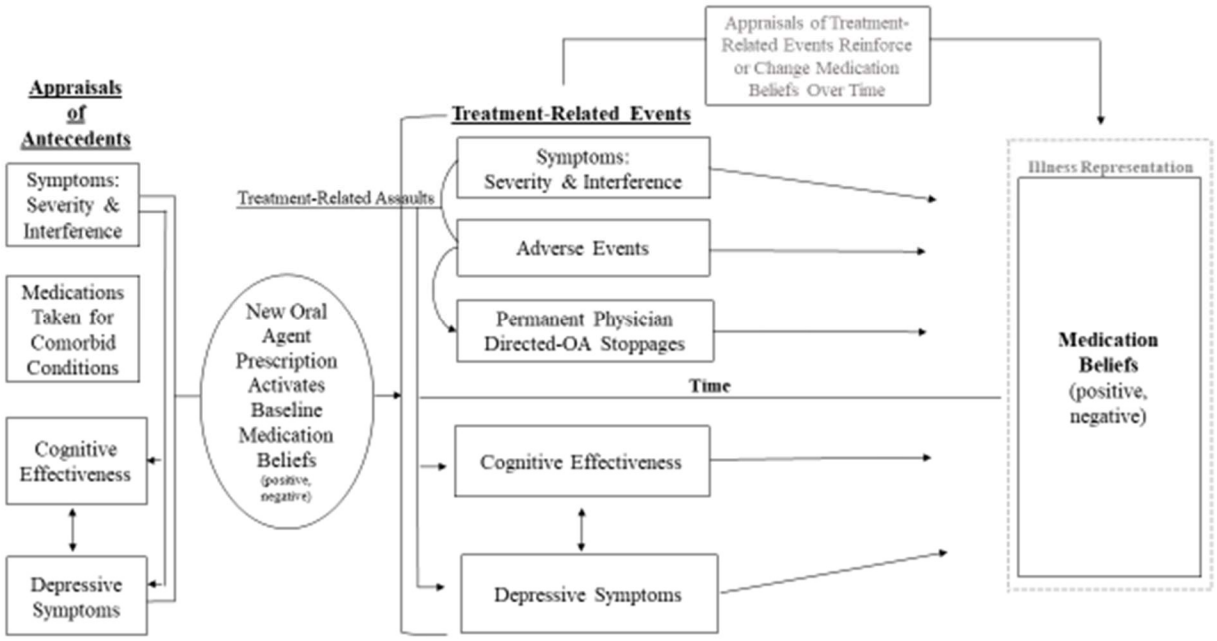

Figure 4.1 The Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). *This model is derived from Extended Common-Sense Model of Self-Regulation. Horne, R. (2003). Derived components from the ECSM that are redefined or modified are highlighted in gray.*

Purpose & Aims

The purpose of this study is to examine select constructs of the Conceptual Model of Medication Beliefs among Advanced Cancer Patients Receiving Oral Oncolytic Agents (Marshall, Lehto, Given, Given, & Sikorskii, 2018). The specific aims of the study include: 1) to explore the relationship of documented adverse events on positive and negative components of medication beliefs at week 12 since the initiation of a new oral oncolytic agent and; 2) to explore

the effect that permanent physician-directed oral oncolytic agent stoppages have on the positive and negative component of medication beliefs.

Methods

Design

This study is a secondary analysis of data from a National Cancer Institute, randomized controlled trial, *Improving Adherence to Oral Cancer Agents and Self Care of Symptoms Using an IVR (1R01CA162401-O1A1*). The parent study tested an intervention to promote symptom management and adherence to OA medication over a 12-week time period after initiating a new OA medication (Given & Given, 2013-2017). Patients were randomized into two groups; experimental or control after the baseline interview using a minimization approach to allocate patients in regard to recruitment location, cancer site, continuous versus intermittent OA dosing, and depressive symptomatology.

Trained personnel interviewed patients via telephone at baseline, 4, 8, and 12 weeks. Baseline interviews were completed within one week of initiating a new OA medication. Control group and experimental groups received weekly interactive voice response calls assessing adherence and symptom management for 8 weeks. Patients in the experimental group received additional daily telephone OA adherence reminders according to their prescribed OA dosing regimen for 4 weeks and an evidence-based symptom management toolkit. Patients in the experimental group were referred to the symptom management toolkit during the first 8 weeks if symptoms were reported as ≥ 4 on a 1-9 rating sale; higher ratings signified more severe symptoms.

The Symptom Management Toolkit provided information on commonly experienced symptoms among cancer patient receiving cancer treatment and strategies to prevent or manage

symptoms in the home environment (Given, Given, & Majeske, 2013). After 8 weeks, adherence and symptom assessment for both trial arms were evaluated for sustainability over the remainder of the study period.

Sample/Setting

Institutional Review Boards (IRB) reviewed and approved the parent study for ethical treatment and protection of human subjects. A secondary analyses of the parent study was approved by the authors' respective university IRB. Personnel trained on the parent study's protocol recruited patients from eight different Midwestern United States cancer centers who met the following criteria: 1) received a new prescription for one of 28 Food and Drug Administration (FDA) approved OAs (see Appendix A); 2) 21 years of age or older; 3) cognitively intact; 4) English speaking; 5) able/willing to complete phone calls and; 6) obtained an Eastern Cooperative Oncology Group performance score of 0–2 (Oken et al., 1982) or a Karnofsky score ≥50 (Karnofsky, 1949), both presented in Appendix B.

Variables & Measures

Patient demographic and cancer/treatment characteristics. Patient demographic, cancer, and cancer treatment characteristics (Table 4.2) were collected during enrollment and at baseline interviews of the parent study. Specific variables included age, sex, race, ethnicity, education, cancer type, cancer stage, cancer recurrence, cancer OA medication information (medication dosing a continuous versus intermittent and drug classification), and whether the patient was receiving concurrent intravenous chemotherapy or radiation (Table 4.2). These variables will be used in this study for purpose of describing the sample (Appendix C). Patients who had intermittent dosing schedules had planned rest periods in which the medication was stopped and then reintroduced after a pre-specified time (e.g. cycling). Continuous dosing refers

to constant dosing patterns without rest periods. Drug classification was organized into four categories including cytotoxics, kinase inhibitors, sex hormone inhibitors, and other. Study group assignment indicated whether patients were in the control group or intervention group as previously described.

Beliefs about medicine questionnaire-specific. Medication beliefs are defined as an individual's perception regarding the benefits and concerns of treatment with medication that arise from cognitive representations of illness. Medication beliefs were measured using the Beliefs about Medicine-Specific (BMQ). The BMQ was developed by Horne and colleagues to quantify medication beliefs about medication prescribed for specific illness using a 10-item questionnaire evaluating cognitive representations reflecting common perceptions about medication (Horne, Weinman, & Hankins, 1999). Medication belief items were rated on a 5-point Likert scale (1 = *strongly disagree* to 5 = *strongly agree*). The BMQ scale in the parent study was adapted to reflect beliefs specific to OA medication. An additional item was also added to the BMQ of the parent study to represent beliefs about unpleasant side effects, which have been well documented in the literature (Appendix D).

Psychometric testing of the original BMQ-Specific revealed two subscales; *Necessity* represents positive medication beliefs that indicate the beneficial nature of taking medication and *Concern* represents negative medication beliefs such as a distrust in medication. The BMQ *Necessity* subscale items include; 1) *My life would be impossible without my oral cancer medications* 2) *Without my oral cancer medications I would be very ill 3) My health, at present, depends on my oral cancer medications* 4) *My oral cancer medications protect me from becoming worse* and 5) *My health in the future will depend on my oral cancer medications*. The BMQ *Concerns* subscales include items; 1) *I sometimes worry about the long-term effects of my*

oral cancer medications 2) *Having to take my oral cancer medications worries me* 3*) I sometimes worry about becoming too dependent on my oral cancer medications* 4) *My oral cancer medications disrupt my life* and 5) *My oral cancer medications are a mystery to me*. The parent study added one item to the Concern subscale; *My oral cancer medications give me unpleasant side effects.*

Responses in the parent study consisted of a five-point Likert scale and were reversed to present a more positive connotation. Responses ranged from 1 (*strongly agree)* to 5 (*strongly disagree)*. Individual item scores of each *Necessity* and *Concerns* subscales were averaged, with total subscale scores ranging from 5 to 25. However, due to an additional item be placed in the Concern subscale for the parent study, the potential total subscale score on the Concern subscale in the current study is 6-30. Item responses will be reversed coded during analyses, to indicate that higher BMQ scores signify stronger beliefs on a continuous scale. For this study, each of the BMQ subscale scores were calculated at 12 weeks by averaging the subscales' corresponding BMQ item scores. The BMQ subscale scores is used as dependent variables to evaluate the relationship that documented adverse events and permanent physician-directed stoppages have on medication beliefs at 12 weeks since initiating a new oral oncolytic agent.

Reliability and validity of the BMQ have been reported among studies examining patients with various chronic conditions using numerous types of medication (Horne et al., 1999; LaPointe et al., 2010; Mahler et al., 2006). Initial instrument internal consistency reliability testing was completed by obtaining Cronbach alpha values (α) for the two BMQ subscales among six different illness groups, yielding acceptable limits ranging from 0.74-0.86 on the *Necessity* subscale and 0.73-0.80 on the *Concerns* subscale among asthmatic, diabetic, and cardiac patients (Horne et al., 1999). The renal sample, which had the lowest sample size (n =

47) yielded an internal consistency reliability of 0.55 for the *Necessity* subscale and 0.73 for the *Concerns* subscale. The general/medical sample revealed an internal consistency reliability of 0.86 for *Necessity* and 0.65 for the *Concerns* subscale and for the psychiatric group 0.74 for *Necessity* and 0.63 for *Concerns*. Original instrument test-retest reliability revealed significant correlations for *Necessity* (0.77) and *Concerns* (0.76). In this study, the 12-week BMQ subscales had a respectable internal consistency reliability of 0.87 for *Necessity* and 0.74 for *Concerns.*

Initial criterion validity during instrument development was evaluated by assessing correlations and expected relationships among the BMQ-Specific *Necessity* and *Concerns* subscales and other valid measures such as the Illness Perception Questionnaire (Weinman, Petrie, Moss-Morris, & Horne, 1996) and the Sensitive-Soma Scale (Diefenbach, Leventhal, & Leventhal, 1996). Discriminant validity has been established by assessing the ability of the instrument to discriminate between patients in different illness groups (Horne et al., 1999). Construct validity was confirmed with use of Principal Component Analysis and Confirmatory Factor Analysis to validate the BMQ two-factor structure (Horne et al., 1999).

Adverse events. Adverse events are defined by the National Cancer Institute as "any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure" (US Department of Health and Human Services, 2009, pg. 2). Due to the criticism raised regarding the bias and reporting of symptoms included in the CTCAE as previously mentioned, only eight objectively measured, clinically evident adverse events documented in the medical record audit from the parent study have been chosen for this study and are listed in Table 4.1. Adverse events included in the study are anemia, bleeding/hemorrhage, confusion/hallucination, dehydration, febrile neutropenia,

neutropenia without fever, hyperglycemia, and thrombocytopenia. Including only the objectively measured or clinically assessed adverse events provides important clinical and diagnostic information such as laboratory findings (e.g. fever, hemoglobin/hematocrit, platelet counts, and white blood cell counts) that the patient may not be able to identify. In addition, to prevent overlap with potential patient symptoms, the selected eight adverse events were chosen because they are not identified as symptoms.

Adverse events were documented in the parent study via medical record audit using the Common Terminology Criteria for Adverse Events (CTCAE) at the end of the study and were coded as either "adverse event present" or "adverse event absent" (Appendix E). Next, a total number of adverse events captured over the 12 weeks were calculated, ranging from 0-8. Although the CTCAE offers a grading of the severity of each adverse event, these grading measures can be quite inconsistent across oncology health professionals. In addition, there were missing data from the parent study in which oncology professionals did not grade the adverse event. Thus, the decision was made to include adverse events in a dichotomous variable as either "present" or "absent" and use the total score of adverse events (range of 0-8) over the 12-week study period. Total number of adverse events are used to examine their relationship on positive and negative medication beliefs at 12 weeks since the initiation of a new OA.

Table 4.1
Adverse Events Collected from the Medical Record Audit

Anemia	Febrile Neutropenia
Bleeding/Hemorrhage	Neutropenia without fever
Confusion/Hallucinations	Hyperglycemia
Dehydration	Thrombocytopenia

Medications taken for comorbid conditions. The number of comorbid conditions requiring medication including but not limited to heart disease, hypertension, emphysema/chronic lung disease, asthma, kidney disease, diabetes, depression, arthritis, and anemia were confirmed using medical record audit (Appendix F). It was expected that total number of chronic conditions requiring medication would be related to medication beliefs based on prior research (Aikens & Piette, 2009; Schüz et al., 2011). Thus, this variable was controlled for during the analyses of the independent variables of positive and negative OA medication beliefs at 12 weeks.

