

University of San Diego

Digital USD

Dissertations

Theses and Dissertations

2020-01-31

Treatments for Cancer Given Orally: Patients' Perceptions of Distress Due to Financial Toxicity

Ellen Carr
University of San Diego

Follow this and additional works at: <https://digital.sandiego.edu/dissertations>



Part of the [Health Economics Commons](#), [Health Policy Commons](#), and the [Other Nursing Commons](#)

Digital USD Citation

Carr, Ellen, "Treatments for Cancer Given Orally: Patients' Perceptions of Distress Due to Financial Toxicity" (2020). *Dissertations*. 165.

<https://digital.sandiego.edu/dissertations/165>

This Dissertation: Open Access is brought to you for free and open access by the Theses and Dissertations at Digital USD. It has been accepted for inclusion in Dissertations by an authorized administrator of Digital USD. For more information, please contact digital@sandiego.edu.

UNIVERSITY OF SAN DIEGO
Hahn School of Nursing and Health Science
DOCTOR OF PHILOSOPHY IN NURSING

TREATMENTS FOR CANCER GIVEN ORALLY:
PATIENTS' PERCEPTIONS OF DISTRESS DUE TO FINANCIAL TOXICITY

by

Ellen Carr

A dissertation presented to the
FACULTY OF THE HAHN SCHOOL OF NURSING AND HEALTH SCIENCE
UNIVERSITY OF SAN DIEGO

In partial fulfillment of the
requirements for the degree
DOCTOR OF PHILOSOPHY IN NURSING

December 2019

DISSERTATION COMMITTEE

Eileen K. Fry-Bowers, PhD, JD, RN, CPNP, FAAN
Chairperson

Kathleen M Stacy, PhD, RN, APRN-CNS
Committee Member

Alison Sanchez, PhD
Committee Member

UNIVERSITY OF SAN DIEGO
Hahn School of Nursing and Health Science, Beyster Institute for Nursing Research

DOCTOR OF PHILOSOPHY IN NURSING

CANDIDATE: Ellen Carr, RN, MSN, AOCN®

DISSERTATION: Treatments for Cancer Given Orally:
Patients' Perceptions of Distress due to Financial Toxicity

DISSERTATION COMMITTEE:

Eileen K. Fry-Bowers, PhD, JD, RN, CPNP, FAAN, Chairperson

Kathleen M Stacy, PhD, RN, APRN-CNS, Committee Member

Alison Sanchez, PhD, Committee Member

ABSTRACT OF THE DISSERTATION

Treatments for Cancer Given Orally:
Patients' Perception of Distress Due to Financial Toxicity

by
Ellen Carr
Doctor of Philosophy in Nursing

University of San Diego, San Diego, 2019
Associate Professor Eileen Fry-Bowers, Chair

Purpose/Aims: For adult participants who have received or are receiving treatment for hematologic and solid tumor malignancies given orally, this study describes the relationship between participants' experience of financial toxicity (FT), the participants' perception of distress associated with FT, and participants' self-identified adherence to prescribed treatments in the context of FT.

Background: FT has emerged as an additional source of distress for cancer patients. The costs of treatments given orally can be prohibitively expensive for patients. Therefore, these patients may experience considerable distress and may not adhere to treatments as prescribed.

Method: Descriptive cross-sectional correlational design study of a sample of adult cancer patients treated with therapy given orally. Study data was analyzed using descriptive and bivariate correlation statistics.

Findings: Data from 136 participants included participant perceptions of FT, distress and adherence at seven days and six months post start of treatment. At both timepoints, patients had moderate scores for FT, according to COST instrument data. At both timepoints for distress, 39-42% of patients had high distress scores related to FT. There was no correlation between FT and distress. Responding to specific COST instrument questions, 80% of participants responded that they feel they have no choice about the cost of care. At seven days post start of treatment, 67.1% of patients reported that OOP expenses were higher than anticipated. At six months post start of treatment 59.4% of patients reported that OOP expenses were higher than anticipated. Most correlations among variables were weak with the exception of a strong correlation between help from pharmaceutical companies/foundations and percentage of financial help from those funding sources ($r = .869, p = <.001$). Based on data from this sample, FT was not established as a predictor of distress or adherence to treatment.

Implications for Nursing: Despite this sample data showing minimal statistically significant correlations, FT has clinical significance. Nurses can mitigate the impact of FT on patients and caregivers by including FT assessment as a component of clinical assessment, referring patients to healthcare FT experts and resources and providing patients and families with support to alleviate FT as a patient stress.

Intentionally Left Blank/Copyright Page

DEDICATION

This study is dedicated to all my teachers—past, present and future.

And as a clinical oncology nurse, I dedicate this study to those who have taught me the most—the patients themselves.

ACKNOWLEDGEMENTS

In gratitude, I sincerely thank the dedicated guidance, support and kindnesses extended to me by my Dissertation Committee: Eileen Fry-Bowers, PhD, JD, RN, CPNP, FAAN (Chair); Kathleen M Stacy, PhD, RN, APRN-CNS; and Alison Sanchez, PhD. In particular as Chair, Dr. Fry-Bowers demonstrated the art and science of mentoring--establishing impeccable, comprehensive standards during all stages of this study so I could present this study with rigor, clarity and relevance.

I am the fortunate beneficiary of a lifetime of remarkable teachers, who provided a foundation of expertise, insight and inquiry. At the University of San Diego Hahn School of Nursing and Health Sciences, I am particularly grateful to Ann M. Mayo, RN, DNSc, FAAN, and Ruth A. Bush, PhD, MPH, who welcomed me to their courses several times during this PhD journey.

I also am grateful for Catherina Madani, PhD, RN, CHPN, who generously helped me sort out the statistical challenges of this study.

I would be remiss if I did not thank Dr. Patricia Roth, now retired as Dean of the Hahn School's PhD Program. Dr. Roth was steadfast in her vision for the PhD Program, always offering inspiration and encouragement to each of my classmates and me.

I also am thankful for the generosity of Andrew and Esther Schorr, who started and have sustained Patient Power®, a trailblazing patient education and advocacy organization. Because of the Schorrs, I was granted access to the Patient Power® community of cancer patients so I could capture this study's data.

Referring to Lady Bird Johnson, former First Lady of the U.S., who once said, “Become so wrapped up in something that you forget to be afraid,” I am thankful for dear friends and family members, who believed in me and lifted me from periods of weariness and doubt.

In particular, I am grateful for the gift of indefatigable support from dear friend, Janice Maienza, RN, MSN, who graduated with me almost forty years ago from the MGH Institute of Health Professions in Boston--at that time one of the few accredited Masters-Entry Programs in Nursing in the U.S. And I also would not have taken on the challenge of this PhD experience without the life force who is Caroline Etland, PhD, RN, AOCN®, ACHPN.

And finally, I am thankful for my family, especially my sister, Miriam, who represents all the dedicated teachers in my family—practitioners in the “Family Business.” Some thanks are difficult to articulate, especially when expressed to family. So I will leave it at that: Thank you beyond what words can convey....

TABLE OF CONTENTS

CHAPTER 1: BACKGROUND and SIGNIFICANCE.....	1
Introduction.....	1
Cancer Care: Advances in Treatments.....	4
Cancer Treatment and Cost.....	5
Financial Toxicity.....	7
Sequelae of Financial Toxicity.....	8
Study Purpose, Aims and Hypotheses.....	8
Content of this Dissertation: Overview of Chapters.....	10
CHAPTER II: CONCEPTUAL FRAMEWORK and REVIEW of the LITERATURE.....	11
Introduction.....	11
Conceptual Framework.....	11
Review of Literature.....	14
Cancer Therapies Given Orally.....	15
Cost of Therapies: Oral Administration.....	16

The Patient's Out of Pocket (OOP) Costs.....	19
The Medicare Donut Hole.....	20
Cancer Treatment and Distress.....	21
Cancer Care, Financial Toxicity and Distress.....	22
Cancer Patients and Financial Toxicity.....	24
Out-of-Pocket Expenses.....	25
Out-of-Pocket Costs as Source of Distress.....	27
Financial Hardship.....	27
Financial Toxicity and Quality of Life.....	29
Financial Toxicity Non-Adherence to Treatment.....	30
Gap Analysis.....	32
Summary of Literature.....	35
CHAPTER III: METHODS.....	37
Purpose and Specific Aims.....	37
Study Design.....	37
Sample.....	37
Setting.....	38
Sample Size.....	41
Protection of Human Subjects.....	41

Study Procedures.....	42
Recruitment of Participants.....	42
Data Collection.....	43
Data Management.....	43
Study Measurements.....	44
Operational Definitions of Terms.....	44
Instruments.....	46
Data Analysis.....	47
Strengths and Limitations of Methods.....	48
CHAPTER IV: RESULTS.....	50
The Study.....	50
Data Collection.....	50
Study Aim #1.....	51
Aim #1.....	51
Aim #1: Analysis.....	51
Demographic Characteristics.....	52
Clinical Characteristics.....	53
Financial Characteristics.....	53
Covering the Cost of Cancer Treatment Given Orally.....	54

Participant Experience of Financial Toxicity.....	55
Out of Pocket Expenses.....	56
Financial Toxicity and Perception of Distress.....	56
Financial Toxicity (FT) and Adherence to Treatment.....	57
Study Aim #2.....	57
Aim #2.....	57
Aim #2 Analysis.....	58
Relationships between Financial Toxicity and	
Demographic, Clinical and Financial Variables.....	58
Relationships between Financial Toxicity and Perception of Distress.....	60
Relationships between Financial Toxicity and	
Adherence to Treatment.....	60
Study Aim #3.....	61
Aim #3.....	61
Aim #3: Analysis.....	61
CHAPTER 5: DISCUSSION.....	89
Introduction.....	89
Healthcare Costs.....	89
FT and Study Results.....	90
Demographics.....	90

FT Experience.....	93
Out of Pocket Expenses for Treatment.....	95
Financial Support for Treatment.....	95
Distress Experience.....	96
Adherence to Treatment.....	97
FT Relationships.....	100
Summary: FT and Study Results.....	101
Limitations.....	101
Study Design.....	101
Sample Population.....	101
Instruments in Study.....	102
Clinical Practice Implications.....	103
Nursing Care.....	104
Assessment.....	104
Referrals.....	105
Support.....	105
Decision Making.....	105
Future Research.....	107
Opportunities for Research.....	107
Survivorship.....	108
Federal Policy & Drug Costs.....	108

Legislative and Regulatory Initiatives.....	109
Legislation.....	110
Regulations.....	110
Federal Policy and Values.....	112
Conclusion.....	112
References.....	114

List of Figures

Chapter 2

- Figure 2-1. Conceptual Framework of Financial Toxicity
in the Treatment of Patients with Cancer.....13
- Figure 2-2. US Food and Drug Administration (FDA)-Approved
Cancer Therapies Given Orally (2016-2017)
and the Approximate Cost of Treatment.....18

Chapter 3

- Figure 3-1. Patient Power Community Demographics (2016).....40
- Figure 3-2. Patient Power Membership/Subscrip.....40

List of Tables

Chapter 4

- Table 4-1. Participant Characteristics.....62
- Table 41a. Demographic Characteristics.....62
- Table 41b. Clinical Characteristics..... 63
- Table 41c. Financial Characteristics.....65
- Table 4-2
- Table 4-2a. Experience of FT (COST scores),
@ seven days after Start of Treatment.....66
- Table 4-2b. Experience of FT (COST scores),
@ six months after Start of Treatment.....68
- Table 4-3. OOP Expenses (Demographics Survey).....70
- Table 4-4. Levels of Distress.....70

Table 4-5. Perceived Stresses (Distress Thermometer Instrument).....	71
Table 4-6. Correlation COST Scores to Distress Thermometer @ 7 days and 6 mons.....	72
Table 4-7. Correlation COST Scores @ seven days to Demographic Variables.....	73
Table 4-8. Correlation COST Scores @ six mons to Demographic Variables.....	74
Table 4-9. Correlation COST Scores @ seven days to Clinical Variables.....	75
Table 4-10. Correlation COST Scores @ six months to Clinical Variables.....	76
Table 4-11. Correlation COST Scores @ seven days to Financial Variables.....	77
Table 4-12. Correlation COST Scores @ six months to Financial Variables.....	78
Table 4-13. Correlation COST Scores @ seven days and 6 months to Adherence.....	79
Table 4-14. Correlations among Demographic Variables.....	79
Table 4-15. Correlations among Clinical Variables.....	80
Table 4-16. Correlations among Financial Variables.....	81
Table 4-17. Correlation Distress Thermometer @ seven days to Demographic Variables.....	82
Table 4-18. Correlation Distress Thermometer @ six mons to Demographic Variables.....	82
Table 4-19. Correlation Distress Thermometer @ seven days to Clinical Variables.....	83