Permanent physician-directed medication stoppages. Permanent OA medication stoppages were verified by medical record audit in the parent study. Some patients were prescribed more than one OA medication during the study. Therefore, permanent physician-directed medication stoppages were defined as at least one cancer treatment OA medication included in the study's outlined protocol (see Appendix G) being stopped by the physician with no intent to restart the medication. OA stoppages were measured within the designated 4-week time period between data collection points (baseline, 4, 8, and 12 weeks) and only one stoppage per study participant is recorded for the secondary analyses. Permanent stoppages were divided into a binary variable indicating "yes" for an OA stoppage (as defined above) or "no" if the patient did not experience a physician-directed OA stoppage at any time over the 12-week parent study period. Permanent physician-directed OA stoppages are used to compare medication beliefs as measured by the BMQ at 12 weeks among those experiencing a permanent physician-directed OA stoppage (group "yes") and those study participants not experiencing a permanent physician-directed OA stoppage (group "no") over the first 12 weeks since initiating a new OA. Only those patients who completed the BMQ at 12 weeks after having experienced a physician-

directed stoppage were used for the analysis and identified as a limitation in the study due to low sample sizes.

Data Management

Data a from the parent study were acquired by trained interviewers, entered into a secure database and stripped of all identifiers prior to any secondary data analyses. No outliers were present and therefore patients cannot be identified based on outlying values.

Scales were scored per established instrument manual guidelines. Data for the secondary data analyses were stored in electronic format on a password protected database maintained by the College of Nursing at Michigan State University and archived according to university policy.

Data Analyses

Statistical analyses were performed in SPSS. Descriptive statistics summarized the distributions of age, sex, race, ethnicity, level of education, site of cancer, and cancer medication characteristics (see Table 4.2). Distributions of the 12-week interview BMQ subscales scores (outcome variables) and explanatory variables including selected adverse events and physician-directed oral oncolytic stoppages were evaluated (Table 4.3).

Aim 1 Analyses

Aim 1 analyses explored the relationship between adverse events and the positive and negative components of medication beliefs. Select documented adverse events according to the National Cancer Institute Common Toxicity Criteria scale (version 4) were extracted via oncology medical record documentation (Table 4.1). A regression analysis evaluated the relationship of the total number of adverse events with each of the BMQ subscales (dependent variables) at the 12-week interview, adjusting for baseline BMQ (Table 4.4). Demographic (age, sex, race, ethnicity, and education) and cancer/oral agent medication characteristics (cancer type,

cancer stage, cancer recurrence, continuous OA dosing versus intermittent OA dosing, drug classification, whether the patient was receiving concurrent intravenous chemotherapy or radiation), and the number of chronic conditions requiring medication were also adjusted for (Table 4.5).

Aim 2 Analyses

Aim 2 analyses explored the relationship that permanent physician-directed oral oncolytic agent stoppages had on the positive and negative component of medication beliefs at 12 weeks after initiation of a new oral agent by exploring whether those experiencing a permanent physician-direct OA stoppage hold different medication beliefs after a medication stoppage compared to those with no medication stoppage. For study participants completing the BMQ after a documented permanent physician-directed OA stoppage, a t-test determined differences in positive and negative components of medication beliefs between those who had permanent OA stoppages and those who did not. This unadjusted analysis was followed by the adjusted analysis, in which positive and negative components of medications beliefs at week 12 were related to medication beliefs at baseline, demographic (age, sex, race, ethnicity, and education) and cancer/oral agent medication characteristics (cancer type, cancer stage, cancer recurrence, continuous OA dosing versus intermittent OA dosing, drug classification, and whether the patient was receiving concurrent intravenous chemotherapy or radiation), and permanent physician-directed oral agent stoppage (Table 4.5).

Results

The sample size for those completing the BMQ at 12 weeks was 164 and a complete list of patient demographic and cancer/cancer treatment characteristics is listed in Table 4.2. The sample consisted of 47% (N = 77) males and 53% (N = 87) females. The mean age was 62.60

(SD 10.46). The sample was predominantly Caucasian (88%, N = 144). Over 70% (N = 118) of the study sample had an education level beyond high school. Fifteen different cancer types were represented (Table 4.2). Breast cancer was most prevalent (25.6%, N = 42) followed by GI cancers (22.6%, N = 37) and prostate cancer (12.2%, N = 20). A majority of the sample had stage IV cancer (72%, N = 118). Three main oral oncolytic agents were represented including cytotoxics (33%, N = 55), kinase inhibitors (46%, N = 75) and sex hormones (12%, N = 19). Treatment dosing of OA medications was evenly represented; continuous (49%, N = 81) and intermittent dosing (51%, N = 83). Patients had on average 3.51 (SD 2.08) comorbid conditions requiring medications.

Descriptive statistics for the BMQ are provided in Table 4.3. The distribution of the 12-week BMQ was normally distributed for both Necessity and Concern subscales. The mean Necessity score was 3.81 (SD .85) and the mean score for Concerns was 2.52 (SD.74). Reliabilities were computed using Cronbach's alpha. The 12-week BMQ Necessity revealed a Cronbach's alpha of 0.86 and was 0.74 for Concerns (Table 4.3). There was a weak negative correlation between the two BMQ subscales.

The relationship of adverse events and medication beliefs exhibited a nonlinear pattern. A total number of eight adverse events were included in the study. Patients experienced between 0-5 adverse events, with 34% (N = 56) of patients experiencing zero, 30% (N = 49) experiencing one, 20% (N = 32) experiencing two, and 12% (N = 19) experiencing three or more adverse events (Table 4.3). Due to the distribution and nonlinear pattern of adverse events, their number was categorized as zero, one, two, and three or more adverse events (Table 4.4).

Aim one of the study was to explore the relationship of adverse events on positive and negative components of medication beliefs at 12 weeks since the initiation of a new OA. Results

of the regression analyses between adverse events and BMQ revealed that significant differences in Necessity (positive) beliefs exist between the patients experiencing varying levels of adverse events in the unadjusted (Table 4.4) and adjusted models (Table 4.5). Chi square tests were completed to explore the relationship of covariates in the adjusted model with adverse events and no significant results were noted. Those experiencing zero (B = 0.50, SE = 0.21, p = .02), one (B = 0.70, SE = 0.21, p = .01) and two (B = 0.82, SE = 0.23, p < .01) adverse events have significantly higher Necessity (positive) beliefs compared to those experiencing three or more reported adverse events (Table 4.5), which indicate that once patients experience three or more adverse events, their Necessity (positive) beliefs decline significantly.

Medication Concern (negative) beliefs were not associated with the number of adverse events experienced in either the unadjusted (Table 4.4) and adjusted models (Table 4.5). In the adjusted analysis, those with stage four cancers had significantly lower Concerns (negative) beliefs (B = -0.39, SE = 0.13, P < .01) compared to those with lower stage cancers and those who had cancers that were not staged (Table 4.5).

Aim two of the study explored whether patients who experience a permanent physician-directed stoppage differ in their medication beliefs compared to those who have not experienced a permanent physician-directed OA stoppage. Results of the independent t- tests showed that those completing the BMQ after a permanent OA stoppage had significantly lower mean Necessity (positive) beliefs compared to who had no permanent stoppage over the 12-week study period (Table 4.6). The adjusted analysis revealed similar significant results and showed those with stage four cancers had significantly less concerns than those with lower stage cancers and those who had not had their cancers staged (data not shown). None of the patients who

experienced a permanent physician-directed stoppage were documented to have entered hospice. Reasons for permanent physician-directed stoppages are provided in Table 4.7.

Discussion

Participants in this study had a significant decline in Necessity (positive) beliefs when they experienced 3 or more adverse events. A total of eight adverse events were examined. Patients experienced between 0-5 adverse events over the course of the 12-week study. A majority of participants had only 0-2 reported adverse events and this could have been due to the relatively limited time on the oral oncolytic agent. Patients may have also experienced temporary stoppages or dose reductions of the oral oncolytic agents that could have resulted in a decreased number of reported adverse events. However, temporary OA stoppages and dose reductions were not analyzed in this study. The relationship of a significant decline of Necessity (positive) beliefs for those experiencing 3 or more adverse events is line with advanced stage cancer patients striving for survival despite experiencing adverse effects of medication and the assumption that experiencing such adverse events could weaken Necessity (positive) beliefs per the conceptual model. There may be a threshold of adverse events that patients are willing to accept before Necessity (positive) beliefs decline. In this sample, that threshold was significant at 3 or more adverse events. A significant decrease in Necessity (positive) beliefs once experiencing 3 or more adverse events could also be a result of conversations the patients had with their oncologist to discuss the possibility that the medication is causing more harm than benefit.

Medication Concern (negative) beliefs were not associated with adverse events at any level. Although this may seem initially surprising, it is important to keep in mind that objectively measured adverse events were selected to be reviewed in this study. According to the conceptual model, adverse events would be expected to influence and potentially strengthen Concern

(negative) beliefs, however in the study design we chose to include only objective measures of adverse events. Therefore, patients may not perceive the adverse events as a concern, unless this adverse event resulted in the experience of a symptom and recognized by the patient as being related to the adverse event. Patients may or may not have been aware of or been able to identify adverse events and therefore Concern (negative) beliefs were not influenced. For example, patients do not perceive objectively measured adverse events such as thrombocytopenia as measured in this study. They must be told by the oncology professional that such adverse event, measured via laboratory testing, is present. Prior research using patient-reported symptoms would be expected to influence Concern (negative) beliefs because symptoms are perceived and appraised by the patient (Basch et al., 2014). Results underscore the importance of including patient reported (PRO) symptomatic adverse events in conjunction with the CTCAE (Basch et al., 2014) and supports the criticisms of the original CTCAE to appropriately measure and capture symptomatic toxicities (DiMaio et al., 2015). In the adjusted models we found that Concern (negative) beliefs were significantly lower for those with stage four cancers compared to lower stage cancer and those who had cancers that were not staged. This has been previously supported in the literature and may have also contributed to the relationship between adverse events and Concern beliefs as patients are attempting to strive for survival no matter the cost of experiencing adverse events (Balmer et al., 2011; Can et al., 2016; Gruneld et al., 2006; Harrington & Smith, 2008; Matsuyama et al., 2006; Silvestri et al., 1998). Patients striving for survival are willing to accept adverse events and toxicities even for little benefit of sustaining life and may be more focused on the benefit of treatment, thus Concern beliefs were not impacted (Balmer et al., 2011).

There was a significant decline in Necessity (positive) beliefs for patients who experienced a permanent physician-directed OA stoppage. Conceptually, positive medication beliefs refer to providing some benefit to the patient such as a relief in cancer symptoms or delayed disease progression. For those who experienced a stoppage, the oncologist may have decided that the benefit was no longer apparent by evidence of adverse events or disease progression despite treatment. These findings have implications regarding the discussions surrounding end of life planning and the initiation of hospice. Eliciting patient's beliefs about their oral cancer medication may reveal that they no longer see the medication as a benefiting their health and this would be an opportunity to discontinue cancer treatment and initiate timelier end of life planning and hospice care.

Patients receiving OAs are starting new cancer treatments closer to the end of life (Earle et al., 2004; Harrington & Smith, 2008; Matsuyama et al., 2006; National Cancer Institute, 2017). Patients taking OAs may also be receiving their cancer treatment closer to death than those receiving traditional forms of cancer therapy (Pirl et al., 2015) and are not as likely to enter hospice (Chan et al., 2016). Patients' decision to continue cancer treatment near the end of life may result from having exhausted other treatment options or the belief that the negative effects of treatment are better than choosing no treatment at all (Chan et al., 2016; Koedoot et al., 2003).

Assessing and addressing medication beliefs among patients with advanced stage cancers receiving OAs could prevent treating patients with expensive, toxic medications that can cause a number of adverse events near the end of life without providing the patient any benefit. If oncologists evaluate and address patient's medication beliefs this can open up conversations regarding whether the cost of treatment outweighs the benefits. Many patients with advanced cancer will believe in the need to continue treatment until they are told by their oncologist that

they have exhausted options with current treatment (Harrington & Smith, 2008). Discussion of patient's medication beliefs can help oncology professionals initiate conservations about end of life planning and hospice can be initiated sooner.

Permanent physician-directed stoppages were not associated with Concern (negative) beliefs. This could be a consequence of patients who stopped the medication having relief of adverse events or symptoms that was driving the permanent stoppage. Patients who were no longer taking their OA may not have perceived further concern for their medication and did not perceive any long-term effects from their medication.

Implications for Nursing Practice and Research

Nurses are able to use the BMQ to assess and address patient's medication beliefs in the clinical setting. The BMQ is a reliable instrument that can be administered and scored in an efficient manner during patients' clinical visits. Nurses should elicit medication beliefs when adverse events arise and when permanent stoppages occur, which could assist in the initiation of end of life care planning earlier.

More research is needed using larger and more diverse study samples to explore the relationship of adverse events and permanent physician-directed OA stoppages on medication beliefs. Nurses should advocate for the use of patient-reported outcomes as more objective measures such as the CTCAE cannot fully capture a patient's symptomatic toxicities (Basch et al., 2014). More research involving medication beliefs could inform oncology interventions that may create policy changes on how patients with advanced cancers initiating new oral oncolytic medications are screened prior to and throughout their treatment. Screening medication beliefs can also serve to address more ethical issues regarding how long patients remain on OAs despite minimal benefit.

Limitations

The study assessed medication beliefs at 12 weeks since initiating a new oral oncolytic agent. This time period is relatively short considering the chronic nature of cancer and treatment with oral agents. The study was cross sectional in nature and does not capture potential changes in relationships with regards to adverse events and permanent stoppages on medication beliefs as they occur. The sample was almost entirely Caucasian, non-Hispanic or Latino, which limits the generalizability of findings to other ethnic and racial backgrounds.

The sample size of patients completing the BMQ at 12 weeks after experiencing a permanent physician-directed was restricted to 15 patients. There were two explanations for this limitation. The first is that per study protocol, patients who were no longer taking their OA due to physician stoppage were not required to complete the full study interview at each data collection point and were offered a shortened interview that did not include completing the BMQ. Secondly, many patients who had a permanent OA stoppage also attrited and therefore did not complete the 12-week interview.

In addition, only 8 adverse events were examined to explore their relationship with medication beliefs. The objectively measured results may have limited the ability to detect relationships with a wide array of adverse events that are typical among individuals with advanced stage cancer who are receiving oral agents. We did not include grade of the adverse events for two reasons. First grading can be potentially bias and there was missing data from the parent study in which some adverse events were not graded by oncology professionals. Finally, temporary stoppages and dose reductions were not included to assess the potential influence on adverse events, which may have limited our ability to explain why patients experienced fewer adverse events.

Conclusion

Tracking adverse events is an important tool for oncologists in order to make treatment-related decisions (Atkinson et al., 2017; Di Maio et al., 2016, Trott et al., 2007), however it is important that patient reported measures are also included to adequately capture patient's perceptions of these potential symptomatic toxicities. Adverse events can impact a patient's Necessity (positive) beliefs once a specific threshold in these events is reached. However, the pathway in which patients recognize adverse events may rely on discussions with oncology professionals in which these toxicities are reviewed with the patient. Necessity (positive) beliefs significantly decline once the OA is permanently stopped which can open up discussions regarding end of life planning and initiation of hospice care. Concern (negative) beliefs were not associated with objectively measured adverse events or permanent stoppages among individuals with advanced stage cancer receiving oral oncolytic agents. Ultimately, adverse events and permanent stoppages influence Necessity (positive) beliefs but are not associated with Concern (negative) beliefs. Patients must receive communication from the oncology professional and appraise the new information before medication beliefs are influenced, which is in contrast to the symptom experience in which patients perceive physical or emotional disturbances. Nurses can easily elicit and address medication beliefs in the clinical setting.

Table 4.2.

Descriptive Statistics of Demographics, Cancer, and Cancer Treatment Characteristics of Patients Completing 12-week BMQ

N = 164

Characteristic	**N (%)**
Sex	
Male	77 (47)
Female	87 (53)
Race	
Caucasian	144 (88)
Other	20 (12)
Ethnicity	
Hispanic or Latino	2 (1)
Not Hispanic or Latino	162 (99)
Education Level Completed	
High school or less	45 (28)
Some college or completed college	89 (54)
Graduate or professional degree	29 (18)
Missing	1
Group Assignment	
Experimental	86 (52)
Control	78 (48)
	Mean (SD)
Age	62.60 (10.46)
Number of comorbid conditions treated with medications	3.51 (2.08)
Cancer/Cancer Treatment Characteristic	**N (%)**
Site of cancer	
Breast	42 (25.6)
GI (Colorectal, Esophageal, Pancreatic)	37 (22.6)
Leukemia/Lymphoma	16 (9.8)
Liver	4 (2.4)
Lung	9 (5.5)
Melanoma	6 (3.7)
Myeloma	4 (2.4)
Prostate	20 (12.2)
Renal	16 (9.8)
Sarcoma	7 (4.3)
Brain	1 (0.6)
Other	2 (1.1)
Stage of Cancer	
I-III/Unknown	46 (28)
IV	118 (72)
Recurrent Cancer	
Yes	69 (42)
No	83 (51)
Unknown/Missing	11 (7)
Cancer Treatment Dosing	
Continuous	81 (49)
Intermittent	83 (51)

Table 4.2 (cont'd)

Cancer/Cancer Treatment Characteristic	N (%)
Cytotoxics	55 (33)
Kinase Inhibitors	75 (46)
Sex Hormone Inhibitors	19 (12)
Other	15 (9)
Concurrent Treatment	
Intravenous Chemotherapy	38 (23)
Radiation	5 (3)

Table 4.3

Descriptive Statistics for Dependent & Independent Variables & Reliabilities for 12 Week BMQ Subscales

N = 163

Characteristic	**12 Week Mean (SD)**
Dependent Variables	
BMQ-*Necessity*	3.81 (0.85)
BMQ-*Concerns*	2.52 (0.74)
BMQ Necessity Reliabilities	**Cronbach's Alpha (α)**
12 Weeks	0.86
BMQ Concern Reliabilities	**Cronbach's Alpha (α)**
12 Weeks	0.74
BMQ Necessity & Concern Subscale Correlations	**Inter-Scale Correlations**
12 Weeks	-0.12
Independent Variables	**N (%) Adverse Events at 12 Week Medical Record Audit**
Total Number of Adverse Events Reported over 12 Weeks	
0 adverse event documented	56 (34)
1 documented adverse events	49 (30)
2 documented adverse event	32 (20)
3+ documented adverse events	19 (12)
Missing	7 (4)
Permanent Physician-Directed Stoppage	**N (%)**
Yes	15 (9)
No	148 (91)
Missing	1

*BMQ = Beliefs about Medicines Questionnaire

Table 4.4

Regression Analysis Depicting Relationship of Adverse Events on BMQ Subscales at 12 Weeks Adjusting for baseline Necessity Beliefs

	BMQ Necessity at 12 weeks Parameter Estimates				**BMQ Concerns at 12 weeks Parameter Estimates**			
Predictor variable	**coefficient**	**Std. Error**	**t**	**p**	**coefficient**	**Std. Error**	**t**	**p**
Adverse Events (AE)								
0 AE	0.50	0.21	2.40	0.02	0.00	0.18	0.02	0.98
1 AE	0.70	0.21	3.27	<0.01	0.00	0.18	0.01	0.99
2 AE	0.82	0.23	3.58	<0.01	-0.25	0.19	-1.28	0.10
3+ AE (ref.)								
Baseline Medication Beliefs Necessity/Concerns	0.02	0.09	0.23	0.82	-0.09	0.09	-1.03	0.30

*BMQ = Beliefs about Medicine Questionnaire

Table 4.5

Adjusted Regression Analysis Depicting Relationship of Adverse Events on BMQ Subscales at 12 Weeks

	BMQ *Necessity* at 12 Weeks Parameter Estimates				**BMQ Concerns at 12 Weeks Parameter Estimates**			
Predictor Variables	**B**	**Std. Error**	**t**	**P**	**B**	**Std. Error**	**t**	**P**
Adverse Events (AE)								
0 AE	0.50	0.21	2.35	0.02	0.20	0.19	1.04	0.30
1 AE	0.70	0.21	3.26	<0.01	0.32	0.19	1.60	0.11
2 AE	0.82	0.23	3.45	<0.01	0.37	0.21	1.77	0.08
3+ AE (ref.)								
Baseline BMQ	0.02	0.09	0.23	0.82	-0.04	0.09	-0.47	0.64
Number of medications Taken for Comorbid Conditions	-0.04	0.03	-1.19	0.24	0.05	0.03	1.60	0.11
Education								
High school or less	0.27	0.21	1.31	0.19	0.16	0.18	0.91	0.36
Some college or graduated from college	0.26	0.18	1.40	0.17	0.09	0.16	0.57	0.57
Graduate school (ref)								
Cancer Stage								
Stage IV	0.20	0.15	1.35	0.18	-0.39	0.13	-2.9	<0.01
Stage I-III/Other (ref)								
Sex								
Male	-0.01	0.13	-0.11	0.92	0.22	0.12	1.87	0.06
Female (ref)								

Table 4.6

Differences in 12 Week BMQ Subscale among Patients Who Experience a Permanent Physician-Direct Oral Oncolytic Stoppage versus Patients with No Permanent Physician-Directed Stoppage

	BMQ Necessity					BMQ Concerns				
	t	**df**	**p**	**Mean Diff**	**Std. Error Diff**	**t**	**df**	**p**	**Mean Diff**	**Std. Error Diff**
Permanent Physician OA Stoppage	2.30	15.15	0.04	0.74	0.32	0.29	15.69	0.78	0.07	0.25
	Necessity					**Concerns**				
Stoppage	N = 15		Mean/(SD) = 3.15 (1.22)			Mean/(SD) = 2.46 (.94)				
No stoppage	N = 148		Mean/(SD) = 3.89 (.77)			Mean/(SD) = 2.53 (.72)				

*BMQ = Beliefs about Medicines Questionnaire

Table 4.7

Reasons for Permanent Physician-Directed Oral Oncolytic Stoppages

Reasons for Permanent Physician-Directed Oral Oncolytic Stoppages
Pulmonary problems
Cardiovascular problems
Anemia
Arthralgia/Myalgia
Neutropenia
Disease Progression/No response to treatment
Blood pressure control
Peripheral neuropathy
Drug changed
Hand foot reaction

APPENDICES

APPENDIX A: FDA Approved Oral Agents Included in the Parent Study

Table 4.8

FDA Approved Oral Agents Included in the Parent Study

Oral Oncolytic Agents Organized Alphabetically by Trade Name	
Afinitor (Everolimus)	Stivarga (Regorafenib)
Bosulif (Bosutinib)	Sutent (Sunitinib)
Gilotrif (Afatinib)	Tafinlar (Dabrafenib)
Gleevec (Imatinib)	Tarceva (Erlotinib)
Ibrance (Palbociclib)	Tasigna (Nilotinib)
Imbruvica (Ibrutinib)	Temodar (Temozolomide)
Inlyta (Axitinib)	Tykerb (Lapatinib)
Lenvima (Lenvatinib)	Votrient (Pazopanib)
Lonsurf (Tipiracil & Trifluridine)	Xalkori (Crizotinib)
Lynparza (Olaparib)	Xeloda (Capecitabine)
Nexavar (Sorafenib)	Xtandi (Enzalutamide)
Pomalyst (Pomalidomide)	Zydelig (Idelalisib)
Revlimid (Lenalidomide)	Zykadia (Ceritinib)
Sprycel (Dasatinib)	Zytiga (Abiraterone acetate)

APPENDIX B: Eastern Cooperative Oncology Group Scale of Performance Status & Karnofsky Status Performance Scale

Table 4.9

Eastern Cooperative Oncology Group Scale of Performance Status & Karnofsky Status Performance Scale

WHO/ECOG Grade	WHO/ECOG Activity	Karnofsky Grade	Karnofsky Activity
0	Fully active, able to carry on all normal activities without restriction	100%	Normal no complaints; no evidence of disease
		90%	Able to carry on normal activity; minor signs or symptoms of disease
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80%	Normal activity with effort; some sign or symptoms of disease
		70%	Cares for self; unable to carry on normal activity or do active work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours	60%	Requires occasional assistance, but is able to care for most personal needs
		50%	Requires considerable assistance and frequent medical care
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours	40%	Disabled; requires special care and assistance
		30%	Severely disabled; hospitalization admission is indicated, although death not imminent
4	Completely disabled. Cannot carry on any self-care, totally confined to bed or chair.	20%	Very sick; hospital admission necessary; active support treatment is necessary
		10%	Moribund; fatal processes progressing rapidly
5	Dead	0%	Dead

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T., & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology*, *5*(6), 649-656.