Table 4-20. Correlation Distress Thermometer @ six mons to Clinical Variables.....	84
Table 4-21. Correlation Distress Thermometer @ seven days to Financial Variables.....	85
Table 4-22. Correlation Distress Thermometer @ six mons to Financial Variables.....	86
Table 4-23. Demographic Correlations to Adherence.....	86
Table 4-24. Clinical Correlations to Adherence.....	87
Table 4-25. Financial Correlations to Adherence.....	88

List of Appendices

Appendix A: USD IRB Approval.....	136
Appendix B: Study Blurb.....	137
Appendix C: Web Site #1 Content.....	139
Appendix D: Web Site #2 Content.....	142
Appendix E: Instrument # 1: Demographic Questionnaire.....	148
Appendix F: Instrument #2: Comprehensive Score for Financial Toxicity (COST).....	152
Appendix G: Instrument #3: National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT) (version 2.2018).....	153

CHAPTER 1

BACKGROUND and SIGNIFICANCE

Introduction

By the year 2026, healthcare spending is expected to account for more than 19% of the U.S. economy (Health and Human Services, 2018). And from 2019 estimates, healthcare spending is expected to top \$4.3 trillion (Schnipper et al., 2016). For the consumer of healthcare, the pace of yearly healthcare costs is increasing at a steady clip, yet has slowed somewhat in the last few years. For the period 1990-2007, the cost of healthcare increased on average 7.3% yearly. For the period 2017-2026, healthcare spending is expected to increase on average 5.5% a year (HHS, 2018). This rise in healthcare costs can, in part, be attributable to an aging population—the primary consumer of healthcare—and the rise in the cost of prescription and specialty drugs that include prescription (non-generic) medications, newly FDA-approved and early in their patent period. Therefore, prescription and specialty drugs are more costly than generic or standard formulary medications (Bradley et al., 2016; Shih et al., 2015; Davidoff et al., 2013).

Contributing to increased healthcare costs, the rise in prescription drugs is expected to increase 6.3% yearly (HHS, 2018). With the high cost of healthcare, third-party private and government health care insurers have transferred more of the burden for healthcare costs to patients, specifically through co-payments, deductibles and any out of

pocket (OOP) costs not covered by the insurer (Galbraith et al., 2011). Yet those with coverage are the lucky ones who at least have some type of healthcare insurance coverage despite the limitations of that coverage that increase expenses to the patient (Gaba et al., 2016; Guy et al., 2013; Guy et al., 2014).

Further, the expense of annual insurance deductibles for health plans has been steadily rising (Claxton et al., 2015). On average in 2017, covered workers contributed 18% of the premium for single coverage and 31% of the premium for family coverage. Since 2012, family coverage premiums have increased 19%. Since 2007, family coverage premiums have increased by 55%. (Kaiser Family Foundation, 2017). A study by the Kaiser Family Foundation reported only 53% of respondents had household incomes that could cover an annual deductible of \$2,400. And when choosing a less robust insurance plan with a higher deductible of \$5,000 annually, only 45% of respondents could afford that expense (Claxton et al., 2015).

Moreover, for those in treatment for cancer, OOP costs can exceed \$5,000 annually (Bernard, Farr, & Fang, 2011; Davidoff et al., 2016). Significantly, the annual medical cost of cancer care was estimated to be \$124.6 billion in 2010 and is projected to increase to \$157.8 billion by 2020 (Mariotto et al., 2011).

In the context of burgeoning healthcare costs, the concept of *financial toxicity* (FT) has emerged, especially for those diagnosed with cancer (IOM, 2013; Tucker-Seeley et al., 2016). FT can be defined as a constellation of financial challenges for patients. These can include high medical payments during or after treatment ends as well as lower

income due to job interruption or job loss due to treatment (Zafar & Abernethy, 2013a; Delgado-Guey et al., 2015).

The Commonwealth Fund has estimated that 23% of insured adults have OOP healthcare costs that are equivalent to more than 10% of their household income (Ell et al., 2008). In 2013, a Medicare Current Beneficiary Survey estimated that 28% of cancer survivors reported high OOP expenses compared to 16% with no cancer history (Davidoff et al., 2013). Moreover, individuals covered by public insurance report high proportional OOP expenses, especially when those individuals cannot work due to illness.

In a 2014 report, the Center for Diseases Control (CDC) estimated annual healthcare expenses and related productivity losses for male survivors of cancer to be \$4,187, an estimated \$1,459 more than those without a history of cancer. For female survivors of cancer, FT had sustaining effects with their estimated annual healthcare expenses and related productivity loss at \$3,293 compared to those without a history of cancer, estimated at \$1,330 (Ekwueme et al., 2014). In a 2016 Medical Expenditure Panel Survey of 1,202 cancer survivors, an average 20.4% of these survivors reported financial hardship associated with their cancer or treatment and extended period of recovery. From this sample of patients, 7.1% reported borrowing to pay their bills or go into debt, and almost 12% of patients reported they were unable to cover their OOP costs and that led to psychosocial hardship (Yabroff et al., 2016).

Therefore, the concept of FT and its impact on cancer patients has gained visibility and parity with other treatment side effects that require management (ASCO,

2018; Delgado-Guey et al., 2015). FT, as an unwanted side effect from cancer treatment, has been shown to affect cancer patients in treatment with similar distress as other side effects or toxicities from cancer treatment such as fatigue, nausea and vomiting, anxiety and sleep disturbance (Bestvina et al., 2014; Delgado-Guay et al., 2015; Ubel et al., 2013). A study of 300 cancer patients in treatment reported that 39% of them experienced greater financial burden from their care than they expected and 19% stated they were overwhelmed due to financial distress (Chino et al., 2017). According to a systematic review of studies about cancer patients and financial distress, an estimated 28-73% of cancer survivors report FT (Gordon et al., 2017).

Cancer Care: Advances in Treatments

This is a time of breakthroughs in the treatment of cancer, which include the promise of molecular and genetic-based treatments for those diagnosed with hematologic or solid tumor malignancies. As additions to multi-modality approaches to treat cancer, these new therapies are advancing the number of treatment options available to patients. These treatments can further refine the precision of prescribed treatments since they are based on the patient's own genetic and metabolic profile (Haslem et al., 2018). In part due to these breakthrough treatments, in the U.S. cancer continues to be one of the most expensive and difficult health challenges to treat (Bradley et al., 2016; Andrews, 2015).

Treatments for cancer have included surgery, radiation therapy, chemotherapy and biologics therapies, either alone or in combination (Shih et al., 2015; Nair & Kong, 2018). With the addition of targeted therapies—many of them formulated in an oral form—some cancer patients can take a pill to treat their cancer rather than the

operationally-complex treatments of surgery, radiation or infusion chemotherapies (Haslem et al., 2018; Nair & Kong, 2018). Moreover, advances in molecular biology and genetics have expanded these cancer treatment options given orally, with these treatments becoming a frequent source of FT (Bayer et al., 2017; Ginex et al., 2017). Although such targeted treatments given orally have been shown to be more effective and easier to tolerate (Garraway et al., 2013), OOP copayment costs to the patient can be staggering, even when insurance pays a large component of the treatment cost (McNulty & Khera 2015; Meisenberg, 2015).

Cancer Treatment and Cost

Targeted therapies in oral form, developed from extensive and often prolonged clinical trials by pharmaceutical companies and academic facilities, can be very expensive. A 1995-2013 analysis of 58 approved anticancer drugs reported that adjusted for inflation, the costs of these drugs increased annually by 10% or approximately \$8,500 a year (Howard et al., 2015). Mariotto and colleagues estimated that by 2020, the cost of cancer care in the U.S. that includes these pricey cancer treatments will be almost \$158 billion (using models that account for incidence, survival and cost). This is a 27% increase over estimates of the cost of cancer care from 2010 (Mariotto et al., 2011).

Even if a third-party payor provides coverage of these treatments and supportive therapies, the OOP cost to the patient can be steep (ASCO, 2018). In a 2017 analysis of insurance coverage, 57% of employees with single (non-family) coverage by employer-supported insurance had an annual OOP maximum of more than \$3,000. And another 18% had an OOP maximum of more than \$6,000 (KFF, 2017). And patients may not

know the OOP cost of these treatments until well after treatment starts since the amount of the OOP costs for these treatments can vary depending on insurance coverage, facility discounts with the medication manufacturer and/or pharmaceutical or patient advocacy assistance programs (Zafar et al., 2103a, 2013b; Zafar et al., 2013c; Zafar, 2016; Henrikson, & Shankaran, 2016).

In addition, studies show that oncologists are reluctant to bring up the cost of medications with patients due to a variety of factors, such as not knowing the cost of the medication themselves, limited data on the clinical value (outcomes based on quality of life and survivorship), and the patients themselves not wanting to know the cost (Gidwani-Marszowski et al., 2018; Carrera et al., 2018; Tucker-Seeley & Yabroff, 2016). In June 2017 in a position statement, the American Society of Clinical Oncology (ASCO), the professional organization for clinical oncologists, expressed concern about the affordability of oncology specialty drugs due to unaffordable coinsurance rates and their OOP expense to the patient (ASCO, 2017).

The costs of receiving care for cancer extend beyond the OOP costs associated with prescription drugs or co-pays. These costs add up. The extra costs of care include a constellation of expenses that are in addition to treatment costs. The cost of receiving care for cancer includes costs of transportation to and from clinic appointments and treatments, parking fees, hotel stays, over the counter medications, child care while in treatment, the cost of non-covered second opinions, special diets and other needs. Especially for low-income patients, transportation issues are a focus of FT and a primary stressor (Massa et al., 2018; Carrera et al., 2018).

Moreover, studies estimate that a range of 25-40% of cancer patients are more likely to miss work or require reduced work hours while in treatment or recovering from declining health (Ferrell et al., 2018; Huntington et al., 2015; Jagsi et al., 2014). A 2017 systematic review of studies about cancer survivors reported some form of financial distress because of the patients' cancer treatment. Studies included in the review reported that survivors' mean annual productivity loss was \$380-\$8,236, with 12-62% reporting that treatment caused them to be in debt (Altice et al., 2017). A study of cancer patients in Washington State reported the bankruptcy risk for the general cancer population at 2.1% approximately 2.5 years after cancer diagnosis (Ramsey et al., 2013).

Financial Toxicity

In cancer care, the objective and subjective financial consequences of cancer treatment may include significant OOP costs, loss of income, and caregiver burden. Since 2011, the term *financial toxicity* also has been associated with patients diagnosed with cancer who face financial challenges related to precision medicine treatments (Carrera, 2017; Zhang, Hueser, & Hernandez, 2017). FT is considered akin to hair loss or nausea from cancer treatment given the distress that patients feel as a result of experiencing financial burden (Carrera et al., 2018). Yet the concept of FT as it relates to patients with cancer is not fully understood (Altice et al., 2017; Gordon et al., 2017). FT as a clinical concept lacks standard strategies to screen and measure (Carrera et al., 2018; Gilbert et al., 2017). And the ability to pay, especially when related to life-saving treatment, is a very personal and individual challenge (Gidwani-Marszowski et al., 2018; Guy et al., 2015). These financially-impacted choices can affect when and whether an individual

agrees to treatment, the impact of medical expenses on household finances and the impact of cancer and treatment on the individual's quality of life (McNulty & Khera., 2015; Kale & Carroll, 2016).

Sequelae of Financial Toxicity

In cancer care, with the cost and initial lack of transparency for these OOP costs to patients, the care team needs to address and better manage FT (Doyle, 2017). The effects of FT create an additional layer of distress for the patient during a time when the cancer patient should focus on treatment and management of functional and emotional side effects. For the patient, FT-related distress can manifest itself as depression and anxiety (Zafar & Abernethy, 2013a, 2013b; 2016; Perrone, et al., 2016). FT has also been suggested as a contributing factor to patients not adhering to a costly cancer treatment regimen given orally.

Due to the high OOP costs, some patients just cannot afford the full cost of the treatment or decide to partially take the prescribed treatment so they can attempt to benefit from some of the treatment effects (Bestvina et al., 2014; Wheeler et al., 2018). Few studies have focused on FT as a factor in care delivery--its effect on the patient's adherence to treatment and the wellbeing of patients and their caregivers when patients are treated (Bestvina et al., 2014; Kale & Carroll, 2016).