Karnofsky, D. A. (1949). The clinical evaluation of chemotherapeutic agents in cancer. *Evaluation of Chemotherapeutic Agents*. In MacLeod CM (Ed), Evaluation of Chemotherapeutic Agents, Columbia University Press, New York.

APPENDIX C: Screening/Baseline Data Collection Tools for Cancer/Cancer Demographic and Treatment Characteristics

What is your highest level of education completed?

- No formal education
- Completed grade school
- Completed some high school
- Completed high school
- Completed some college or technical college or associate degree
- Completed college
- Completed graduate/professional degree (post baccalaureate degree)
- Refused

What is your current marital status?

- Never married
- Married
- Divorced/Separated
- Widowed
- Living together
- Refused

What is your ethnic background?

- Hispanic or Latino
- Not Hispanic or Latino
- Unknown
- Refused

What is your race or ethnic background?

- American Indian or Alaskan Native
- African American or Black
- Asian
- Native Hawaiian or Pacific Islander
- White
- More than one race
- Unknown
- Refused

Screening Eligibility Form from Parent Study
(Collecting patient and disease characteristics)

Gender:

- Male
- Female

Ethnicity:

- Hispanic/Latino
- Not Hispanic/Latino

Race (check all that apply):

- American Indian/Alaska Native
- Asian
- Native Hawaiian/Pacific Islander
- Black/African American
- White

Cancer Site:

- Breast
- Colorectal
- Gastrointestinal
- Leukemia
- Liver
- Lung
- Lymphoma
- Melanoma
- Myeloma
- Pancreatic
- Prostate
- Renal
- Sarcoma

Stage:

- I
- II
- III
- IV
- Other

If 'Other' write in stage: _____

On Concurrent IV chemotherapy?:

- Yes
- No
- If yes, medication and frequency:_____
-

On Concurrent Radiation?

- Yes
- No
- If yes, treatment name and frequency: _____

Patient Eligibility:

- Yes
- No
-

(If NO to ANY of the questions below, patient is NOT eligible)

Can hear on telephone?

- Yes
- No

Can read and understand English?

- Yes
- No

21 or older?

- Yes
- No
- Age:_____

ECOG Performance status within 0-2 or Karnofsky performance status within 50-100?

- Yes
- No
- Score:_____

Has a land line/cell phone with touch pad numbers?

- Yes
- No

Is on an eligible oral cancer medications?

- Yes
- No

Date Screened: _____

Recruiter Initials: _____

Eligibility:

- Eligible
- Ineligible

Enrollment Status:

- Consented
- Refused
- Lost to follow-up

Reason, if refused:

- Too ill
- Too busy
- Lack of interest
- Other

APPENDIX D: Adapted Beliefs about Medicine Questionnaire

Table 4.10

Adapted Beliefs about Medicine Questionnaire

	Strongly Agree 1	Agree 2	Uncertain 3	Disagree 4	Strongly Disagree 5	Refused 6
My health, at present, depends on my oral cancer medications.						
Having to take my oral cancer medications worries me.						
My life would be impossible without my oral cancer medications.						
Without my oral cancer medications I would be very ill.						
I sometimes worry about the long-term effects of my oral cancer medication.						
My oral cancer medications are a mystery to me.						
My oral cancer medications give me unpleasant side effects.						
My health in the future will depend on my oral cancer medications.						
My oral cancer medications disrupt my life.						
I sometimes worry about becoming too dependent on my oral cancer medications.						
My oral cancer medications protect me from becoming worse.						

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, *14*(1), 1-24.

Table 4.11
Adverse Event Reporting: Medical Record Audit

Complete Table 2

PATIENT COMPLICATIONS, TOXICITY AND SIDE EFFECTS (C/SE) DURING CURRENT ORAL AGENT AUDIT TREATMENT PERIOD

Table 2 is a summary from the NCI toxicity criteria that you may use for all complications and side effects (C/SE). Please date the C/SE.
For all C/SE, please check and estimate toxicity if it is not stated explicitly then make grade not known (check box Grade Unknown).

PLEASE CHECK GRADE AT MOST SEVERE LEVEL AND DATE WHEN IT OCCURRED.

Table 2: Patient Complications, Symptoms, Toxicity and Side Effects (C/SE) During Current Oral Agent Treatment Period

PLEASE CHECK THE APPROPRIATE GRADE							
Adverse Effect/Complication	**Documented in chart? Yes / No**	**Date Noted in Chart**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade Unknown** *Check if not known*
1. Anemia			☐10.0/gdl or higher; 100g/L	☐8.0-10.0/gdl; <100-80 g/L	☐6.5-7.9/gdl; <80-65 g/L	☐<6.5/gdl; <65 g/L	☐
2. Anorexia			☐Loss of appetite without alteration in eating	☐Oral intake altered without weight loss or malnutrition; oral nutrition supplement	☐Weight loss or malnutrition (e.g., inadequate oral caloric or fluid intake); IV fluids or TPN	☐Life-threatening consequences	☐
3. Arthralgias/ Myalgias			☐Mild pain with inflammation	☐Moderate or severe, transient pain with swelling and inflammation	☐Severe, unrelenting pain with joint suffering; interfere with ADL	☐Immobility, unable to move	☐
4. Bleeding/Hemorrhage			☐Mild without transfusion; few symptoms <Male 4.7 – 6.1 million per MCL (write in levels) <Female 4.2 – 5.4 million per MCL (write in levels)	☐Symptomatic loss of 1 liter of blood	☐Transfusion indicated; 2 liters of blood	☐Catastrophic bleeding, major blood replacement	☐
5. Confusion/Hallucination			☐Mild disorientation or mild hallucinations / Perceptual distortions	☐Moderate disorientation limiting ADL / Moderate hallucinations	☐Severe disorientation limiting self care & safety / Severe & frequent hallucinations	☐Life threatening, totally unmanageable, threats of harm to self or others / Threats due to hallucinations, needs hospitalization	☐
6. Constipation			☐Mild	☐Moderate	☐Severe	☐Ileus> 96hrs	☐
7. Cough			☐Dry hacking	☐Dry cough, treatment needed	☐Unrelenting, interferes with sleep and ADL	☐Severe continuous wet cough	☐

Table 4.11 (cont'd)

Patient ID _____

Table 2: Patient Complications, Symptoms, Toxicity and Side Effects (C/SE) During Current Oral Agent Treatment Period

PLEASE CHECK THE APPROPRIATE GRADE							
Adverse Effect/Complication	**Documented in chart? Yes / No**	**Date Noted in Chart**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade Unknown** *Check if not known*
8. Dehydration			☐↑ Oral fluids indicated; dry mucous membrane; ↓ skin turgor	☐IV fluids indicated <24 hours	☐IV fluids indicated ≥24 hours	☐Life-threatening consequences (e.g., hemodynamic collapse)	☐
9. Diarrhea			☐↑ of 2-3 stools /d over pre-Rx	☐↑ of 4-6 stools/d moderate cramping nocturnal stools	☐↑ of 7-9 stools/d severe cramping incontinence	☐↑ of >10 stools/d parenteral support grossly bloody stools	☐
10. Dyspnea (shortness of breath)			☐Dyspnea on exertion, can walk 1 flight of stairs without stopping	☐Dyspnea on exertion unable to walk 1 flight of stairs or 1 city block (0.1 km) without stopping	☐Dyspnea with ADL	☐Dyspnea at rest; intubation/ventilator indicated	☐
11. Edema; limb, facial			☐5-10% inter-limb discrepancy in volume or circumference visible difference; swelling; pitting edema	☐>10-30% inter-limb discrepancy in volume or circumference apparent obstruction of anatomic structure; obliteration of skin folds	☐>30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL	☐Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling	☐
12. Fatigue (asthenia, lethargy, malaise)			☐Mild fatigue over baseline	☐Causing difficulty performing ADL	☐Severe fatigue interfering with ADL	☐Disabling	☐
13. Febrile Neutropenia (ANC <1.0x109/L, fever >38.5°C)			☐38.0 – >39.0°C (100.4 – 102.2°F) with neutropenia	☐39.0 – >40.0°C (102.3 – 104.0°F) with neutropenia	☐ ≤40.0°C (≤104.0°F) for ≤24 hours with neutropenia	☐Life-threatening (e.g., septic shock, hypotension, acidosis) ≤40.0°C (≤104.0°F) for >24 hrs with hypotension	☐
14. Fever without Neutropenia			☐38.0 – >39.0°C (100.4 – 102.2°F)	☐39.0 – >40.0°C (102.3 – 104.0°F)	☐ ≤40.0°C (≤104.0°F) for ≤ 24 hours	☐ ≤104°F for 24 hours with shock like symptoms	☐
15. Hand and Foot Skin Reaction			☐Skin changes; no pain	☐Skin changes with pain; no functional interference; peeling, blisters	☐Skin changes interfering with function; pain, ulcers, edema	☐Disability due to function interference and pain	☐

Table 4.11 (cont'd)

Patient ID _____

Table 2: Patient Complications, Symptoms, Toxicity and Side Effects (C/SE) During Current Oral Agent Treatment Period

PLEASE CHECK THE APPROPRIATE GRADE							
Adverse Effect/Complication	**Documented in Chart? Yes / No**	**Date Noted in Chart**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade Unknown** *Check if not known*
16. Hyperglycemia			☐ 160 mg/dL; 8.9 mmol/L	☐> 160-250 mg/dL; >8.9 – 12.9 mmol/L	☐> 250-500 mg/dL; 13.9 – 27.8 mmol/L; hospitalization indicated	☐> 500 mg/dL; >27.8 mmol/L; life-threatening consequences	☐
17. Insomnia (difficulty sleeping)			☐Occasional, not interfering with function	☐Interferes with function but not with ADL	☐Frequent, interfering with ADL	☐Disabling	☐
18. Memory impairment/ Cognitive Changes			☐Not interfering with function	☐Interferes with function, but not interfering with ADL	☐Interfering with ADL	☐Amnesia	☐
19. Mucositis / Stomatitis			☐Erythema, painless ulcers, mild soreness	☐Painful erythema, edema, ulcers can eat	☐Painful erythema, edema, ulcers	☐Parenteral or enteral support	☐
20. Nausea			☐Able to eat but lack of appetite	☐About to eat, diminished intake	☐Unable to eat, 0 intake, inadequate fluids, dehydration, weight loss	☐Life threatening	☐
21. Pain			☐Mild, not interfering with function	☐Moderate, interfering with function, but not interfering with ADL	☐Severe, interfering with ADL	☐Disabling	☐
22. Platelets (PLT) (x 1000/mm3)			☐<75.0x10^9/L <75000/mm^3	☐≥50.0-<74.9x10^9/L ≥50000-<75000/mm^3	☐≥25.0-<50x10^9/L ≥10000-≤20000/mm^3	☐<10.0x10^9/L-<25.0x10^9/L <10000/mm^3	☐
23. Pruritus			☐Mild or localized	☐Intense, widespread, little to no discomfort	☐Widespread with discomfort	☐Widespread, open and weeping discomfort	☐
24. Skin/Macular/Rash			☐Scattered macular or popular rash or erythema that is asymptomatic	☐Scattered macular or papular rash or erythema with pruritus or other symptoms	☐Generalized symptomatic macular, popular, or vesicular rash	☐Exfoliative or ulcerating dermatitis	☐
25. Vomiting			☐1 episode in 24 hours	☐2-5 episodes in 24 hours; IV fluids indicated <24 hours	☐≥6 episodes in 24 hours; IV fluids, or TPN indicated ≥24 hours	☐Life-threatening consequences	☐

APPENDIX F: Comorbid Conditions Requiring Medication: Medical Record Audit

PRESCRIBED MEDICATIONS OTHER THAN CHEMO OR ORAL CANCER MEDICATIONS

Please list all medications (other than chemotherapy agents listed in Table 1) that were prescribed during the audit period, as well as medications that the patient was on for comorbid conditions during the audit period.