Study Purpose, Aims and Hypotheses

For adult participants who have received or are receiving treatment for hematologic and solid tumor malignancies given orally, this study will describe the

relationship between participants' experience of financial toxicity (FT), the participants' perception of distress associated with FT, and participants' self-identified adherence to prescribed treatments in the context of FT.

The aims of this study are:

1. To describe sociodemographic, clinical and financial characteristics, the experience of FT, perception of the level of distress, and adherence to treatment in a sample of adult participants who have received or are receiving treatment given orally for hematologic or solid tumor malignancies.
2. To describe relationships between participant sociodemographic, clinical and financial characteristics, participants' experience of FT, participants' perception of distress, and participants' adherence to treatment.

Hypotheses:

- Participant experience of FT will be related to participant perception of distress while controlling for statistically significant demographic, financial and clinical characteristic covariates.
 - Participant experience of FT will be related to participant adherence to the treatment given orally, while controlling for statistically significant demographic, financial and clinical characteristic covariates.
3. To explore the likelihood that participant experience of FT predicts participant perception of distress and non-adherence to the treatment given orally.

Hypotheses:

- The participant experience of FT predicts the likelihood of participant perception of the level of distress.
- Participant experience of FT predicts the likelihood of participant nonadherence to the treatment given orally.

Content of this Dissertation: Overview of Chapters

As a foundation for this study, Chapter 1 has introduced the concepts of FT as a source of distress for cancer patients prescribed treatment given orally. The costs of treatments given orally can be prohibitively expensive for patients. Therefore, patients may experience distress and may not adhere to the treatments as prescribed.

Chapter 2 reviews and critiques peer-reviewed literature about FT associated with cancer patients receiving therapies orally, patient perception of distress related to FT and adherence related to FT.

Chapter 3 describes the study methods, including the study design, a description of the population, protection of human subjects, procedures for recruiting patients, data collection procedures, and the plan for statistical analysis.

Chapter 4 presents the study results organized in order of the study aims.

Chapter 5 discusses the study findings in the context of clinical practice, implications for practice, future research and policy implications.

CHAPTER II
CONCEPTUAL FRAMEWORK
and
REVIEW of the LITERATURE

Introduction

For patients receiving treatment for hematologic and solid tumor malignancies given orally, the purpose of this study is to determine the relationships between the patient experience of financial toxicity (FT), patient perception of distress, adherence to prescribed treatments and OOP costs of prescribed treatments. This chapter begins with a review of the conceptual framework underpinning this study: Carrera’s Conceptual Framework of Financial Toxicity in the Treatment of Patients with Cancer (Carrera, 2017; Kantarjian, & Binder, 2018). The chapter continues with a review of the literature as a foundation for the study and specifically addresses cancer treatments given orally, the cost of those treatments, cancer treatment and distress, and components of FT for patients in treatment for cancer. Finally, the chapter provides a gap analysis, based on the literature review, which supports this study’s purpose and aims.

Conceptual Framework

The concept of FT has been referred to in the medical literature since 2001. Its attributes include a subjective and objective response by cancer patients to the cost of their cancer therapies. That response is considered a “hardship” or source of “distress”

due to the financial burden that impacts patients, who are already dealing with the impact of a cancer diagnoses on their lives (Carrera et al., 2018).

The research conceptual framework for this study is the *Conceptual Framework of Financial Toxicity in the Treatment of Patients with Cancer*, which is adapted from Carrera's work on the topic (Carrera, 2017; Carrera et al., 2018). The Framework presents a foundation for FT, created by a back and forth platform that flows among the patient's expenditures, wealth, anxiety and discomfort. That platform leads to the patient's objective financial burdens, such as the direct costs of treatment and expenditures associated with treatment. Examples of the patient's subjective financial burdens are the patient's perception and experience of financial distress, resulting in worry and anxiety about decreased household income and savings (Carrera, 2017; Carrera et al., 2018).

The conceptual framework, *Financial Toxicity in the Treatment of Patients with Cancer*, is shown in Figure 2-1. Evidence to support the interrelated components of the conceptual framework actually begins with early studies about FT by Zafar and colleagues, and later studies led by Carrera and Schnipper (Carrera et al., 2018; Schnipper et al., 2016). Zafar and colleagues were the first to publish about FT affecting patients' adherence to treatment. They also proposed strategies to better approach patients' experience of FT that included having frank and open discussions among patients and for health care professionals to take a broader perspective toward treatment decisions that go beyond strict clinical guidelines (Zafar, 2016; Zafar & Abernethy 2013a; Zafar et al., 2013).

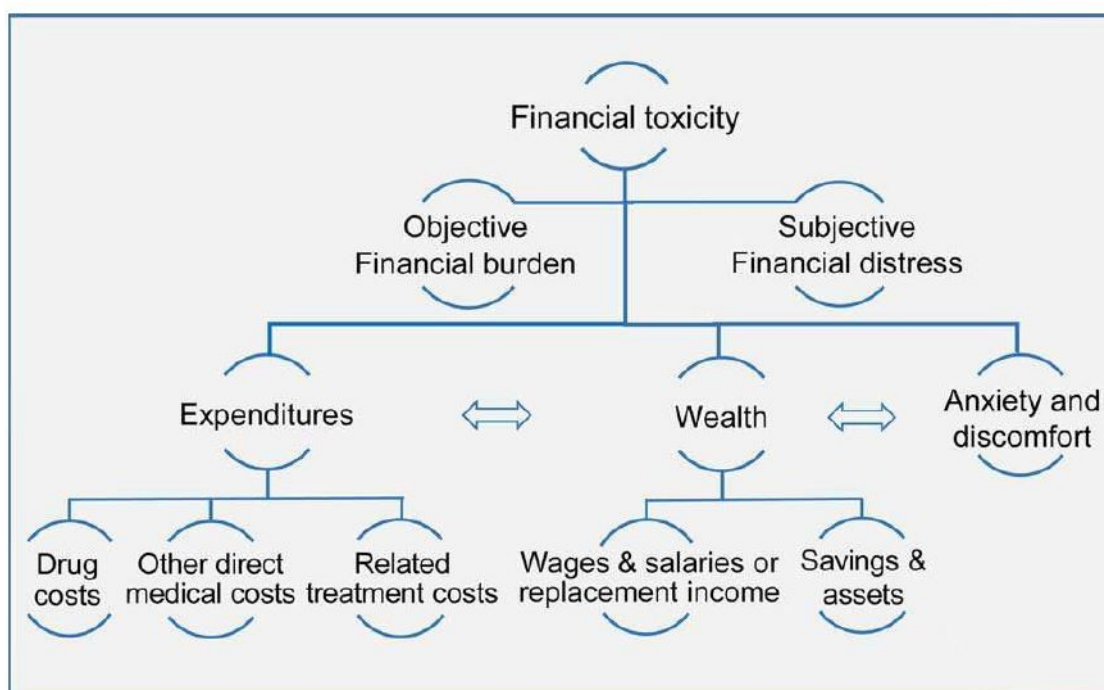


Figure 2-1

Conceptual Framework of Financial Toxicity in the Treatment of Patients with Cancer
(Used with Permission, John Wiley and Sons: from Carrera et al., 2018)

Based on clinical experience and studies to date, Carrera and colleagues suggest that the relationship of costs, expenditures and anxiety are on a continuum, increasing discomfort for the patient. They suggest that this level of patient discomfort merits effective multidisciplinary approaches to address FT as a toxicity from treatment, just as more familiar clinically-based toxicities require attention (Carrera, 2017; Carrera et al., 2018).

Addressing the assessment of value of cancer treatment options, Schnipper and colleagues have published trailblazing work on behalf of the American Society of

Clinical Oncologists addressing FT in clinical care. This ongoing work discusses FT based on value assessment, objective and subjective distress, and shared decision-making (Schnipper et al., 2015).

As represented in this conceptual framework, FT can be associated with the cost of newer cancer therapies and with the cost of the therapies (OOP copays and larger deductibles), which are more the burden of the patient rather than the insurer (Gordon et al., 2017; Altice et al., 2017; Claxton, Rae & Panchal, 2015).

Therefore, for this study, this conceptual framework suggests relationships between the patient's experience of FT and patient perception of distress (subjective burden). Based on that FT/distress relationship, the framework also serves as a foundation for FT-associating patient perception of distress (subjective financial distress) and/or patient adherence to prescribed medication (result of objective financial burden).

Review of Literature

The literature review was based on peer-reviewed articles, published in English from 2010-2018, that were retrieved from these databases: PubMed, CINAHL, OVID and Google Scholar. The literature search included the words and phrases, *financial distress*, *financial toxicity*, *patient distress*, *treatment adherence*, *cancer oral drugs*, *cancer treatments*, *oncolytics*, *cost of cancer care*, *oral cancer drug prices* and *OOP cost of cancer care*. In addition, the reference list of articles was reviewed for further pertinent resources. Approximately 165 articles were reviewed. The review included studies primarily of adult patients in the United States.

Cancer Therapies Given Orally

This is a period of promising cancer treatment made possible by advances in molecular biology, bioinformatics, pharmacometrics and genetic and genomic-engineering (Maeda & Khatami, 2018). Development of new molecular/genomic treatment strategies has been advancing over the past 40 years, with the first Federal Drug Administration (FDA)-approved monoclonal antibody treatments for cancer first introduced into practice settings in 2000-2005 (Brassil & Ginex, 2018; Bayer et al., 2017).

FDA-approved applications for these immunotherapies or so-called targeted therapies administered orally have continued at a steady clip, with almost 40 treatments approved as of 2018. The rate of these FDA approvals continues with new targeted therapies or applications added to therapy options every few months. To support their FDA approval, these new treatments given orally must show effectiveness as alternative treatment strategies, as additional options to treat frail patients or treatments for those who have exhausted standard treatment options (Shih et al., 2015). Additional applications for targeted therapies include more advanced-stage hematologic malignancies and more and later-stage solid tumor malignancies (Nair & Kong, 2018; Shih et al., 2015).

Targeted therapies given orally include monoclonal antibodies, cytokine therapies, immune checkpoint inhibitors, oncolytic viral therapies and targeted therapies (Brassil & Ginex, 2018; Garraway, Verweij & Ballman, 2013). They contribute to the future platform for cancer treatment termed *precision medicine*. These treatments, using a scientific development platform called transformational medicine, target the molecular

level of cancer cells themselves with specificity to an individual patient's malignancy, rather than reverting to a standard, broad, systematic approach to treatment. The staple of standard systemic treatments continues to be chemotherapy or chemotherapy-radiation therapy combination treatment protocols (Haslem, Chakaraty & Fulde, 2018; Nair et al., 2018).

In addition to precision-medicine treatments given orally, oral formulations of supportive therapy—prescribed to lessen or manage treatment side effects—also continue to advance in their development. Examples of these supportive therapies include growth factors that reduce cancer treatment-prompted neutropenia (reduced white and red blood cell effectiveness and production), anti-nausea and vomiting agents and anti-inflammatory agents (Irwin & Johnson, 2015).

Cost of Therapies: Oral Administration

Insurance coverage of these prescribed oral medications is based upon the classification of the pharmaceutical therapy into one of three categories: brand, generic and specialty (Hoadley et al., 2015a, 2015b). A brand name medication is a medication developed by a pharmaceutical company that holds the patent for the medication and, as such, possesses exclusive rights to the manufacturing and sale of the medication. Once a patent expires, other companies can produce copies of brand-name drugs, known as generic medications, that have the same dosage, intended use, effects, side effects, route of administration, risks, safety, and strength as the original drug. Because generic drugs are not exclusive to a single manufacturer, they are usually less expensive. A specialty medication is a high-cost prescription therapy prescribed to treat complex, chronic

conditions (FDA, 2018). Most cancer treatments given orally, sometimes called oncologics, are considered specialty medications. Usually, these specialty medications are not included in the formulary of the insurance carrier and as such may not be considered a covered medication by the insurer (Hoadley et al., 2015b). In some cases, the cost or partial cost of a specialty medication can be covered if the prescriber provides clinical justification for the therapy. Whether a specialty medication is a covered benefit by the insurer is based on the insurer's policies, guidelines and discussion with medical experts (Carrera et al., 2018; Schnipper et al., 2016).

Overall, the cost of these oral cancer therapies is exceedingly high. For example, in 2015, the annual cost of the oncologic ponatinib, a treatment for chronic myeloid leukemia (CML), was an estimated \$138,000. As of 2015, the cost of induction (initial) treatment for chronic lymphocytic leukemia (CLL) with omacetaxine is \$28,000 per year, followed by \$14,000 annually for maintenance doses. The cost of another oncologic agent given orally, bosutinib, is \$118,000 per year (McNulty and Khera, 2015). CLL treatment and management is expected to outpace other cancer diagnoses in its costs. Figure 2 lists FDA-approved medications as of 2018 given orally as treatment for malignancies and their monthly cost (Carrera et al., 2018).