Table 4.12
Comorbid Conditions Requiring Medication: Medical Record Audit

NAME OF DRUG	**DATE PRESCRIBED** ***IF DURING THE AUDIT PERIOD***

APPENDIX G

Permanent Stoppages Measured Via Medical Record Audit

Table 4.13

Permanent Oral Agent Stoppages: Medical Record Audit

Patient ID _____

Table 1: Cancer Protocols and Drugs during Audit Period: PROTOCOL 1

Name of Drug(s) in Protocol 1 (Injection, Infusion, Patch)	Date Prescribed	Dose or Injection (mg per pill or mg/ml)	No. Pills/Day or Injections, Infusions or Patches	Continuous Dosing	Start on Cycle Day	No. of Days On in a Cycle	Number of Days Off in a Cycle	Drug Ongoing	Discontinuation Permanent (P) or Temporary (T) & Date(s)	If stopped (changed), Why? (choose Reason Number below)
Drug 1 (Protocol 1):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 1	___/___/___			**Yes / No**				**Yes / No**		
Drug 2 (Protocol 1):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 2	___/___/___			**Yes / No**				**Yes / No**		
Drug 3 (Protocol 1):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 3	___/___/___			**Yes / No**				**Yes / No**		

Use this table to determine the **Reason Number** to complete the final column 'If Stopped, changed or discontinued...' above. Write in all that apply

#	Reason	#	Reason	#	Reason - Delay of Drugs / Stoppage
1	Anemia	12	Dyspnea (Shortness of Breath)	23	Peripheral Neuropathy
2	Anorexia	13	Edema, Limb	24	Pruritus / Skin Problem / Rash
3	Arthralgias/Myalgias	14	Fatigue (Asthenia, Lethargy, Malaise)	25	Pulmonary problems
4	Bleeding/Hemorrhage	15	Febrile Neutropenia	26	Renal Failure
5	Cardiac Problems	16	Fever without Neutropenia	27	Thrombocytopenia (low platelets)
6	Completed prescribed protocol	17	Insomnia (Difficulty Sleeping)	28	Protocol completed
7	Constipation	18	Mucositis (Stomatitis)	29	Patient decision to stop treatment
8	Cost of Medication	19	Nausea and or vomiting	30	Patient entered hospice (date) ___/___/___
9	Cough	20	Neutropenia	31	**Disease progression—no response to therapy**
10	Deep Vein Thrombosis	21	Pain	32	Drug was changed
11	Diarrhea	22	Pericardial Effusion	33	Other *please write in* _____

Table 4.13 (cont'd)

Patient ID _____

Table 1: Cancer Protocols and Drugs during Audit Period: PROTOCOL 2

Name of Drug(s) in Protocol 2 (Injection, Infusion, Patch)	Date Prescribed	Dose or Injection (mg per pill or mg/ml)	No. Pills/Day or Injections, Infusions or Patches	Continuous Dosing	Start on Cycle Day	No. of Days On in a Cycle	Number of Days Off in a Cycle	Drug Ongoing	Discontinuation Permanent (P) or Temporary (T) & Date(s)	If stopped (changed), Why? (choose Reason Number below)
Drug 1 (Protocol 2):	___/___/___			Yes / No *(Circle one)*				Yes / No *(Circle one)*	P or T (date stopped) (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 1	___/___/___			Yes / No				Yes / No		
Drug 2 (Protocol 2):	___/___/___			Yes / No *(Circle one)*				Yes / No *(Circle one)*	P or T (date stopped) (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 2	___/___/___			Yes / No				Yes / No		
Drug 3 (Protocol 2):	___/___/___			Yes / No *(Circle one)*				Yes / No *(Circle one)*	P or T (date stopped) (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 3	___/___/___			Yes / No				Yes / No		

Use this table to determine the **Reason Number** to complete the final column 'If Stopped, changed or discontinued...' above. Write in all that apply

#	Reason	#	Reason	#	Reason - Delay of Drugs / Stoppage
1	Anemia	12	Dyspnea (Shortness of Breath)	23	Peripheral Neuropathy
2	Anorexia	13	Edema, Limb	24	Pruritus / Skin Problem / Rash
3	Arthralgias/Myalgias	14	Fatigue (Asthenia, Lethargy, Malaise)	25	Pulmonary problems
4	Bleeding/Hemorrhage	15	Febrile Neutropenia	26	Renal Failure
5	Cardiac Problems	16	Fever without Neutropenia	27	Thrombocytopenia (low platelets)
6	Completed prescribed protocol	17	Insomnia (Difficulty Sleeping)	28	Protocol completed
7	Constipation	18	Mucositis (Stomatitis)	29	Patient decision to stop treatment
8	Cost of Medication	19	Nausea and or vomiting	30	Patient entered hospice (date) ___/___/___
9	Cough	20	Neutropenia	31	Disease progression—no response to therapy
10	Deep Vein Thrombosis	21	Pain	32	Drug was changed
11	Diarrhea	22	Pericardial Effusion	33	Other *please write in* _____

Table 4.13 (cont'd)

Patient ID _____

Table 1: Cancer Protocols and Drugs during Audit Period: PROTOCOL 3

Name of Drug(s) in Protocol 3 (Injection, Infusion, Patch)	Date Prescribed	Dose or Injection (mg per pill or mg/ml)	No. Pills/Day or Injections, Infusions or Patches	Continuous Dosing	Start on Cycle Day	No. of Days On in a Cycle	Number of Days Off in a Cycle	Drug Ongoing	Discontinuation Permanent (P) or Temporary (T) & Date(s)	If stopped (changed), Why? (choose Reason Number below)
Drug 1 (Protocol 3):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 1	___/___/___			**Yes / No**				**Yes / No**		
Drug 2 (Protocol 3):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 2	___/___/___			**Yes / No**				**Yes / No**		
Drug 3 (Protocol 3):	___/___/___			**Yes / No** *(Circle one)*				**Yes / No** *(Circle one)*	**P or T (date stopped)** (circle one) ___/___/___ Date restart if T ___/___/___ If intermittent circle one: Cycle continued; Cycle reset from restart date	
Dose Change Drug 3	___/___/___			**Yes / No**				**Yes / No**		

Use this table to determine the **Reason Number** to complete the final column 'If Stopped, changed or discontinued...' above. Write in all that apply

#	Reason	#	Reason	#	Reason - Delay of Drugs / Stoppage
1	Anemia	12	Dyspnea (Shortness of Breath)	23	Peripheral Neuropathy
2	Anorexia	13	Edema, Limb	24	Pruritus / Skin Problem / Rash
3	Arthralgias/Myalgias	14	Fatigue (Asthenia, Lethargy, Malaise)	25	Pulmonary problems
4	Bleeding/Hemorrhage	15	Febrile Neutropenia	26	Renal Failure
5	Cardiac Problems	16	Fever without Neutropenia	27	Thrombocytopenia (low platelets)
6	Completed prescribed protocol	17	Insomnia (Difficulty Sleeping)	28	Protocol completed
7	Constipation	18	Mucositis (Stomatitis)	29	Patient decision to stop treatment
8	Cost of Medication	19	Nausea and or vomiting	30	Patient entered hospice (date) ___/___/___
9	Cough	20	Neutropenia	31	**Disease progression—no response to therapy**
10	Deep Vein Thrombosis	21	Pain	32	Drug was changed
11	Diarrhea	22	Pericardial Effusion	33	Other *please write in* _____

REFERENCES

REFERENCES

Aikens, J. E., & Piette, J. D. (2009). Diabetic patients' medication underuse, illness outcomes, and beliefs about antihyperglycemic and antihypertensive treatments. *Diabetes Care*, *32*(1), 19-24. doi:10.2337/dc08-1533.

Arriola, K. R. J., Mason, T. A., Bannon, K. A., Holmes, C., Powell, C. L., Horne, K., & O'Regan, R. (2014). Modifiable risk factors for adherence to adjuvant endocrine therapy among breast cancer patients. *Patient Education and Counseling*, *95*(1), 98-103.

Atkinson, T. M., Hay, J. L., Shoushtari, A., Li, Y., Paucar, D. J., Smith, S. C., ... & Milhem, M. M. (2017). Relationship between physician-adjudicated adverse events and patient-reported health-related quality of life in a phase II clinical trial (NCT01143402) of patients with metastatic uveal melanoma. *Journal of Cancer Research and Clinical Oncology*, *143*(3), 439-445.

Balmer, C. E., Thomas, P., & Osborne, R. J. (2001). Who wants second-line, palliative chemotherapy?. *Psycho-Oncology*, *10*(5), 410-418.

Basch, E. (2010). The missing voice of patients in drug-safety reporting. *New England Journal of Medicine*, *362*(10), 865-869.

Basch, E., Jia, X., Heller, G., Barz, A., Sit, L., Fruscione, M., ... & Culkin, A. (2009). Adverse symptom event reporting by patients vs clinicians: Relationships with clinical outcomes. *JNCI: Journal of the National Cancer Institute*, 101(23), 1624-1632.

Basch, E., Reeve, B. B., Mitchell, S. A., Clauser, S. B., Minasian, L. M., Dueck, A. C., ... & Bruner, D. W. (2014). Development of the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). *Journal of the National Cancer Institute*, *106*(9), dju244.

Bender, C. M., Gentry, A. L., Brufsky, A. M., Casillo, F. E., Cohen, S. M., Dailey, M. M., ... & Sereika, S. M. (2014, May). Influence of patient and treatment factors on adherence to adjuvant endocrine therapy in breast cancer. *Oncology Nursing Forum 41*(3), 274-285.

Chan, W. L., Lam, K. O., Siu, W. K., & Yuen, K. K. (2016). Chemotherapy at end-of-life: An integration of oncology and palliative team. *Supportive Care in Cancer*, *24*(3), 1421-1427.

Cimprich B. (1992). Attentional fatigue following breast cancer surgery. *Research in Nursing & Health*, *15*:199–207. doi: 10.1002/nur.4770150306.

Cimprich, B., So, H., Ronis, D. L., & Trask, C. (2005). Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psycho-Oncology*, *14*(1), 70-78.

Cimprich, B., Visovatti, M., & Ronis, D. L. (2011). The Attentional Function Index—a self-report cognitive measure. *Psycho-Oncology*, *20*(2), 194-202.

Clarke, G., Johnston, S., Corrie, P., Kuhn, I., & Barclay, S. (2015). Withdrawal of anticancer therapy in advanced disease: A systematic literature review. *BMC Cancer*, *15*(1), 892-900.

Corter, A. L., Findlay, M., Broom, R., Porter, D., & Petrie, K. J. (2013). Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology*, *18*(1), 168-181.

Diefenbach, M., Leventhal, H., and Leventhal, E.A. (1996) The Sensitive Soma Scale. Unpublished.

Di Maio, M., Basch, E., Bryce, J., & Perrone, F. (2016). Patient-reported outcomes in the evaluation of toxicity of anticancer treatments. *Nature Reviews Clinical Oncology*, *13*(5), 319-325.

Ding, P. N., Lord, S. J., Gebski, V., Links, M., Bray, V., Gralla, R. J., ... & Lee, C. K. (2017). Risk of Treatment-Related Toxicities from EGFR Tyrosine Kinase Inhibitors: A Meta-analysis of Clinical Trials of Gefitinib, Erlotinib, and Afatinib in Advanced EGFR-Mutated Non–Small Cell Lung Cancer. *Journal of Thoracic Oncology*, *12*(4), 633-643.

Earle, C. C., Neville, B. A., Landrum, M. B., Ayanian, J. Z., Block, S. D., & Weeks, J. C. (2004). Trends in the aggressiveness of cancer care near the end of life. *Journal of Clinical Oncology*, 22(2), 315-321.

Given, B.A., & Given, C.W. (2013–2017). *Improving adherence to oral cancer agents and self-care of symptoms using an IVR (1R01CA162401-O1A1)*. [National Cancer Institute clinical trial]. Retrieved from https://clinicaltrials.gov/ct2/show/NCT02043184.

Given, B.A., Given, C.W., Majeske, C. (2013). Medication Management & Symptom Management Toolkit. East Lansing, MI. Michigan State University.

Grunfeld, E. A., Maher, E. J., Browne, S., Ward, P., Young, T., Vivat, B., ... & Richards, M. A. (2006). Advanced breast cancer patients' perceptions of decision making for palliative chemotherapy. *Journal of Clinical Oncology*, *24*(7), 1090-1098.

Harrington, S. E., & Smith, T. J. (2008). The role of chemotherapy at the end of life: "When is enough, enough?". *Journal of the American Medical Association*, *299*(22), 2667-2678.

Heisig, S. R., Shedden-Mora, M. C., Blanckenburg, P., Rief, W., Witzel, I., Albert, U. S., & Nestoriuc, Y. (2016). What do women with breast cancer expect from their treatment? Correlates of negative treatment expectations about endocrine therapy. *Psycho-Oncology*, *25*(12), 1485-1492.

Horne, R. (2003). Treatment perceptions and self-regulation. In The self-regulation of health and illness behavior. In L. D. Cameron, & H. Leventhal (Eds.), *The self-regulation of health and illness behavior* (pp. 138–153). New York, NY: Routledge.

Horne, R., & Weinman, J. (1999). Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal of Psychosomatic Research*, *47*(6), 555-567.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health, 14*(1), 1–24. doi:10.1080/08870449908407311.

Jansen DA. (2006). Attentional demands and daily functioning among community-dwelling elders. *Journal of Community Health Nursing*, *23* (1), 1–13. doi: 10.1207/s15327655jchn2301_1.