TABLE 1. US Food and Drug Administration-Approved Oral Cancer Drugs in 2016 to 2017 and Costs of Treatment^a

GENERIC NAME	BRAND NAME	CANCER TYPE	COST PER MONTH OF TREATMENT, US\$
Brigatinib	Alunbrig	NSCLC, ALK	12,868.76
Cabozantinib	Cabometyx	Renal cell carcinoma, FLT3, KIT, MET, RET, VEGFR2	15,156.59
Enasidenib	Idhifa	Acute myeloid leukemia, IDH2	25,141.37
Midostaurin	Rydapt	Acute myeloid leukemia, FLT3 positive	15,798.72
Neratinib	Nerlynx	Breast cancer, HER2 positive	10,613.75
Niraparib	Zejula	Ovarian cancer, PARP1, PARP2	14,430.19
Ribociclib	Kisqali	Breast cancer, HER2 negative	8476.31
Rucaparib	Rubraca	Ovarian cancer, BRCA	20,162.74
Venetoclax	Venclexta	Chronic lymphocytic leukemia, BCL2	7514.41

Abbreviations: ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; ER, estrogen receptor; FLT3, fms-related tyrosine kinase 3; HDAC, histone deacetylase; HER2, human epidermal growth factor receptor 2; IDH, isocitrate dehydrogenase; KIT, stem cell factor receptor; NSCLC, nonsmall cell lung cancer; PARP, poly(ADP-ribose) polymerase; VEGFR2, vascular endothelial growth factor receptor 2.

^aEstimated monthly prices for chemotherapy drugs are based on the allowable Medicare charge and were calculated according to a methodology used by Dr. Peter B. Bach, Director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center, in a previously published article on cancer drug prices (Bach 2009¹⁷). Since 2005, Medicare has reimbursed at 106% of the Average Sales Price (ASP) for Part B drugs. ASPs are reported in quarterly files released by the Center for Medicare and Medicaid Services.¹⁸ If a drug's ASP is not available, then Medicare calculates the payment limit as 95% of the Average Wholesale Price (AWP). The AWP's were obtained using Thomson Healthcare's Red Book (Thomson Healthcare 2010¹⁹). For Part D drugs, current prices are retrieved from Medicare's publicly available, Web-based "PlanFinder" tool (US Food and Drug Administration [FDA] 2017²⁰). The price we report for these drugs is the "Full Cost of Drug," as reported in the PlanFinder for the Humana Enhanced Prescription Drug Plan, for a beneficiary living within zip code 10021. Payment limits for prior years vary and are described briefly in the table below and in more detail within the previously mentioned article.¹⁷ In all cases, the relevant payment limit is applied to a 12-week dosing regimen for an "average" adult weighing 70 kg, or with a body area of 1.7 m², and divided by 2.77 to arrive at a monthly price (on average, there are 2.77 months in 12 weeks). The 12-week dosing regimen is retrieved from the FDA-approved label for the drug, which are available in the FDA's "Drugs@FDA" database (FDA 2017²¹). The lowest total dosing regimen within the first FDA-approved indication for the drug is used in all cases. The prices shown are for the listed drug only; costs for supportive care or administration fees are not included.

Figure 2-2 (reproduced Table)

(Used with Permission, John Wiley and Sons: from Carrera et al., 2018)

Since 2010, the FDA has approved more specialty drugs than standard therapy drugs for the treatment of cancer. Specialty drugs are estimated to account for 25% of drug spending and constitute one of the largest expenditures for employee health benefit plans (Business Group Health, 2018). The costs of these drugs are projected to increase at a rate of at least 10% per year, which is probably an unrealistically low estimate (Dusetzina et al., 2014). Specialty pharmacies that focus on the distribution of these drugs have recently emerged to take advantage of these expensive and lucrative medications, even though only 4% of patients are treated with specialty medications (Business Group Health, 2018).

The Patient's Out of Pocket (OOP) Costs

Cancer treatments have rarely been affordable without insurance coverage, but insurance coverage in the past has been robust enough to cover most of the costs of traditional, standard treatment (Soni, 2016; Bradley et al., 2016; Shih et al., 2015). Specialty medications, however, are usually not covered under the patient's prescription drug benefit. Coverage of these medications is not like that of intravenous treatments, which are often administered in an in-patient or out-patient setting, and as such, are covered under most insurer's medical benefit plans (KFF, 2018). Now with these new, promising treatments being given orally, the cost to patients can be significant with an increased share of the cost of treatment shifting to the patient (Schnipper et al., 2016; Shih et al., 2015; Morrison, 2015).

As an example, the tyrosine kinase inhibitor imatinib was introduced in 2001 as a first-line treatment for CLL. By 2012, the cost of treatment was approximately \$92,000/year (Dusetzina et al., 2014). In 2015, depending on a patient's insurance coverage and the insurer's policies about specialty medication coverage, the OOP cost of imatinib for patients could be nearly \$700 per month for 58 months (Shanafelt et al., 2015). In another estimated calculation about the OOP cost of imatinib in 2014, the annualized OOP costs were estimated at \$8359 (Kantarjian et al., 2014). Since 2015, additional second-generation tyrosine kinase inhibitors have become treatment options for CLL. Yet the yearly cost of these second-generation therapies has climbed to more than \$100,000, accompanied by a higher range of OOP costs to the patient (Dusetzina et al., 2014).

Some estimates have these OOP costs as much as ten times higher than OOP costs for other medications partially covered on the insurer's formulary (Hoadley et al., 2015b). OOP costs can escalate based on whether the price of the medication is based on classification as generic or brand drug and whether the medication is on the insurer's formulary as a covered medication (Rotenstein, Dusetzina & Keating, 2018). Moreover, the increase in cost-sharing for more expensive oral specialty drugs has escalated from 3% in 2004 to an estimated 25% in 2013 (Meisenberg 2015). Further, Davidoff and colleagues estimated that 50 % of Medicare beneficiaries with a cancer diagnosis spend at least 10% of their income on OOP costs of their cancer treatment (Davidoff et al., 2013).

The Medicare Donut Hole

Most Medicare patients participate in Medicare Part D, a prescription drug benefit, which provides coverage for medications through commercial insurance plans. Conversely, non-Medicare patients may or may not have a prescription drug benefit (Printz, 2014). Even if medications are covered under a plan, Medicare Part D or otherwise, prescription coverage varies widely (Hoadley et al., 2015b). For example, in 2018, once a Medicare patient enrolled in Part D hits the plan's initial deductible and coverage limits, they become responsible for paying drug costs until they meet the annual out-of-pocket threshold. This period when costs are the responsibility of the patient is called the coverage gap, also referred to as the "donut hole". For example, in the case of specialty drugs, costs quickly escalate and land a patient in the donut hole. Only after

their OOP expenditures then reach the upper threshold established for the donut hole will the insurer resume payment for a percentage of those costs (Medicare, 2018).

In 2018, the donut hole threshold was \$3820. Due to changes in Medicare coverage due to the Bipartisan Budget Act of 2018, provisions related to the donut hole will change. Among factors that affect the cost of drugs to the Medicare Part D beneficiary include the beneficiary's income, whether the medication is brand or generic and some additional cost breaks to the beneficiary by the drug manufacturer.

With the donut hole calculation ending for Part D beneficiaries, the change in how medications are charged to the patient is expected to benefit patients required to pay the bulk of their prescription costs until they reach the limit of costs established in the hole (Medicare, 2018). With the elimination of the donut hole, it is not yet clear how Medicare Part D will cover specialty medications, including oral cancer therapies (Cubanski, Rae & Panchal, 2018). It seems likely that patients, Medicare and non-Medicare, will continue to bear increasing responsibility for the costs of oral cancer therapy due to their insurer's prescription drug benefit limits (Printz, 2014).

Cancer Treatment and Distress

Among the many stresses associated with a cancer diagnosis are pain, suffering and the fear of death. For patients who have gone through treatment and are considered survivors, they also experience distress that includes fear of recurrence, physical challenges from rehabilitation after treatment (i.e., a new normal), financial concerns related to continued clinical follow-up and the prospect of more treatment (Massa et al., 2018; Nipp, Sonet & Guy, 2018). Studies confirm that cancer patients in treatment--or

after treatment--report decreased quality of life (QOL) due to factors associated with FT (Kale & Carroll, 2016; Delgado-Guay et al., 2015). These patients or cancer survivors are at risk or suffer from depression and various anxiety disorders (Kale & Carroll, 2016). To establish clarity about the impact that FT has on patients, Gordon and associates conducted a systematic review of FT and cancer patients, covering 25 studies published from 2013-2016. From this review, the most common factors associated with FT included being female, having a low income, being treated with additional therapies after standard treatments and a recent diagnosis (Gordon et al., 2017).

Cancer Care, Financial Toxicity and Distress

Since patients treated for cancer have been shown to be at higher risk for FT than non-cancer patients, FT is of particular clinical concern in cancer care (Soni, 2015). In addition to the cost of cancer therapies, the cost of supportive therapies, which reduce neutropenic, nausea and vomiting, and anemia can also be high and have increased (Ell et al., 2008).

A cancer patient's distress, responding to the cost of cancer diagnosis and treatment, can be amplified by the additional burden of FT (Kale & Carroll, 2016). For patients in distress from FT, this distress can appear as worry, anxiety and/or depression (Massa et al., 2018; Chino et al., 2017). Already challenged by the complexities of getting through treatment, the stress of paying medical bills is common among these patients, with studies estimating that 20-64% of cancer survivors reporting financial stress and burden (Guy et al., 2014, Guy et al., 2013: Bernard, Farr & Fang, 2011).

A cross-sectional study of 120 insured patients with cancer explored the relationship between financial distress, emotional symptoms and overall distress. The data, gathered from the InCharge Financial Distress/Financial Well-being Scale and the National Comprehensive Cancer Network's Distress Thermometer, showed that 65% of respondents had clinically significant overall distress scores accompanied by at least one emotional symptom (i.e., worry, depression, anxiety). The study also reported that due to financial concerns, 40% of the sample needed to continue working to pay for treatment and medical bills (Meeker et al., 2016).

Davidoff and colleagues surveyed 1868 Medicare beneficiaries from 1997-2007 (n = 10,047). These patients spent a greater proportion of their incomes, often fixed, on medical costs compared to those not diagnosed with cancer. Beneficiaries with cancer had statistically significant mean higher OOP costs (\$4,727) compared to those without cancer (\$3,209) ($p < .001$) (Davidoff et al., 2013).

In a 2015 review of literature about financial hardship and cancer treatment focusing on 13 studies published between 2011-2014, McNulty and Khera determined that patients are carrying more of the costs of cancer treatment. Based on their review of studies, they identified risk factors associated with FT as patient and family sociodemographics, employment and cancer diagnosis-related factors. Consequences of FT included patient and family disability status, loss of income, lifestyle changes due to reduced income and effect on cancer treatment—including nonadherence or discontinuing cancer treatment (McNulty & Khera, 2015).

Cancer Patients and Financial Toxicity

Current evidence examining the effect of FT on cancer patients is limited in scope and consistency. Researchers use various methods and measurements and instruments, including some unvalidated surveys and questionnaires. Examples include the Health-Related Quality of Life (HRQOL), the Edmonton Symptom Assessment System (ESAS), the Hospital Anxiety and Depression Scale (HADS), the Functional Assessment of Cancer Therapy-General (FACT-G), the Comprehensive Score for Financial Toxicity (COST instrument), health plan claims, medical record reviews, SEER Medicare data and Medical Expenditure Panel Survey Data. These studies include a wide variety of variables, disparate sample populations (advanced cancer patients, cancer survivors, specific cancer diagnoses, older cancer patients) and frequently targeted sites limited to just one health care system (Wheeler, Spencer & Pinheiro, 2018; deSouza et al., 2017, Winn, Keating & Duestzina, 2016; Delgado-Guay et al., 2015; Huntington et al., 2015). As a result, comparisons across studies are challenging. Therefore, as Meisenberg stated in his 2015 commentary, it is difficult to establish the impact of financial hardship for those patients undergoing treatment as well as those who have completed treatment (Meisenberg, 2015). Two studies stand out as examples, however.

First, Yabroff and colleagues analyzed the experience of 1,202 cancer survivors with financial hardship, based on survey results from the 2011 Medical Expenditure Panel Survey (MEPS) Experiences with Cancer questionnaire. Respondents reported financial hardship due to their cancer diagnosis if they had filed for bankruptcy, had problems paying their medical bills, had borrowed money or had to adjust their finances

due to cancer treatment. The analysis showed that younger cancer patient survivors (18-64 years old) experienced more financial hardship (28.4%) than older cancer survivors (> 65 years; 13.8%). Those younger survivors, who were uninsured and had lower family income, experienced more psychological financial hardship (Yabroff et al., 2016).

Ekwueme and colleagues studied costs of cancer for survivors. For the period 2008–2011, male cancer survivors had mean annual health care expenditures of \$8,091, compared with \$3,904 among males with no cancer history. Study results for female survivors had mean annual medical expenditures of \$8,412, compared with \$5,119 among women without a cancer history. (Ekwueme et al., 2014).

Out-of-Pocket (OOP) Expenses

OOP expenses are considered any expense or bill that is the responsibility of the patient and not covered by health insurance or outside sources of health expense coverage. These OOP expenses can be deductibles and copayments that insurance does not cover. They also can be the expense of access to ongoing medical care, which can include transportation, hotel, food, medications not covered by insurance (Cabrera et al., 2018; Altice et al., 2017; Chino et al., 2017).

Cancer survivors have reported higher OOP spending on healthcare than non-cancer survivors. In a review of medical and productivity costs of cancer survivors from 2008-2011, Ekwueme and colleagues estimate that ongoing medical bills for those diagnosed with cancer are 160-260% higher than noncancer patients (Ekwueme et al., 2014).

McNulty and Khera's 2015 MEDLINE literature review of articles published 1986-2014 about financial hardship and cancer treatment compiled risk factors and consequences of FT to patients and families. Among the risk factors were patient and family socio-economic status, employment, logistics to get to and receive treatment and the stage and trajectory of disease. Consequences from FT included decreased adherence to treatment, lifestyle changes (avoiding purchases, reduced spending on food and staples in the household), borrowing money and bankruptcy (McNulty and Khera, 2015).

A 2017 study of 400 breast, colo-rectal, lung and prostate patients in rural Australia documented that 21 weeks after their cancer diagnosis, 11% had spent more than 10% of their household income on treatment-related costs. For this sample of patients, OOP costs were on average \$2,179AU (2018 AUD dollars were 1.39 > US dollars) (Newton et al., 2018). Rotenstein and colleagues conducted a retrospective analysis of commercial insurer prescription drug claims for seven years for 13 FDA approved oral oncolytics. The range of monthly OOP costs representing monthly prescriptions for 44,113 patients was found to be a range of no cost to as high as \$14,157 with a mean monthly per prescription cost of \$82.82. The mean monthly OOP was \$2,901 (Rotenstein et al., 2018). Based on data from a 2008–2012 MEPS, Guy and colleagues compared 4,271 adult cancer survivors with 96,780 individuals without a history of cancer to determine their OOP cost burden. The analysis showed that cancer survivors were more likely to report high OOP expenses, especially when they were poor

(18.4%). In addition, cancer patients were more likely to delay medical care (21.6%) or delay medical care (19.2%) (Guy et al., 2014).

Out-of-Pocket Costs as Source of Distress

A 2018 qualitative study by Ferrell and associates confirmed that from the patient and family member perspective, financial distress can be more distressing even than the physical, emotional and spiritual distress from cancer and its treatment. The study results were based on a convenience sample of 20 family caregivers of cancer patients with solid tumors, who were interviewed one time for 20-40 minutes each as part of a larger randomized trial about support interventions. The caregivers described their own physical, psychological, social and spiritual wellbeing and financial strain related to the patient's cancer diagnosis and treatment. The researchers reported that caregivers had extensive financial concerns; most said they were struggling to pay for care as OOP expenses, pay household bills and maintain their credit. They stated among the costs associated with medical care were last minute airplane flights, gasoline, overnight hotel stays, restaurant meals and vehicle maintenance. For caregivers with self-reported financial stability with adequate healthcare coverage, they also stated they were anxious about their ability to cover future health care expenses (Ferrell et al., 2018).

Financial Hardship

In an analysis of 19.6 million cancer survivors from 2011 MEPS data, 28.7% reported financial burden due to cancer diagnosis and treatment. Respondents reported that 7.6% had borrowed to pay their bills or incurred debt, with 4.2% borrowing less than \$10,000 and 3% borrowing more than \$10,000. Of the respondents, 1.4% had declared bankruptcy. Approximately 21% of these cancer survivors were worried about their

medical bills, especially as they mushroomed, with 11.5% stating they could not cover their medical bills. Based on accompanying physical and mental component scores, those with financial challenges had increased depression and worried more about recurrence (Kale & Carroll, 2016).

Using a 2012 LIVESTRONG database of 4,719 cancer survivors, Banegas and colleagues determined that approximately one-third of cancer survivors had gone into debt, and 3% had filed for bankruptcy. Of those going into debt, 55% of respondents had a debt of \$10,000 or more (Banegas et al., 2016).

Zheng and associates analyzed MEPS data from 2008-2012 to determine the economic burden experience by cancer survivors: breast (n = 1568); prostate (n = 1170) and colorectal (n = 540). That burden experience included high medical bills and lost productivity (missed work; days in bed). Their analysis indicated that cancer patients experience a statistically higher economic burden compared with those without a cancer history (Zheng et al., 2016).

From a pilot study Zafar and colleagues reported about OOP costs and the FT experience of 246 cancer patients with solid tumors. They reported that 42% of patients receiving chemotherapy or hormonal therapy reported significant financial burden associated with their OOP expenses. For those who did not receive financial assistance with the OOP costs of their treatment, their median monthly OOP cost for cancer treatment was \$708. Not surprisingly, results indicated that FT increased when patients were non-white, lower income and had higher psychosocial distress (Zafar et al., 2013).

In a study of 2,494 women surveyed from the Carolina Breast Cancer Study through the North Carolina Cancer Registry (2008-2013), Black women treated for breast cancer experienced worse financial impact when compared to white breast cancer patients. Based on the study's multivariable logistic regression analysis, black women experienced significantly worse financial impact during their cancer treatment. Additional factors affecting the experience of FT included loss of job and income and challenges with transportation (Wheeler et al., 2018).

Financial Toxicity and Quality of Life

Studies have explored relationships among the experience of FT, patient's decreased QOL and patient mortality. Zafar and colleagues have proposed factors that may be associated with cancer patients experiencing a perception of high FT that affects mortality (Zafar, 2016). These factors include decreased QOL, poorly-perceived wellbeing (defined as an "undesirable lifestyle") and less care due to OOP costs (less care associated with non-adherence to prescribed treatments) (Zafar, 2016). Additional studies have looked at copay thresholds, when cancer patients may decide not to take prescribed medications given orally because they cannot afford the OOP cost of treatment (Dusetzina et al., 2013).

In a cross-sectional study by Delgado-Guay and associates, which evaluated overall suffering and QOL in 144 advanced cancer patients treated at a comprehensive cancer center and a public hospital in Texas, more than 30% of patients reported that financial distress was more than physical distress or distress from family relationships or emotional distress. Study data was compiled from validated depression, functional

assessment QOL and social support instruments. Moreover, study results reported that patients treated at the public hospital had twice the financial distress compared to those treated at the cancer center.

According to this study's results, distress manifested as depression, anxiety and that the patient's perception of QOL had deteriorated. The authors went on to report that for patients with advanced cancer, financial distress is rarely evaluated or reported. Delgado-Guay and associates suggest that the impact of financial distress is not yet quantified related to other distress-related factors during diagnosis and treatment (Delgado-Guay et al., 2015).

In a 2014 observational, cross-sectional study by Chino and associates of 174 advanced cancer patient perception of financial burden, 47% reported significant or catastrophic financial burden. The study results suggest that addressing the financial burden with cancer patients can affect their general satisfaction with the quality of their cancer care and may positively affect adherence to treatment and patient QOL outcomes (Chino et al., 2014).

Financial Toxicity Non-Adherence to Treatment

A few studies have established a relationship between health care decision-making tempered by financial distress. These decisions have resulted in patients taking less than their prescribed medications, less monitoring of treatment side effects, less attention to signs of recurrence, lifestyle changes that avoid regular primary care visits, eating less healthy diets and exercising less regularly. These behavior-based decisions

impact whether cancer patients can do well when treated for their malignancies (Wheeler et al., 2018; de Souza et al., 2017; Bestvina et al., 2014).

Desetzina and colleagues reported in a 2014 analysis about patient adherence to imatinib, a tyrosine kinase inhibitor, used as a treatment for patients with CML. They reported 2002 thru 2011 data from large employers, health plans and government insurers for 1,541 patients with initial insurance coverage for the treatment. The monthly copayment for the medication averaged \$108 with a range of copayments \$0 to \$4,792. The study data suggests that when OOP costs of the treatment were higher, patients had lower adherence to the treatment, estimating 42% of patients were more likely to be nonadherent to the treatment with higher copays. Therefore, patients with higher copayments were more likely to be nonadherent or discontinue treatment. Moreover, 70% of the respondents were most likely to stop taking the therapy within six months of starting therapy when the monthly co-pay was more than \$53 (Desetzina et al., 2014).

From a cross-sectional survey of 164 patients participating in a copay assistance program and treated for solid tumor malignancies 2019-2011, Zullig and colleagues reported that 45% of the patients reported not adhering to prescribed prescriptions due to the cost of treatment. This non-adherence included not filling their prescriptions, taking less than the prescribed treatment or taking medication that was prescribed for others. The results also indicated that those who were non-adherent to the prescribed treatment spent less of their household income on food and clothing and were more likely to use credit cards to pay for medication (Zullig, Peppercorn & Schrag, 2016).

Winn and associates evaluated the affordability of anti-cancer therapies (tyrosine kinase inhibitor) given orally for CML. Using the SEER-Medicare database from 2007-2011 of 393 patients, only 68% started therapy within three months of diagnosis. The researchers suggested that the OOP costs may prevent patients from starting therapy as prescribed. From the study, factors contributing to nonadherence to treatment decreased with age, especially for patient 80 years or older (Winn et al., 2016).

Finally, in a 2014 cross-sectional survey study at Duke Cancer Institute, 300 patients during 2012-2013 were asked if they had discussed with their oncologists the OOP costs for their cancer treatment given orally. Only 19% of them reported they had discussed costs with their oncologist. As to OOP cost of the therapy affecting whether they followed the medication instructions as prescribed, 27% stated they did not follow through taking the medication as prescribed, 14% stated they missed medication doses and 11% stated they took less than the medication prescribed—all due to the cost of the medication (Bestvina et al., 2014).

Gap Analysis

This study attempts to fill a gap in what is known about the experience of FT for patients treated for cancer with therapies given orally and the relationship of that experience with the patient's perception of distress and adherence to the prescribed treatment. Few studies have focused on FT experienced by cancer patients. In September 2017, a search of the PubMed database of studies from the past ten years resulted in few studies about FT and cancer (44), financial hardship and cancer (61) and financial distress and cancer (44). This accounting of studies compared with a PubMed search not linked to

the word “cancer” of FT (55), financial hardship (433) and financial distress (152) (Carrera et al., 2018).

A 2016 systematic review of the previous six years of peer-reviewed studies looked at the cost of illness and its effect on cancer patients. The review confirms that FT studies lack consistency of rigor in their design and methods (Gordon et al., 2017). Gordon’s review identified 25 relevant studies, with only 15 from the United States. Eighteen studies were cross-sectional; the remainder of studies were prospective or retrospective cohort studies. The study measures varied with some reporting FT as a subjective measure, with 15-73% of respondents reported experiencing FT. Objective measures of FT included non-adherence to treatment, delays in starting treatment, not proceeding with treatment and changes in insurance coverage affecting the patient’s experience of FT. This systematic review confirms there are precious few rigorous studies about FT with cancer patients and any comparison of data or conclusion across studies is problematic (Gordon et al., 2017).

To date, studies of FT in cancer patient populations have adopted various study designs, procedural methods and data analysis. In general, studies have had small sample sizes or have performed secondary data analysis, extracting data about patients’ financial toxicity experience based on broad interpretations (Gupta et al., 2018; Huntington et al., 2015; Pelletier & Bona, 2015; Delgado-Guay et al., 2015).