Karnofsky, D. A. (1949). The clinical evaluation of chemotherapeutic agents in cancer. Evaluation of Chemotherapeutic Agents. In C. M. MacLeod (Ed.), *Evaluation of Chemotherapeutic Agents*. New York, NY: Columbia University Press.

Koedoot, C. G., De Haan, R. J., Stiggelbout, A. M., Stalmeier, P. F. M., De Graeff, A., Bakker, P. J. M., & de Haes, J. C. J. M. (2003). Palliative chemotherapy or best supportive care? A prospective study explaining patients' treatment preference and choice. *British Journal of Cancer*, *89*(12), 2219.

Krebber, A. M. H., Buffart, L. M., Kleijn, G., Riepma, I. C., Bree, R., Leemans, C. R., ... & Verdonck-de Leeuw, I. M. (2014). Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology*, *23*(2), 121-130.

LaPointe, N. M. A., Ou, F. S., Calvert, S. B., Melloni, C., Stafford, J. A., Harding, T., ... & Peterson, E. D. (2010). Changes in beliefs about medications during long-term care for ischemic heart disease. *American Heart Journal*, *159*(4), 561-569. doi:10.1016/j.ahj.2009.12.025

Mahler, C., Hermann, K., Horne, R., Jank, S., Haefeli, W. E., & Szecsenyi, J. (2012). Patients' beliefs about medicines in a primary care setting in Germany. *Journal of Evaluation in Clinical Practice*, *18*(2), 409-413. doi: 10.1111/j.1365-2753.2010.01589.x.

Marshall, V., Lehto, R., Given, C.W., Given, B., Sikorskii, A. (2018). Conceptualization of medication beliefs among advanced cancer patients receiving oral oncolytic agents using a theory derivation approach. *Unpublished doctoral dissertation, Michigan State University, East Lansing Michigan*.

Matsuyama, R., Reddy, S., & Smith, T. J. (2006). Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *Journal of Clinical Oncology*, *24*(21), 3490-3496.

Mohammed, S., Peter, E., Gastaldo, D., & Howell, D. (2016). The "Conflicted Dying": The active search for life extension in advanced cancer through biomedical treatment. *Qualitative Health Research*, *26*(4), 555-567.

Müller-Schwefe, G., Ahlbeck, K., Aldington, D., Alon, E., Coaccioli, S., Coluzzi, F., ... & Kress, H. G. (2014). Pain in the cancer patient: Different pain characteristics CHANGE pharmacological treatment requirements. *Current Medical Research and Opinion*, *30*(9), 1895-1908.

National Cancer Institute. Quality of End-of-Life Care in Patients with Advanced Cancer. (2017). www.cancer.gov/about-cancer/advanced-cancer/planning/end-of-life-hp-pdq#link/_14_toc. Accessed October 12, 2017.

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T., & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology, 5*(6), 649–655. doi:10.1097/00000421-198212000-00014.

Pirl, W. F., Greer, J. A., Irwin, K., Lennes, I. T., Jackson, V. A., Park, E. R., ... & Temel, J. S. (2015). Processes of Discontinuing Chemotherapy for Metastatic Non–Small-Cell Lung Cancer at the End of Life. *Journal of Oncology Practice*, *11*(3), 405-412.

Rizvi, N. A., Mazières, J., Planchard, D., Stinchcombe, T. E., Dy, G. K., Antonia, S. J., ... & Otterson, G. A. (2015). Activity and safety of nivolumab, an anti-PD-1 immune checkpoint inhibitor, for patients with advanced, refractory squamous non-small-cell lung cancer (CheckMate 063): A phase 2, single-arm trial. *The Lancet Oncology*, *16*(3), 257-265.

Rosenberg, J. E., Hoffman-Censits, J., Powles, T., Van Der Heijden, M. S., Balar, A. V., Necchi, A., ... & Srinivas, S. (2016). Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: A single-arm, multicentre, phase 2 trial. *The Lancet*, *387*(10031), 1909-1920.

Salgado, T. M., Davis, E. J., Farris, K. B., Fawaz, S., Batra, P., & Henry, N. L. (2017). Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment*, *163*(2), 311-319. doi: 10.1007/s10549-017-4177-9.

Schnipper, L. E., Lyman, G. H., Blayney, D. W., Hoverman, J. R., Raghavan, D., Wollins, D. S., & Schilsky, R. L. (2013). American Society of Clinical Oncology 2013 top five list in oncology. *Journal of Clinical Oncology*, *31*(34), 4362-4370.

Schüz, B., Wurm, S., Ziegelmann, J. P., Warner, L. M., Tesch-Römer, C., & Schwarzer, R. (2011). Changes in functional health, changes in medication beliefs, and medication adherence. *Health Psychology*, *30*(1), 31-39. doi:10.1037/a0021881.

Silvestri, G., Pritchard, R., & Welch, H. G. (1998). Preferences for chemotherapy in patients with advanced non-small cell lung cancer: Descriptive study based on scripted interviews. *British Medical Journal*, *317*(7161), 771-775.

Spoelstra, S. L., Given, B. A., Given, C. W., Grant, M., Sikorskii, A., You, M., & Decker, V. (2013). An intervention to improve adherence and management of symptoms for patients prescribed oral chemotherapy agents: An exploratory study. *Cancer Nursing*, *36*(1), 18-28.

Tipton, J. M. (2015). Overview of the challenges related to oral agents for cancer and their impact on adherence. *Clinical Journal of Oncology Nursing*, *19*(3), 37-40.

Trotti, A., Colevas, A. D., Setser, A., & Basch, E. (2007). Patient-reported outcomes and the evolution of adverse event reporting in oncology. *Journal of Clinical Oncology*, *25*(32), 5121-5127.

US Department of Health and Human Services. (2009). Common terminology criteria for adverse events (CTCAE) version 4.0. *National Institutes of Health, National Cancer Institute*, *4*(03). www.evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf. Accessed October 5, 2017.

Weinman, J., Petrie, K. J., Moss-Morris, R., & Horne, R. (1996). The illness perception questionnaire: A new method for assessing the cognitive representation of illness. *Psychology and Health*, *11*(3), 431-445. doi:10.1080/08870449608400270.

CHAPTER 5: CONCLUSION

The purpose of this dissertation was to examine how medication beliefs among advanced stage cancer patients receiving oral oncolytic agents (OAs) change over the first 12 weeks since initiating a new OA medication and determine what factors are associated with these changes. The three manuscripts address significant gaps in the literature. First, to address the lack of conceptual clarity surrounding medication beliefs, a derived conceptual model was developed. Next, derived model components were examined to determine how the separate positive and negative components of medication beliefs change over time among advanced cancer patients receiving OAs and variables associated with these changes. The effect that adverse events and permanent physician-directed medication stoppages of OAs have on medication beliefs was also examined. This chapter provides a summary of the three manuscripts and collaborative discussion regarding findings, interpretations, limitations and implications for future nursing practice, research and policy.

Manuscript one offers conceptual clarity regarding how medication beliefs are formed, how medication beliefs may change over time, and factors associated with changes in medication beliefs using a derived conceptual model. Manuscript two examined portions of the derived model including the effect of symptom severity and interference, depression, and cognitive effectiveness on medication beliefs over time. Finally, manuscript three explored the influence that adverse events and permanent physician-directed OA stoppages have on medication beliefs 12 weeks after initiating a new OA.

Overview of Manuscript One

Manuscript one advanced conceptual clarity of the phenomenon of medication beliefs among individuals with advanced cancer receiving OAs using a theory derivation approach. The need for a conceptual model explaining medication beliefs and how medication beliefs might

change over time for individuals with advanced stage cancer receiving OAs became evident after an extensive literature and integrative review process (Marshall & Given, 2018). Several gaps existed in research examining the phenomenon of medication beliefs among patients with cancer, including: 1) the cross sectional nature of studies investigating medication beliefs among cancer patients with limited reports of longitudinal studies explaining how medication beliefs change over time; 2) the limited research on medication beliefs among late-stage cancer patients receiving cancer treatment with current studies comprising of earlier stage cancers (Bender et al., 2014; Corter et al., 2013; Grunfeld et al., 2005); 3) the limited research describing potential changes in the positive and negative components of medication beliefs; 4) the unknown factors associated with potential changes in medication beliefs, such as the impact of treatment-related assaults and physician-directed medication stoppages; 5) the restricted number of studies examining medication beliefs of patients receiving OAs; and 6) the lack of conceptual framework that describes the phenomena of medication beliefs.

The use of the BMQ to elicit and quantify medication beliefs in the empirical literature was shown to further confuse the understanding of the relationship between the positive and negative components of medication beliefs by presenting these dimensions as having an inverse relationship. Positive and negative components of medication beliefs are distinct constructs and influenced by different factors, but individuals hold both positive and negative medication beliefs at the same time. The distinction between positive and negative components of medication beliefs is critical to understanding how the two components can change differently over time as they are influenced by different treatment-related factors. Positive medication beliefs represent beliefs that the patient will benefit from the medication (Horne, 2003). Positive medication beliefs among cancer patients are not associated with treatment-related assaults such

as symptoms (Heisig et al., 2017; Salgado et al., 2017). Thus, it is hypothesized that the positive medication beliefs are more stable over the 12-week cancer treatment trajectory in response to treatment-related assaults. However, positive medication beliefs can strengthen as patients confirm medication efficacy or weaken if a patient experiences a permanent physician-directed OA stoppage. Once the oncologist stops the medication, the medication can be appraised as having no further benefit for the patient's health.

Negative medication beliefs represent concern for taking OAs (Horne, 2003). Negative medication beliefs among cancer patients appear to be impacted by treatment-related assaults, such as symptoms and adverse events (Bhattacharya, Easthall, Willoughby, Small, & Watson, 2012; Salgado et al., 2017), which are common among patients receiving OAs (Tipton, 2015). Because of the experience of treatment-related events along the 12-week OA treatment trajectory, it was hypothesized that the negative medication beliefs are more vulnerable to change over time. In contrast, the positive medication beliefs are not impacted by OA treatment-related assaults, such as symptoms and adverse events, and therefore remain more stable until a permanent physician-directed OA stoppage occurs or medication efficacy is confirmed. The following manuscripts examine these relationships within the derived conceptual model using a sample of patients with advanced cancer receiving oral oncolytic agents.

Overview of Manuscript Two

Manuscript two focused on testing relationships among variables of a derived model presented in Manuscript one as a means to explain and describe medication beliefs among advanced stage cancer patients across the first 12 weeks after initiating a new oral oncolytic agent. The study included the longitudinal examination of medication beliefs over 12 weeks since initiation of a new oral oncolytic agent by adjusting for baseline medication beliefs and

using three data collection points at 4 weeks, 8 weeks and 12 weeks. First, positive and negative components of medication were evaluated for change over time. Next, the influence of summed symptom severity and interference indices on the positive and negative components of medication beliefs in independent models over time were investigated. An exploratory analysis was then performed to investigate the specific symptoms from CSEI that could be driving the effect found on Concern beliefs, using the six most prevalent patient-reported symptoms of fatigue, weakness, pain, loss of appetite, numbness and tingling, and sleep disturbance. Lastly, the distinct influence of depression and cognitive effectiveness on the positive and negative dimensions of medication beliefs over time and over and above the summed symptom severity and interference indices was examined.

Results from this study demonstrated Necessity (positive) beliefs strengthened from 4 to 12 weeks, mean difference 0.112, SE (0.055), $p = .04$. Increases in Necessity (positive) beliefs could be a result of cognitive reappraisals of the benefit of medication, which has been previously supported in the cancer literature (Jansen et al., 2005), but was not measured in the study. Baseline Necessity (positive) beliefs were significantly associated with Necessity (positive) beliefs ($B = 0.701$, $SE = 0.049$, $p < .01$) at 4, 8, and 12 weeks, which is consistent with the derived conceptual model beliefs. Higher levels of depressive symptoms were significantly associated with lower Necessity (positive) beliefs ($B = -0.012$, $SE = 0.004$, $p < .01$), although the mean depressive symptoms in the study were surprisingly low and may have been why no decline in Necessity beliefs across the three repeated measures was noted. Findings support that patients with depressive symptoms negatively impact perceptions and inhibit the ability to view the positive benefits of medication. Necessity (positive) beliefs were not associated with symptom severity or interference, which supports the hypothesis in the derived conceptual model

that Necessity (positive) beliefs remain stable with respect to symptoms compared to Concern (negative) beliefs. Results reflect that patients can experience the benefit of medication such as delayed disease progression, despite experiencing symptoms.

Changes in Concern (negative) beliefs over time were only apparent when symptom severity and interference indices were added to the LME model. An increase in Concern (negative) beliefs were significantly associated with symptom severity and interference, depressive symptoms, cognitive effectiveness, and the number of chronic conditions requiring medication, which was consistent with the literature review and hypotheses drawn from the derived conceptual model. Therefore, in line with previous research, the experience of symptoms leaves patients vulnerable to the development of negative medication beliefs about their cancer treatment (Bhattacharya et al., 2012; Salgado et al., 2017) over time and threatens the stability of existing medication beliefs. These negative beliefs may be reinforced as patients appraise the interruption that symptoms cause in their daily lives. In addition, patients with increased depressive symptoms and compromised cognitive effectiveness are vulnerable to developing increased Concern beliefs. Depressive negatively impact perceptions that result in bias towards the negative aspects of mediation, thus increasing negative medication beliefs. In this study, those with higher cognitive effectiveness had less Concern (negative) beliefs, perhaps because they were still able to direct attention towards inhibiting negative aspects of medication. Those with later stage cancers had significantly lower Concern beliefs compared to those with lower stage cancer and those with cancers that were not staged, which is consistent with other studies (Heisig et al., 2016). Patients with later staged cancers may be willing to accept the negative aspects of medication in exchange for the benefit of extended survival, thus resulting in lower Concern (negative) beliefs. In addition, patients with comorbid condition requiring medication

had higher Concern (negative) beliefs, which could indicate concerns for interaction among medications, the complexity of self-managing multiple medication regimens, or cost of the OA.

This study supports that Necessity (positive) beliefs are a more stable construct and not influenced by as many treatment related factors compared Concern (negative) beliefs. This study demonstrates the need for nurses to assess and address treatment related concerns such as symptoms, depressive symptoms, and compromised cognitive effectiveness, and polypharmacy as these factors can increase Concern (negative) beliefs, making patients vulnerable to nonadherence of the OA treatment.

Overview of Manuscript Three

Manuscript three concentrated on the relationships of objectively measured adverse events and permanent physician-directed OA stoppages on the positive and negative components of medication beliefs at 12 weeks since the initiation of a new OA. Patients completing the 12-week BMQ were included in the analyses. The relationship of adverse events and medication beliefs exhibited a nonlinear pattern. Patients in the study sample experienced between 0-5 adverse events. Adverse events experienced were not normally distributed. A number of patients experienced either zero (34%, N = 56), one (30%, N = 49) or two (20%, N = 32) adverse events, perhaps due to the relatively short time since initiating a new OA. Therefore, adverse events were categorized into four different groups; those experiencing zero, one, two, and three or more.

Results revealed those who experienced zero, one, and two adverse events had significantly higher Necessity (positive) beliefs compared to those experiencing three or more reported adverse events. Such findings indicate there may be a specific threshold of adverse events the patient is willing to experience before medication beliefs are influenced or may indicate medication beliefs are influenced after the physician discusses the potential for

medication interruption or permanent physician-directed stoppage as a result of multiple adverse events. Concern (negative) beliefs were not associated with objectively measured adverse events. included in the study. Unlike perceived symptoms, patients may not be aware of adverse events they are experiencing, such as neutropenia, and may need to rely on the oncologist to bring these adverse events to their attention. Thus, results do not necessarily conflict with the derived conceptual model that Concern (negative) beliefs are associated with treatment related assaults including adverse events. Future research should include adverse events as reported by PRO-CTCAE to better understand the relationship of adverse events as defined by the National Cancer Institute and Concern (negative) beliefs.

Patients experiencing a permanent OA stoppage had significantly lower mean Necessity (positive) beliefs compared to those who had no permanent stoppage over the 12-week study period. Important to note was that none of the patients who experienced a permanent physician-directed stoppage were documented to have entered hospice, which has implications for future nursing practice and research. Findings could suggest that patients are either not ready to discuss end of life care such as hospice even after an OA stoppage or oncologists are not initiating end of life conversations. While some patients experiencing a permanent physician-directed OA stoppage had a drug change and continued on another oral agent, others had disease progression or no response to treatment. At such point in a patient's cancer care, this would be an opportunity for nurses to intervene and implement end of life care planning with education and referral to palliative care and hospice. More research is needed to determine if interventions such as eliciting medication beliefs when the OA is stopped increases palliative care and/or hospice referrals. Initiation of timely palliative and hospice care has been reported to increase quality of life at the end of life (Parikh, Kirch, Smith, & Temel, 2013). Nurses should be aware that

patients experiencing changes to the OA regimen such as a permanent stoppage can be vulnerable to developing weakening Necessity beliefs.

Limitations

Limitations of the dissertation research include a largely Caucasian sample. Only 2% (N=5) Hispanic/Latino and 9% (N=25) represented races other than Caucasian. Medication beliefs are culturally-determined, and this research may represent a more Westernized view of medication beliefs in which medications are perceived to benefit the patient in some way and concerns are contextual and sensitive to factors such as symptoms. Another limitation is the developmental age of the sample, which had a mean age over 60 years. There was only a small representation of hematological cancers. Hematological cancers potentially yield a younger sample of patients receiving OAs (American Cancer Society, 2018). Younger patients may hold different beliefs compared to their older counterparts, although the literature is inconclusive (Bickell, Weidmann, Fei, Lin, & Leventhal, 2009; Bond, Hirota, Fortin, & Col, 2002; Salgado et al., 2017). In addition, over 70% of patients had stage four cancer. Results may not be generalized to more diverse racial and ethnic backgrounds, younger patients with cancer, or earlier stage cancers. This research has several implications that can be linked to patient outcomes such as adherence to OAs, however, adherence was not included the studies. First, the goal of the research was to examine medication beliefs as dependent variables and investigate the factors influencing mediation beliefs over the first 12 weeks of the treatment trajectory with OAs. Secondly, adherence in advanced stage cancer illness does not carry the same implications for adherence as for lower stage cancers or those receiving OAs with the intent to cure the cancer (e.g. select hematological cancers). This research does, however, have implications for utilizing medication beliefs to advance the science for quality of life at the end of life.

Nursing Implications

Nursing Practice

Oncology nurses can elicit medication beliefs in the clinical area using the BMQ, a convenient and reliable instrument. Assessing and addressing medication beliefs are important to determine potential areas where oncology nurses may need to intervene. Patients may not readily share concerns that they have regarding their OAs. Eliciting medication beliefs can help the patient realize their own perceptions about their medication and help them to initiate important discussions with oncology professionals. Discussions may include how well patients believe their medication is working or potential concerns they have regarding taking the OAs. In addition, results of measuring medication beliefs in the clinical setting can help nurses initiate conversations about patients' perceptions regarding their medication and may be the gateway to discussing patient care such as uncontrolled symptoms or end of life care and hospice. Nurses should also be aware of the factors that can increase medication Concern (negative) beliefs over time, such as symptom severity and interference, depression, decreased cognitive effectiveness, and polypharmacy. Such factors should be assessed over time. Nurses can then target these specific areas of Concern to improve medication beliefs and improve the chances of patient adherence to OAs.

Nursing Research

The research presented in this dissertation has limitations in the representation of patients with diverse racial and ethnic backgrounds. Future research with a more diverse sample is needed to generalize findings. Most patients in the study were diagnosed with stage four cancer. Patients with advanced stage cancer have been reported to have different medication beliefs

(Heisig et al., 2016). Therefore, future research should include the longitudinal examination of medication beliefs among individuals diagnosed with lower stage cancers.

This dissertation presents one of the first examinations of the longitudinal analyses of medication beliefs among patients receiving oral cancer therapy. In addition, constructs of a derived conceptual model describing the phenomenon of medication beliefs were examined and provided preliminary data regarding the factors associated with the positive and negative components of medication beliefs over time in patients receiving oral oncolytic agents. Now that preliminary investigation has been completed on the factors associated with medication beliefs in this population, future research including adherence measures are indicated. However, adherence may not be of importance for advanced stage cancer at the end of life and adherence may be more appropriate to explore among earlier stage cancers. Patients with advanced stage cancers are taking OAs with the intent to treat cancer in order to relieve symptoms of cancers or prolong life, but patients will not be cured. Patients with lower staged cancers and/or of whom have the ability to have their cancer cured, such as select hematological cancers, need to be adherent to the OA for the best patient outcomes. Therefore, adherence would be a viable outcome to monitor in those with lower stage cancers.

Questions that remain for future research are many. First, further research regarding the mechanism by which depressive symptoms impact medication beliefs are needed as the sample in this study had a very low mean of depressive symptoms. In addition, more research is needed to determine the relationship and potential mediating and moderating factors between depressive symptoms, symptom severity and interference, and medication beliefs.

Secondly, the relationship between cognitive effectiveness and medication beliefs in this stud were used by examining the AFI on a continuous scale. There have been established AFI cut

off values to determine low, moderate and high cognitive fatigue (low cognitive effectiveness), however, cutoff values are not established for the 13-item AFI scale that was used in this research. Understanding how medication beliefs may be influenced by differing levels of cognitive effectiveness may help nurses intervene and change the way in which educational material regarding the OA medication is provided. Potential research aims could focus on at what level of compromised cognitive effectiveness begin to influence the ability for patients to understand education regarding their diagnosis and medication and at what level of compromised cognitive effectives are medication beliefs vulnerable to change?

In Chapter 4, the Necessity (positive) beliefs of those experiencing zero, one, or two adverse events were significantly higher compared to those who experience three or more adverse events. Research is needed to determine if there are specific adverse events that are more influential on Necessity (positive) beliefs than others or if there is a specific amount of time that these adverse events are tolerated before medication beliefs are influenced. The full spectrum of adverse events experienced were also not included in the study because of the overlap with symptoms. Future research may benefit from using the PRO-CTCAE (Basch et al., 2014) to capture the effect of both patient-reported and physician-reported adverse events on medication beliefs over time instead at one time point that was used in this research.

It would be interesting to determine whether eliciting medication beliefs at each clinic visit would result in greater number of palliative care or hospice referrals for patients with advanced cancer. It would be expected that eliciting medication beliefs would increase discussions regarding the benefits and risks of medications and that if concerns outweighed benefit, a greater number of patients may prefer to initiate such end of life planning or be referred to such resources. It would also be noteworthy to explore whether eliciting medication

beliefs initiates conversations about stopping the OA medication prior to uncontrolled symptoms or toxicities and when benefit of the medication is not apparent. Another future point of research is to determine if eliciting medication beliefs in the clinical setting makes end of life discussions easier to approach for oncology professionals. Prior research has determined that end of life discussions are difficult (Udo, Lövgren, Lundquist, & Axelsson, 2018) and may be stalled by physicians until symptoms are uncontrolled or all viable treatment options have been exhausted (Keating et al., 2010).

Research needs to focus on the value of cancer treatment with OAs, especially for those with stage four cancers. Eliciting medication beliefs may be important to discuss benefits, symptoms/adverse events, and cost of the medication for patients initiating new treatment. The American Society of Clinical Oncology (ASCO) is currently working on a framework that can be used as a tool for oncologists to determine such value in treatment (American Society of Clinical Oncology, 2015). ASCO points out that value in cancer treatment does not necessarily mean just monetary cost (Asco, 2015). The meaning of value is individualized for patients and entails shared decision making between the oncologist and patient to weigh the clinical benefits of cancer treatment and the costs in terms of side effects and toxicities as well as financial hardship (Schnipper et al., 2015). Some patients with advanced stage cancers may value cancer treatment because it offers them extended survival, even if that survival is limited to weeks or months. Other patients with advanced cancers may value not having to face the possibility of side effects or toxicities of the cancer treatment at the end of life and enjoy the of quality of life that they have left. In addition, some patients may not want to bear the financial hardship associated with cancer treatment that in turn has limited long-term benefit and leaves their family in a compromised financial state. Therefore, individualized conversations about the value of cancer

care and what it means to patients facing advanced cancer disease is essential. Eliciting medication beliefs about OAs is a way to begin discussing what value patients hold for treatment and assisting them to weigh their options (ASCO, 2015; Schnipper et al., 2015).

Importantly, the Concerns subscale of the BMQ does not include the issue of cost. As many patients struggle with the cost of their oral cancer medications (Shih, Smieliauskas, Geynisman, Kelly, & Smith, 2015), an additional item on the BMQ may be warranted. Another suggestion for future research may include the use of additional instruments to operationalize concepts important at the end of life such as quality of life, or quality versus quantity of life measures, in addition to the BMQ. In addition, future research should confirm the two-factor structure of the BMQ in patients with advanced cancer who are receiving or oncolytic agents.

Lastly, the adherence literature supports that social support influences adherence to oral cancer medications (Greer et al., 2016), but less is known about the influence of caregivers or perceived medication social support on medication beliefs. Future research should include scales that can elicit the medication beliefs of caregivers who are actively involved in supporting the patients to take their medication and examine if relationships exist between the medication beliefs among patients and their caregivers.