The literature review for this study confirms that measuring FT in cancer patients is a new focus of clinical care. Only one measurement instrument, the Comprehensive Score for Financial Toxicity (COST), has a published evaluation of its reliability and

validity (deSouza et al., 2014). Otherwise, the assessment of FT in cancer patients is based on a broad list of instruments. Without a focus on FT, many instruments are not established as reliable, without published psychometric evaluations related to FT and specific populations (Gupta et al., 2018; Pelletier & Bona, 2015; Delgado-Guay et al., 2015; Chino et al., 2014; Bestvina et al., 2014). In some studies, there has been a focus on evaluating clinical depression or anxiety as equivalent to the experience of FT and distress (Kale & Carroll, 2016; Meeker et al., 2016). Data has also been gathered from surveys, the medical record or large insurance claim or cancer-registry data bases (Yabroff et al., 2016; Chino et al., 2014; Guy et al., 2014; Guy et al., 2013; Wheeler et al., 2013).

Several thought leaders in the emerging field of FT have weighed in with insightful commentaries about the need to further study FT and its relationship with the patient's psychosocial status and adherence to treatment (Meisenberg, 2015; Zafar, 2015; Kantarjain et al., 2014; Light & Kantarjian, 2013; Ubel, Aberneth & Zafar, 2013). But those commentaries refer to few published studies based on clinical data, with their commentaries urging the need for further research. They state that a foundation to build effective interventions to address FT requires clinical attention and study. Data-based studies form the foundation for clinical care, which can lead to more open discussions between patients and their providers about the value of treatments within a care plan. Studies also can serve as a foundation for more effective decision-making and guidelines for standards of care (Santacroce, Tan & Killea, 2016; Delgado-Guay et al., 2015).

Moreover to date, FT studies do not focus on cancer patient populations with any specificity or acknowledgment of complexity. These studies are limited in their insights about cancer patients with a particular diagnosis, stage of their cancer, choice of novel treatments, time or duration of their treatment or survivorship status (Wheeler, et al., 2018; McNulty & Khera, 2015). Analysis of health care expenditures associated with insurance carriers provide some understanding of the financial burden of care. But little is known about FT when insurance coverage changes, when those changes affect the patient's OOP costs and financial burden (Gupta et al., 2018; Fessele, 2017; Fenn et al., 2014).

Summary of Literature

This review of the literature related to FT in cancer patients confirms a challenge to patients undergoing treatment that is becoming more concerning. Moreover, the high costs of cancer therapies given orally have become more the responsibility of the patient (KFF, 2018; Guy et al., 2015; Hoadley, 2015a). These OOP costs are the source of distress to patients, as evident by patients' reports of more worry, depression and anxiety (Massa et al., 2018; Chino et al., 2017; Delgado-Guay et al., 2015).

Studies about FT associated with cancer treatment have focused on financial burden of treatment (Guy et al., 2013; Guy et al., 2014; Bernard et al., 2011). To define the components and impact of FT, studies have used a variety of study designs, measurement strategies and instruments (Gupta et al., 2018; Huntington et al., 2015). Some FT measurement instruments have been evaluated for reliability and validity of findings (deSouza et al., 2017). The majority of studies have not used reliable

measurement instruments that can produce reliable, valid data (Gupta et al., 2018, Pelletier & Bona, 2015; Delgado-Guay et al., 2015. Chino et al., 2014; Bestvina et al., 2014).).

The first documented reliable FT instrument to produce valid data is the COST. Since it is the first FT instrument tested as reliable, use of the COST instrument is a method to establish standard FT measurement across different studies (deSouza et al., 2017).

Gaps in what is known about the relationship of FT to the experience of patients treated for cancer include the nuances of financial distress and adherence to treatment, decision-making and patient preferences about their plan of care (Santacroce et al., 2016; Delgado-Guay et al., 2015). Those who have studied FT recommend establishing coherence in the approach to FT, understanding the context in which FT occurs and conducting more studies with robust designs using reliable measurements and instruments (Carrera et al., 2018; Altice et al., 2017). Yet no studies to date have studied cancer patients receiving therapies given orally and the relationships to their adherence to prescribed treatment, their experience with FT and their perception of distress.

To better inform health care professional discussions with patients about treatment and their impact on patients and their family members, this study intends to better describe the participant experience of FT and its relationship with patient distress and non-adherence to treatments given orally.

CHAPTER III

METHODS

This chapter includes a discussion of the study design; a description of the population, study procedures for participant recruitment and data collection, and the plan for data management and statistical analysis.

Purpose and Specific Aims

The purpose of this study was to describe the relationships between the patient experience of financial toxicity (FT), patient perception about distress and patient adherence to prescribed therapy in a sample of cancer patients treated with therapy given orally.

Study Design

This study used a descriptive cross-sectional correlational design to describe the relationships between the patient experience of FT, patient perception about distress and patient adherence to prescribed treatment in a sample of cancer patients treated with therapy given orally.

Sample

The sample of participants had received or are receiving treatment for hematologic and solid tumor malignancies given orally.

The inclusion criteria for participants were adult patients (21 years or older) who are Spanish or English speaking, have the ability to read English and have an initial

diagnosis of these malignancies: Breast cancer, head and neck cancer, Hodgkin's Lymphoma, lung cancer, leukemia, lymphoma, melanoma, multiple myeloma, myeloproliferative neoplasms, pancreatic cancer and prostate cancer. Participants' oncologists had prescribed a cancer treatment regimen for at least four weeks and given orally. The participants' health insurance coverage included private health insurance or coverage by Medicare (Medicare Fee for Service (FFS), Medigap or Medicare Part C (Advantage)).

The exclusion criteria for study participants included patients who had not been prescribed cancer treatment given orally (i.e. infusion only, radiation and/or surgery only) and those receiving in-patient cancer treatment. In addition, excluded study participants were those covered by Medicaid or those without health insurance coverage.

Setting

The patient education/advocacy organization Patient Power® was the setting for the study. Patient Power® provides education, information, resources and support to patients diagnosed with cancer, their family members and caregivers.

Patient Power® is a service of Patient Power®, LLC, based in Carlsbad, CA with members participating from around the world (Patient Power, 2018). In 2005, two health communications pioneers, Andrew and Esther Schorr, founded Patient Power®. The Schorrs have extensive professional and career experience in healthcare communications. Moreover, their commitment to Patient Power® is based on their own experience with cancer: Andrew is a two-time cancer survivor (chronic lymphocytic

leukemia (CLL); myelofibrosis (MF). He was first diagnosed in 1996. Esther has been his care partner over 20+ years.

The foundation for Patient Power®'s communication and exchange is its open-access web site: www.patientpower.info. As of September 2018, Patient Power had approximately 23,000 contactable community members. For a participant to become a contactable community member (registered, receiving a free subscription to Patient Power's information and resources), the participant is required to register (establish a password and submit the participant's e-mail address to Patient Power®). With membership, the participant receives e-Alerts and invitations to online and in-person events.) Tables 3-1 shows the demographics of the Patient Power® membership. Table 3-2 provides a breakdown of its membership.

In 2018, the Patient Power® site had approximately 70,000 visits to the site per month. Patient Power® also builds traffic to its site from its Facebook community page (35,000 visits/week) and from additional website platforms: LinkedIn, Twitter, and other social media channels.

Patient Power® follows HIPAA privacy guidelines to protect membership data. It complies with the HONcode Standard for trustworthy health information. It is in partnership with major medical institutions and advocacy groups to continually ensure the veracity of its information and resources. Among its collaborative partners for education and advocacy are the Leukemia and Lymphoma Society, CLL Research Foundation, Myeloma Crowd, MD Anderson Cancer Center and City of Hope National Medical Center.

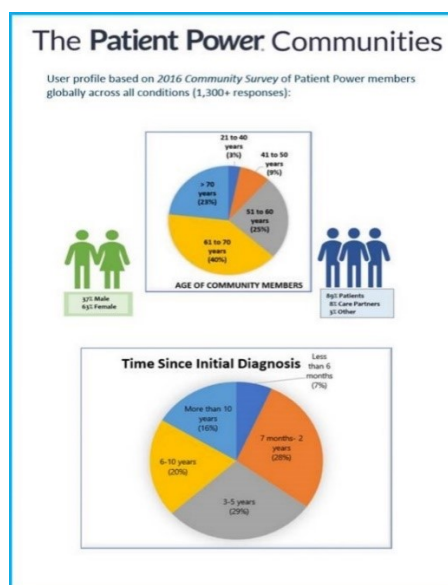


Figure 3-1
Patient Power® Community Demographics (2016)
(Used with Permission, Patient Power®)

Subscriptions	
Topic	TotalCnt
Chronic Lymphocytic Leukemia	6396
Multiple Myeloma	3808
Myeloproliferative Neoplasms	3611
Care Partner Center	1831
Non-Hodgkin Lymphoma	1151
Lung Cancer	1092
Chronic Myelogenous Leukemia	1039
Prostate Cancer	818
Acute Myeloid Leukemia	696
Hodgkin Lymphoma	669
Acute Lymphoblastic Leukemia	495
Breast Cancer	489
Phenylketonuria	365
Melanoma	313
Pancreatic Cancer	225
Head and Neck Cancer	181
Leukemia	95

Figure 3-2
Patient Power® Member/Subscriptions (2018)
(Used with Permission, Patient Power®)

Sample Size

This study's target sample size was based on an *a priori* analysis from three previous studies about FT as a clinical factor in patient care (Gupta et al., 2018; Shankaran et al., 2018; Huntington et al., 2015). Samples from those studies included sample sizes of 118, 34 and 100 patients. In addition to supporting a target sample size, a power analysis was calculated using G*Power version 3.1.9.2. The G*Power calculation used a medium effect size of 0.15, based on a one-way independent analysis of variance (ANOVA) at 0.95 power, eight anticipated predictors and significance of 0.05. The G*Power calculation resulted in 89 participants. Therefore, taking into account previous study samples, the G*Power calculation and anticipated incomplete, missed and outlier data, this study's sample size was targeted at a minimum of 120 participants for responses to contribute to the data analysis.

Protection of Human Subjects

The study was reviewed by the Institutional Review Board of the University of San Diego. (Appendix A.) This review confirmed that study participants were recruited according to the National Institute of Health (NIH) guidelines Protecting Human Research Subjects (NIH, 2018). The study design did not present inherent adverse physical effects or undue burden for the participants.

Study Procedures

Recruitment of Participants

The study investigator recruited a convenience sample of participants by accessing participants (patients only) from the Patient Power® community. With permission from the Patient Power® site administrator, the study investigator posted information about the study (including the inclusion/exclusion criteria) on the Patient Power® website. (Study Blurb: Appendix B.) If potential participants were interested in reviewing more information about the study or proceeding to sign up as a study participant, the study instructions guided interested members from the Patient Power® community to proceed via link to Website #1, managed by the investigator, with more information about the study and procedures provided about joining the study (Appendix C, Web site #1 content.).

On Website # 1, the Study Investigator provided potential interested participants with a study synopsis, FAQs about the study and the Study Investigator's contact information if potential participants had questions or need further clarification about the study. Website #1 also included instructions to sign up for the study, which included instructions to complete the informed consent and the informed consent itself.

If after reviewing the study information on WebSite #1, the participant did not want to participate in the study, there was no further contact with the Patient Power® member.

Data Collection

When a participant responded that he/she wanted to sign up for the study (signed informed consent posted), the Study Investigator contacted the participant via e-mail with instructions to proceed to a participant password-protected site to complete the three study instruments (Appendix D. Web site #2). Web site #2 (Advantage Survey Monkey platform) included the study synopsis (again), contact information about the Study Investigator and instructions to proceed to complete surveys listed in Appendix E, F and G. Participant's responses were automatically entered into a .csv file within Advantage Survey Monkey® and only accessible to the investigator.

At all times, participation in the study remained voluntary. Participants could choose to answer only those questions they chose to answer.

Data Management

To secure the data and ensure confidentiality, participants and their survey responses were deidentified. The study investigator accessed participant data and survey results from a password protected file, provided by the Advantage Survey Monkey® platform (<https://www.surveymonkey.com>). The .csv file was uploaded to the investigator's computer. Files of the dataset were stored in a secured environment (lockable computer system with passwords).

To prepare the data for analysis, the Study Investigator reviewed and cleaned the data, accounting for missing, invalid or outlier data. The data was coded to assess for

internal validity. Data was then transferred to the SPSS v26 Statistical Package for data analysis.

Study Measurements

Operational Definitions of Terms

As a review, here are operational definitions pertinent to this study:

Financial Toxicity (FT): In cancer care, the objective and subjective financial consequences of cancer treatment, which may include significant OOP costs, loss of income, and caregiver burden. Since 2011, the term *financial toxicity* also has been associated with patients diagnosed with cancer who face significant financial challenges related to precision medicine as a foundation for treatment (Carrera, 2017; Zhang, Hueser, & Hernandez, 2017).