Policy Implications

The American Cancer Society estimates that in 2018, over 1.7 million individuals will be diagnosed with cancer (American Cancer Society, 2018). The National Cancer Institute projects individuals living beyond their cancer diagnoses will increase nearly 25% between 2014 and 2024 (National Cancer Institute, 2017). Cancer has now been deemed a chronic illness and more patients are receiving continuous and long-term treatment with OAs.

Nurses are positioned to advocate for health policies that improve the care of individuals with cancer. The Oncology Nursing Society (ONS) has announced their most recent legislative and regulatory policy agenda that highlights strategic goals (ONS, 2017a). The first strategic goal is to advance the quality of cancer care and the safety of patients (ONS, 2017a). Under this goal, promoting comprehensive treatment education, personalized care planning and awareness as well as ensuring access to appropriate pain management and palliative care is highlighted (ONS, 2017).

Nurses must advocate for standardized patient education regarding treatment with oral cancer therapy, demand personalized care planning that entails proper screening of the appropriateness of oral therapy for patients (e.g. screening medication beliefs), and symptom management protocols that ensure established guidelines for symptom management for patients responsible for medication administration in the home environment with proper follow up. The assessment of medication beliefs among patients with advanced cancer receiving OAs is one way nurses can determine potential misconceptions patients may have about their medication, address Concerns (negative) beliefs such as unpleasant symptoms, and determine if the patient believes the medication will improve their health. Addressing Concerns (negative) beliefs such as symptoms is essential for improving medication beliefs and improving patient outcomes such as adherence.

In addition, patients indicating low Necessity (positive) beliefs about their OA medication, may introduce an opportunity for oncology nurses to discuss early palliative care or hospice. Nurses should advocate for additional training in hospice and palliative care and establish programs to train on how to initiate and support end of life decisions (ONS, 2017a). ONS recently supported the Patient Quality of Life Coalition (PQLC), which supports a rule's

provision to establish advanced care planning as its own standalone improvement activity, noting that there is more work to be done to encourage end of life planning discussion with patients (ONS, 2017b). ONS encourages nurses to take advantage of ways to learn more about how to best engage patients in end of life discussions as they are often the first line of communication regarding advanced care planning (ONS, 2017b). Eliciting medication beliefs could be a gateway into these difficult discussions, especially when patient's perceived cost of treatment outweighs the benefits. In addition, when OA medications are permanently stopped, nurses can assist patients with appropriate referrals and provide support for end of life care.

Currently, there is no standard of care describing how patients with advanced cancer are screened for the appropriateness of OA medication. Questions arise regarding ethical care and balancing the benefit of OA medication versus the harm of overwhelming treatment symptoms and toxicities. In addition, cost is very high for OA medication. Treatment can drain financial resources for patients and their families at the end of life, while patients may experience little, if any, benefit of the treatment.

In this study, symptoms were associated with an increase in Concern (negative) beliefs and those experiencing three or more adverse events had significantly lower Necessity (positive) beliefs compared to those experience less than three adverse events. Another initiative outlined by ONS is to establish mechanisms to facilitate the reporting of adverse events utilizing health information technology in cancer care delivery and treatment (ONS, 2017a). Oncology nurses can also promote state of the science technology to increase the remote communication between the patients receiving OA and the oncology team. For example, the Patient-Centered Outcome Research Institute has released a mobile application to encourage the reporting of symptoms, side effects, and medication adherence for patients receiving oral cancer treatments in the

(Patient-Centered Outcomes Research Institute, 2018). The mobile application delivers patient assessments in real time to the oncology team who can facilitate evaluation and needed intervention (Patient-Centered Outcomes Research Institute, 2018). For the use of technology and oncology intervention to be feasible, proper funding and reimbursement must be in place. ONS addresses the need for federal policies to recognize the economic value of nurses' contributions to patient care including patient safety and outcomes by ensuring the Medicare policies and payments capture and cover the full range of both inpatient and outpatient oncology nursing services such as evaluating medication beliefs and follow up to technology-based interventions that promote patient education, supportive care and end of life care (ONS, 2017a). Medication beliefs could easily be screened in the same mobile application as this study demonstrated Concern (negative) beliefs were associated with a number of treatment-related events.

To ensure that new interventions such as assessing and addressing medication beliefs in the clinical area and implementing technology-based interventions are feasible, funding is needed. Nurses can advocate for the reimbursement of remote services provided to patients who are managing care in the home environment and research funding to support the advancement of oncology nursing interventions (ONS, 2017a).

Conclusion

Medication beliefs are defined as an individual's perception regarding the benefits and concerns of treatment with medication that arise from cognitive representation of illness (Horne, 2003). This research has advanced the science forward by providing preliminary evidence of the factors influencing medication beliefs over time in patients receiving OAs. This dissertation fills many gaps in the literature by: 1) introducing a conceptual framework of medication beliefs 2)

examining medication beliefs over time; 3) incorporating patients receiving OAs; 4) examining medication beliefs as dependent variables to evaluate the factors associated with these beliefs; 5) including medication beliefs among patients with advanced stage cancer and; 6) including patients diagnosed with various cancers 7) examining how physician-directed OA stoppages influence medication beliefs and 8) describing the potential link between medication beliefs and end of life planning.

As patients experience the benefits of medication, Necessity (positive) beliefs increase. However, when patients perceive illness in the form of symptoms after initiating a new OA, they develop increasing Concern (negative) beliefs about their medication. Because medication beliefs entail an individual's perceptions, these beliefs are vulnerable to depressive symptoms and compromised cognitive effectiveness. Medication beliefs are influenced by many factors across the first twelve weeks after initiating treatment with a new OA. Patients can hold both positive and negative medication beliefs at the same time and each of these beliefs are influenced by different factors. Concern (negative) beliefs are more vulnerable to factors across the 12-week treatment trajectory, which has implications for oncology nursing intervention. Necessity (positive) beliefs are seemingly more stable across the 12-week treatment trajectory unless patients have three or more adverse events, experience a permanent physician-directed stoppage, or experience depressive symptoms.

Medication beliefs have been linked to patient outcomes such as adherence in patients with cancer, however such outcomes such as adherence may not be important for patients with advanced stage cancer. Outcomes such as end of life planning may be more important for this population. Future research is needed to determine the feasibility of interventions in the clinical

areas to elicit and evaluate medication beliefs and develop intervention to improve medication beliefs in order to improve patient outcomes such end of life care.

In summary, this research has contributed to science by describing the two components of medication beliefs as independent constructs influenced by different factors. Preliminary data has provided information regarding the influence that adverse events and permanent physician-directed stoppages have on medication beliefs, which focus on patient-reported outcomes other than adherence and towards more timely end of life planning and hospice referrals.

REFERENCES

REFERENCES

American Cancer Society. Cancer Facts & Figures. (2018). www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2018.html. Accessed on March 4, 2018.

American Society of Clinical Oncology. 2015. ASCO Publishes Conceptual Framework to Assess the Value of New Cancer Treatment Options. Retrieved from https://www.asco.org/advocacy-policy/asco-in-action/asco-publishes-conceptual-framework-assess-value-new-cancer-treatment. Accessed April 15, 2018.

Bender, C. M., Gentry, A. L., Brufsky, A. M., Casillo, F. E., Cohen, S. M., Dailey, M. M., ... & Sereika, S. M. (2014, May). Influence of patient and treatment factors on adherence to adjuvant endocrine therapy in breast cancer. *Oncology Nursing Forum 41*(3), 274–285.

Bhattacharya, D., Easthall, C., Willoughby, K. A., Small, M., & Watson, S. (2012). Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. *Journal of Oncology Pharmacy Practice*, *18*(3), 333–342.

Bickell, N. A., Weidmann, J., Fei, K., Lin, J. J., & Leventhal, H. (2009). Underuse of breast cancer adjuvant treatment: Patient knowledge, beliefs, and medical mistrust. *Journal of Clinical Oncology*, *27*(31), 5160–5167.

Bond, B., Hirota, L., Fortin, J., & Col, N. (2002). Women like me: Reflections on health and hormones from women treated for breast cancer. *Journal of Psychosocial Oncology*, *20*(3), 39–56.

Corter, A. L., Findlay, M., Broom, R., Porter, D., & Petrie, K. J. (2013). Beliefs about medicine and illness are associated with fear of cancer recurrence in women taking adjuvant endocrine therapy for breast cancer. *British Journal of Health Psychology*, *18*(1), 168–181.

Greer, J. A., Amoyal, N., Nisotel, L., Fishbein, J. N., MacDonald, J., Stagl, J., ... & Pirl, W. F. (2016). A systematic review of adherence to oral antineoplastic therapies. *The Oncologist*, *21*(3), 354-376.

Grunfeld, E. A., Hunter, M. S., Sikka, P., & Mittal, S. (2005). Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Education and Counseling*, *59*(1), 97–102.

Heisig, S. R., Shedden-Mora, M. C., Blanckenburg, P., Rief, W., Witzel, I., Albert, U. S., & Nestoriuc, Y. (2016). What do women with breast cancer expect from their treatment? Correlates of negative treatment expectations about endocrine therapy. *Psycho-Oncology*, *25*(12), 1485–1492.

Horne, R. (2003). Treatment perceptions and self-regulation. In The self-regulation of health and illness behavior. In L. D. Cameron, & H. Leventhal (Eds.), *The self-regulation of health and illness behavior* (pp. 138–153). New York, NY: Routledge.

Horne, R., Graupner, L., Frost, S., Weinman, J., Wright, S. M., & Hankins, M. (2004). Medicine in a multi-cultural society: The effect of cultural background on beliefs about medications. *Social Science & Medicine*, *59*(6), 1307-1313.

Keating, N. L., Landrum, M. B., Rogers, S. O., Baum, S. K., Virnig, B. A., Huskamp, H. A., ... & Kahn, K. L. (2010). Physician factors associated with discussions about end-of-life care. *Cancer*, *116*(4), 998-1006.

Marshall, V. & Given, B. (*In Press*). Factors Associated with Medication Beliefs in Patients with Cancer: An Integrative Review. *Oncology Nursing Forum*.

National Cancer Institute. (2017). Cancer Statistics. www.cancer.gov/about-cancer/understanding/statistics.

Oncology Nursing Society. (2017a). Legislative and Regulatory Health Policy Agenda 115th Congress, 1st Session. Retrieved from: https://www.ons.org/sites/default/files/ONS_HP_Agenda_115th_1st_Session_012317.pdf.Access March 5, 2018.

Oncology Nursing Society. (2017b). CMS's Proposed Rule for Advanced Care Planning Is Important to Oncology Nurses. Retrieved from: https://voice.ons.org/advocacy/ons-shares-views-on-advanced-care-planning-patient-access-to-opioids-in-comment-letter-to. Accessed March 5, 2018.

Parikh, R. B., Kirch, R. A., Smith, T. J., & Temel, J. S. (2013). Early specialty palliative care—translating data in oncology into practice. *New England Journal of Medicine*, *369,*2347-2351.

Patient-Centered Outcomes Research Institute. (2018). Mobile Application for Improving Symptoms and Adherence to Oral Chemotherapy in Patients with Cancer. Retrieved from: https://www.pcori.org/research-results/2013/mobile-application-improving-symptoms-and-adherence-oral-chemotherapy-patients. Accessed March 6, 2018.

Salgado, T. M., Davis, E. J., Farris, K. B., Fawaz, S., Batra, P., & Henry, N. L. (2017). Identifying socio-demographic and clinical characteristics associated with medication beliefs about aromatase inhibitors among postmenopausal women with breast cancer. *Breast Cancer Research and Treatment*, *163*(2), 311–319. doi: 10.1007/s10549-017-4177-9.

Shih, Y. C. T., Smieliauskas, F., Geynisman, D. M., Kelly, R. J., & Smith, T. J. (2015). Trends in the cost and use of targeted cancer therapies for the privately insured nonelderly: 2001 to 2011. *Journal of Clinical Oncology*, *33*(19), 2190.

Schnipper, L. E., Davidson, N. E., Wollins, D. S., Tyne, C., Blayney, D. W., Blum, D., ... & Lyman, G. H. (2015). American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. *Journal of Clinical Oncology*, *33*(23), 2563.

Tipton, J. M. (2015). Overview of the challenges related to oral agents for cancer and their impact on adherence. *Clinical Journal of Oncology Nursing*, *19*(3), 37–40.

Udo, C., Lövgren, M., Lundquist, G., & Axelsson, B. (2018). Palliative care physicians' experiences of end-of-life communication: A focus group study. *European Journal of Cancer Care*, *27*(1), 1-7.