Cancer Treatments given Orally: Molecular and genetically-based cancer treatments that are prescribed in oral form (i.e. not intravenous or intraperitoneal infusions) (Carrera, 2017; Zhang et al., 2017).

Perception of Distress: Perception of Distress is an unpleasant emotional state experienced by an individual, which may affect feelings, thoughts, and actions. It can include feelings of unease, sadness, worry, anger, helplessness, and guilt (NCCN, 2018).

Adherence to Treatment: Taking a prescribed medication or treatment exactly as prescribed, including dose or rate, schedule and formulation (Bestvina et al., 2014; Zullig et al., 2013).

Instruments

Demographic Questionnaire. The first instrument was the Demographics screen. It included standard demographic questions, including cancer diagnosis, gender, age, gross household income, level of education, employment status and insurance coverage, as well as questions about the participant's cancer therapy given orally. (Appendix E).

The study used two validated study instruments:

Comprehensive Score for Financial Toxicity (COST). The COST is a measurement instrument to assess a respondent's experience with FT (Appendix F.). It is an 11-item instrument that covers one financial question, two resource item questions and eight affect-focused questions about the respondent's experience with FT. Lower COST scores indicate higher levels of FT (DeSousa et al., 2017; DeSouza et al., 2014).

The COST measure demonstrates high internal consistency and test-retest reliability. Specifically, COST scores have been shown to correlate with income (correlation coefficient $r = 0.28$; $p < .001$), psychosocial distress ($r = 0.26$; $p < .001$), and in comparison to the Health-Related Quality of Life (HRQOL) instrument, as measured by the FACT-G ($r = 0.42$; $p < .001$) and by the EORTC QOL instruments ($r = 0.33$; $p < .001$) (DeSousa et al., 2017; DeSouza et al., 2014). The COST instrument has a Cronbach alpha value of $> .90$., confirming reliability and that it generates valid data (DeSousa et al., 2017; DeSouza et al., 2014).

The COST instrument is relatively new to research practice with a few studies reporting results when used (Huntington et al., 2015). In a 2013 study by Zafar and associates in two Chicago-area hospitals, the COST measure demonstrated high internal consistency and test-retest reliability when evaluating FT (Zafar et al., 2013c). Although considered a reliable instrument to evaluate FT in cancer patients, the COST is not yet widely used (Huntington et al., 2015).

National Comprehensive Cancer Network (NCCN) Distress Thermometer

(DT). The National Comprehensive Cancer Network (NCCN) Distress Thermometer and accompanying Problem List (DT) (Appendix G) has been widely used internationally and in a variety of clinical cancer patient care settings (NCCN, 2018; Baken & Wooley, 2011). The DT consists of a 1-10 scale (0 = no distress; 10 = extreme distress), identifying any source of distress to the patient. Scores of 4 or higher on the DT suggest clinically significant distress (Ploos van Amstel et al., 2017).

The DT has been shown to effectively assess distress in cancer patients (Mitchell, 2007; Donovan et al., 2014). Its reliability and validity as a measurement instrument has been demonstrated in 38 pooled studies, representing 14,000 patients with cancer. The pooled sensitivity of the DT has been established at 81% (95% CI, 0.79-0.82) at a cutoff score of 4 (Ma et al., 2014). The DT has a specificity of $\alpha = 0.70$ for detecting clinical levels of distress (Jacobsen et al., 2005).

When a patient's score is 4 or greater, the provider can further target the patient's distress by assessing the patient's response to the instrument's 39-item accompanying Problem List. From the Problem List, items are categorized in 5 areas: practical, family,

emotional, spiritual/religious and physical (NCCN, 2018). Under the Practical Problems category, Insurance/Financial is an option that the patient can choose to mark: yes or no. When the patient marks yes, the provider can follow-up on that problem area with education, support and resources (NCCN, 2018). Two studies have validated the DT instrument with the expanded Problem List, which includes Insurance/Financial as a Problem (positive predictive value: 39%; negative predictive value: 95%.) (Graves et al., 2007; Tuinman et al., 2008).

Data Analysis

All data analysis was performed using IBM SPSS Statistics, version 26.

The study's three aims and the statistical analysis plan for each aim follows:

Aim #1. To describe sociodemographic, clinical and financial characteristics, the experience of FT, perception of the level of distress, and adherence to treatment in a sample of adult participants who have received or are receiving treatment given orally for hematologic or solid tumor malignancies.

To meet this aim, descriptive statistics were computed for all study variables to determine the overall characteristics of the sample and the distribution of variables.

Aim #2. To describe relationships between participant sociodemographic, clinical and financial characteristics, participants' experience of FT, participants' perception of distress, and participants' adherence to treatment.

To meet this aim, the study analysis examined relationships between the covariates of participant sociodemographic, clinical and financial characteristics, participants' experience of FT, participants' perception of distress, and participants' adherence to treatment. Variables underwent bivariate analysis and modeling. Analysis was expected to control for the demographic characteristic. Variables were entered in the logistic regression model and examined for linearity, multicollinearity and outliers.

To establish potential associations between the study's variables (categorical), Pearson's Coefficient Correlation analysis was performed. Then nonparametric analysis (Spearman's Rank Order Correlation) was performed on selected variables to determine if any study variables had significant correlation not established with parametric analysis.

Aim #3. To explore the likelihood that participant experience of FT predicts participant perception of distress and non-adherence to the treatment given orally.

From the bivariate analysis completed for Aim #2, variables significant at $p < 0.5$ were to be entered in logistic regression models to determine the likelihood that participant experience of FT predicts participant perception of distress and/or non-adherence to the treatment given orally.

Strengths and Limitations of Methods

By using an on-line patient education/advocacy site to recruit study participants, the participants were self-selected as a) cancer patients, b) cancer patients treated with cancer treatments given orally, and c) cancer patients who were motivated to know and learn about their cancer, its treatment and the operational issues related to their treatment.

Participants recruited from the advocacy site, Patient Power®, were not representative of cancer patients, any standardization of insurance coverage for patients or were receiving treatments prescribed for all cancer patients.

CHAPTER IV

RESULTS

This chapter presents the results of the study, including a narrative description, supported by 25 tables supporting the data analysis. (Tables follow this chapter.) The analysis described the data, using descriptive statistics. Further analysis addressed each of the study's aims, establishing relationships among the study variables and whether the total COST instrument data (representing financial toxicity (FT) could predict patient distress or adherence to treatment.

The Study

This study employed a descriptive, cross-sectional design using convenience sampling and validated survey instruments. The study described characteristics about the sample, relationships among the sample's variables related to the experience of FT, perception of distress and adherence to prescribed cancer treatment given orally.

Data Collection

The study's data were collected on-line from 136 participants, who were members of the patient education/advocacy community, Patient Power[®]. Participants in the study were self-identified as diagnosed with a malignancy and prescribed a cancer treatment given orally. Participants completed three study instruments—the 27-question Demographic Questionnaire, the 11-item, Likert-scale Comprehensive Score for Financial Toxicity (COST) and the 0-10 scaled National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT). The study period was six weeks, March 1 to April 15, 2019.

The study investigator accessed the participant data and survey results from a password protected file, provided by the Advantage Survey Monkey® platform. All data files were uploaded to the investigator's computer and stored in a secured environment (lockable computer system with passwords).

To prepare the data for analysis, the Study Investigator reviewed and cleaned the data, accounting for missing, invalid or outlier data from all three study instruments. Pairwise deletion was the method used to account for any missing data during data analysis. Continuous data were evaluated through parametric testing; linearity was established via scatter plot evaluation.

The data was transferred to SPSS v26 Statistical Package for data analysis.

Study Aim #1

Aim #1

Based on the sample data, to describe sociodemographic, clinical and financial characteristics, the experience of FT, perception of the level of distress, and adherence to treatment in a sample of adult participants who have received or are receiving treatment given orally for hematologic or solid tumor malignancies.

Aim #1: Analysis

To address Aim #1, descriptive statistics, specifically frequencies and percentages, were calculated to provide a summary of the characteristics of the sample population and the measures captured in this study.

Demographic Characteristics

The study sample included 136 participants, who completed or partially completed the study's three on-line surveys. Tables 1a, 1b, 1c compile demographic characteristics about the study's participants. Participants completed the three surveys at one time. For some of the questions related to the COST instrument (FT) and the Distress Thermometer (DT), participants were asked about their perceptions at two time points: 1) Perceptions at one-week post start of treatment prescribed orally, and 2) Perceptions at six months post start of treatment prescribed orally.

More women (n =75, 51.1%) than men (n = 61, 44.9%) participated in the study. More than two thirds of the participants were > 65 years old (n = 93, 68.4%)—an age threshold expected since the study focused on participants diagnosed with malignancies more prevalent with age. In addition, many of the treatments for the cancer diagnoses represented in the study sample are treatments given orally.

The majority of participants were married or had a domestic partner (n = 112, 82.4%). Participants' educational backgrounds skewed to well-educated with almost one third completing some college credits (n = 48, 35.3%). Approximately two thirds of study participants had earned graduate credit and/or graduate degrees (n = 88, 64.7%).

Due to the age of the study participants, most participants at the time of the study period were not employed (n = 93, 74.4%). However, 54% of the study participants reported they were employed when they started their cancer treatment given orally (n = 67, 54%). Of the study participants, two thirds reported that their cancer treatment did not affect their employment (n = 80, 65.6%).

Clinical Characteristics

The most common diagnoses of the study participants were chronic lymphocytic leukemia (CLL) (n = 54, 41.5%) and multiple myeloma (MM) (n = 34, 26.1%), accounting for more than two thirds of the survey participants' diagnoses. The treatments that participants were prescribed in oral formulation were in keeping with the recommended or standard-of-care treatments for their cancer diagnoses. The most frequently cited therapies reported by the participants were imbrutinib (Imbruvica®), lenalidomide (Revlimid®) and ruxolitinib (Jakafi®). Most of participants (n = 118, 86.7%) reported that despite challenges to stay on their treatments given orally, they maintained their treatment dosing schedules.

Only 2.9% (n = 4) of study participants reported that they had skipped taking their cancer treatments given orally due to the cost of treatment. Few study participants reported that they had stopped taking their non-cancer medications (n = 5, 3.8%) or took some of their non-cancer medications (n = 5, 4.0%) or adjusted the dose of their non-cancer medication (n = 8, 6.5%) due to the cost of their cancer treatment (Table 4-1b).

Financial Characteristics

Almost three fourths of study participants responded that they financially supported themselves and a partner (n = 92, 75.5%). Another quarter of the participants responded that they were single, financially supporting only themselves (n = 28, 24.0%). Of those responding to the question about gross income, 70% of participants had a gross

income <\$100,000/year (n = 82, 70.0%) with the remaining participants reporting a gross income of >\$100,000/year (n = 35, 29.8%) (Table 4-1c).

Covering the Cost of Cancer Treatment Given Orally

The majority of the sample participants were covered by health insurance (n = 128, 98.4%), which fully or partially covered their cancer treatments given orally. Health insurance coverage represented in the sample included Medicare alone (n = 32, 27%), Medicare with Medigap coverage (n = 33, 27.5%), Medicare Advantage (a managed care coverage option for Medicare) (n = 7, 6%), and private insurance (n = 46, 39.0%). Most participants had prescription drug coverage, either Medicare Part D (n = 65, 56.0%) or private insurance drug coverage (n = 47, 40.5%) (Table 4-1b)

For study participants receiving financial support from pharmaceutical, foundation or other non-insurance sources to cover their treatment cancer costs, they were generally split between those who received support (n = 57, 46.3%) and did not receive support (68, 54.0%). Of note, approximately half of study participants did not respond to the question about the percentage of financial support received from non-insurance sources. For study participants who did respond about receiving non-insurance support for their treatment (n = 66, 52.8%), 27.2% (n = 34) received 50-100% support; 7.2% (n = 9) received 20-50% support and 10.4% (n = 13) received < 20% support (Table 4-1b).

After cancer treatments given orally were covered by insurance or non-insurance sources, 91% of study participants reported that they were responsible for < 20% of the cost (n = 52, 43%); 20-50% of the cost (n = 22, 18%) and 5-100% (n = 6, 5%). The

remaining participants (n =30, 16.5%) reported they were partially responsible for the cost of their treatment, based on copays and various OOP cost calculations. (Table 4-1b)

Participant Experience of Financial Toxicity

The COST instrument scores, which indicated participants' perception of their FT experience at one week and six months after the start of treatment, were analyzed as percentages, frequencies, means and standard deviations (SDs) (Tables 4-2a, 4-2b).

Comparing the total COST scores (n = 119) at the two time points, the means and range of scores were similar: at seven days post start of treatment (M = 25.13, SD = 5.154, range: 10-39); at six months post start of treatment (M = 25.17, SD = 5.614; range 8-39). (NOTE: Overall range of COST scores: 0-44; COST score cutoff for high FT = ≤ 24 ; for low FT = > 24 .)

For the eleven individual COST items scored on a 5-point Likert scale, Table 4-2a and 4-2b provide frequencies and percentages of responses. For participant perceptions at one week after cancer treatment began, COST items that prompted quite a bit or very much concern were “feel no choice about cost of care” (n = 89, 75.4%), “worry about future financial problems due to illness” (n = 70, 72.2%), “higher than anticipated out of pocket medical expenses” (n = 74, 67.1%), “reduced satisfaction in current financial situation due to cancer treatment” (n = 69, 58.5%), “ability to meet monthly expenses” (n = 60, 52.1%) and “overall financial stress” (n = 53, 45.7% (Table 4-2a).

For participant perceptions at six months after beginning their cancer treatment given orally, items that prompted quite a bit or very much concern were “feel no choice about cost of care” (n = 92, 80.0%), “worry about future financial problems due to

illness” (n = 80, 68.9%), “higher than anticipated out-of-pocket medical expenses” (n = 69, 59.4%), “reduced satisfaction in current financial situation due to cancer treatment” (n = 63, 56.7%), “ability to meet monthly expenses” (n = 59, 50%) and “overall financial stress” (n = 58, 49.5%) (Table 4-2b).

Out-of-Pocket Expenses

Of 115 study participants responding to the Demographics instrument questions about monthly out-of-pocket (OOP) expenses associated with cancer treatment given orally, 66% (n = 78) estimated < \$500/month OOP expenses and 34% (n = 40) estimated > \$500/month OOP expenses.

Study participants responded to the types of OOP expenses on both the Demographics and COST instruments (Tables 4-3, 4-4). From participant responses to the Demographics instrument question, participants’ OOP expenses included transportation (gas and parking) (n = 101, 86.3%), over-the-counter medications (n = 67, 57.2%), hotel costs (n = 35, 29.9%), lost wages (n = 23, 19.7%), miscellaneous costs (pet care, prescription medications, medical marijuana, meals and flights traveling to appointments, chiropractic/massage) (n = 6, 6.0%) and child care (n = 3 2.6%) (Table 4-3).

Financial Toxicity and Perception of Distress

Perceptions of high distress due to FT at one week post start of treatment given orally were 42% (n = 39) and 39% (n = 38) at six months post start of cancer treatment given orally. Of note, 32% of study participants (n = 44) did not respond to the one week

after treatment start question. For perception of distress at six months after start of cancer treatment given orally, 29% of study participants (n = 38) did not respond. (Table 4-4)

From the DT instrument questions about sources of cancer diagnosis-associated distress (categorized as practical, family, emotional, physical and spiritual problems), 55.7% (n = 64) of the participants cited insurance and financial problems as a source of distress (Table 4-5).

Financial Toxicity (FT) and Adherence to Treatment

From study participants responding to the question about adherence to cancer treatment given orally (n = 136), only 8% of participants (n = 11) reported that they stopped, interrupted or altered their prescribed cancer treatment given orally (Table 2).

Study Aim #2

Aim #2

From the study data, describe relationships between sociodemographic and clinical characteristics and

- 1) the participants' experience of FT (Sub Aim #1)
 - 2) the participants' perception of distress (Sub Aim #2)
- and
- 3) the participants' adherence to treatment prescribed orally (Sub Aim #3).

Aim #2: Analysis

The Pearson's Correlation Coefficient was calculated to evaluate bivariate correlation between total COST scores at the two time points and the DT scores at the two time points. (Tables 4-6). The Pearson's Correlation Coefficient was also calculated to evaluate any bivariate correlation relationships between COST scores at the two time points and selected demographic, clinical and financial characteristics—including adherence to treatment (Tables 4-7 through 4-25). Pairwise comparisons were calculated for selected demographic variables, for clinical variables and for financial variables (Tables 4-14, 4-15, 4-16).

Relationships between Financial Toxicity and demographic, clinical and financial variables

For Aim #2, Sub-Aim 1--to describe relationships between sociodemographic and clinical characteristics and the participants' experience of FT--based on Pearson's Correlation Coefficient analysis, weak statistically significant relationships were found, comparing total COST scores at one week and six months after start of cancer treatment given orally for these variables:

At seven days post start of treatment, COST scores to had a drug plan ($r = -.185$, $p = .035$) (Table 4-9); to affected employment ($r = .282$, $p = .002$) (Table- 4-11); and adherence ($r = -.260$, $p = .003$) (Table 4-13). NOTE: Using non-parametric analysis (Spearman's Rank Order Correlation), there also was weak correlation, COST Scores at seven days post start of treatment to OOP costs ($r_s = .259$; $p = .005$) (Table 4-11).

At six months post start of treatment, COST scores to had a drug plan ($r = -.201, p = .022$) (Table 4-10); to affected employment ($r = .326, p < .001$) (Table 4-12); and to adherence ($r = .245, p = .005$) (Table 4-13). NOTE: Using non-parametric analysis (Spearman's Rank Order Correlation), there also was weak correlation, COST Scores at six months post treatment to OOP costs ($r = .340, p < .001$) (Table 4-12)

For demographic variables, correlation coefficients were established between gender and age ($r = .301, p < .001$); gender and living status ($r = .224, p = .009$); and education to living status ($r = -.264, p = .002$) (Table 4-14).

For clinical variables, a moderate correlation coefficient was established between skipping cancer treatment and taking some of the prescribed non-cancer medications ($r = .600, p < .001$). Weak correlation coefficients were established between lowering the prescription of non-cancer medications and taking some of the prescribed non-cancer medications ($r = .386, p < .001$); and being covered by insurance and being covered by a drug plan ($r = .219, p = .013$) (Table 4-15). In addition, adherence was correlated to having a drug plan ($r = .345, p < .001$) (Table 4-24).

For financial variables, weak correlation coefficients were established between employed now and employed when started treatment ($r = .393, p < .001$); treatment affected employment and income support ($r = .238, p = .009$); income support and gross income ($r = .283, p = .002$); gross income and receiving help from pharmaceutical companies/foundations ($r = .354, p < .001$); gross income and percentage of help received from pharmaceutical companies/foundations ($r = .336, p = .001$); received help from pharmaceutical companies/foundations and OOP monthly costs ($r = .351, p = .001$);

and percentage help from pharmaceutical companies/foundations and OOP monthly costs ($r = .274$, $p = .003$). (Table 4-16). In addition, adherence was weakly correlated to income support ($r = -.055$, $p = >.001$) and gross income ($r = .188$, $p = .045$) (Table 4-25).

A strong correlation coefficient was established for received help from pharmaceutical companies/foundations and percentage financial help from those non-insurance sources ($r = .869$, $p = .001$) (Table-4-16)

For perception of distress and demographic, clinical and financial variables, the only statistically significant, albeit weak relationship was perception of distress at six months post start of treatment and the percentage of help from pharmaceutical/foundation sources ($r = .336$, $p = .001$) (Table 4-22).

Relationships between Financial Toxicity and Perception of Distress

For Aim #2, Sub-Aim 2--to describe relationships between the participants' experience of FT at the two time points and participants' perception of distress (DT)—there was no statistically significant relationship calculated in the sample, based on Pearson's Correlation Coefficient calculations.

Relationships between Financial Toxicity and Adherence to Treatment

For Aim #2, Sub-Aim 3--to describe the correlation between the participants' experience of FT and the participants' adherence to treatment, there was a weak negative correlation at both time points at one week ($r = -.260$; $p = .003$) and six months after start of cancer treatment given orally ($r = -.245$; $p = .005$) (Table 4-13).

Study Aim #3

Aim #3

Based on the sample data, to explore the likelihood that participant experience of FT predicts participant perception of distress and non-adherence to the treatment given orally.

Aim #3: Analysis

From frequency, distribution and univariate analysis of study data, both at one week and at six months from start of treatment given orally, there were no significant relationships between total COST scores and Distress Scores at either timepoint: seven days post start of treatment ($r = -.115, p = .276$) and at six months post start of treatment ($r = -.085, p = .405$). (Table 4-6). Therefore, a logistic regression model for FT level (via total COST scores) to predict perception of distress could not be calculated.

COST instrument scores were statistically significant related to adherence at seven days post start of treatment ($r = -.260, p = .003$) and at six months post start of treatment ($r = -.245, p = .005$). For both timepoints, there was a weak negative correlation, FT to adherence. Since FT and adherence were the only two variables, FT level (via total COST scores) could not predict adherence to treatment, based on a logistic regression model (Table 4-13).

**Table 4-1
Participant Characteristics**

**Table 4-1a
Demographic Characteristics**

	n	%
Gender	136	
Women	75	(55.1%)
Men	61	(44.9%)
Age	136	
50-64 years old	43	(31.76%)
>65 years old	93	(68.4%)
Living Status	136	
Married/domestic partner	112	(82.4%)
Single	24	(17.6%)
Education	136	
<12 the grade, some college	48	(35.3%)
Completed college/grad school	88	(64.7%)

Table 4-1b
Clinical Characteristics

	n	%
Cancer Diagnosis	130	
Chronic Lymphocytic Leukemia	54	(41.5%)
Multiple Myeloma	34	(26.1%)
Polycythemia Vera	5	(3.8%)
Essential Thrombosis	2	(1.5%)
Myelofibrosis	7	(5.4%)
Chronic Myelogenous Leukemia, Prostate, Breast, Lung (1 each)	4	(3.1%)
No response	24	(18.5%)
Oral cancer treatments	126	
<i>For CLL:</i>		
Imbrutinib (Imbruvica®)	54	(42.8%)
Venetoclax (Venclexta®)	8	(6.3%)
Acalabrutinib (Calquence®)	3	(2.3%)
<i>For MM</i>		
Hydroxyurea (Hydrea)	9	(7.1%)
Lenalidomide (Revlimid®)	33	(26.2%)
<i>For myelofibrosis, polycythemia vera</i>		
Ruxolitinib (Jakafi®)	10	(8.0%)
Other oral cancer treatments	13	(10.3%)
Currently Receiving Tx Given Orally	128	
Yes	109	(85.1%)
No	19	(14.8%)
On Treatment for Cancer Given Orally	136	
Stayed on	118	(86.7%)
Temporarily stopped	4	(2.9%)
Never started	7	(5.1%)
Stop other non ca meds	132	
Yes	5	(3.8%)
No	127	(96.2%)
Take some non ca meds	129	
Yes	5	(4.0%)
No	124	(96.1%)
Lower dose non ca meds	124	
Yes	8	(6.5%)
No	116	(94.0%)

Table 4-1b
Clinical Characteristics
(continued)

	n	%
Health Insurance	130	
Yes	128	(98.4%)
No	2	(1.5%)
Insurance Carrier	120	
Private/AARP	46	(39%)
Medicare	32	(27%)
Medigap	33	(27.5%)
Medicare Advantage (b)	7	(6.0%)
Tri Care, Medicaid (1 each)	2	(2.0%)
Prescription Plan	130	
Yes	122	(94.0%)
No	8	(6.1%)
Prescription Coverage	116	
Part D	65	(56%)
Private	47	(40.5%)
Part #, Tri Care (1 each)	2	(1.7%)
Advantage	2	(1.7%)
Responsible for Cancer Cost	121	
<20% of the cost	52	(43.0%)
20-50% of the cost	22	(18.0%)
50-100% of the cost	6	(5.0%)
Co pay (no amount)	10	(8.2%)
Clinical Trials	5	(4.1%)
Grants	3	(2.4%)
Donut, pay % overage	2	(1.6%)
All OOP	2	(1.6%)
Co pay \$10/mon	1	(0.8%)
Co pay \$25/mon	1	(0.8%)
Co pay \$ 40/mon	1	(0.8%)
Co pay \$50/mon	1	(0.8%)
Co pay \$150/mon	1	(0.8%)
Co pay \$200/mon	1	(0.8%)
Co pay \$500/mon	1	(0.8%)
Co pay \$2000	1	(0.8%)
No response/skipped	11	(9.0%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%).

Table 4-1c
Financial Characteristics

	n	%
Employed now	125	%
Fulltime/Part-time	32	(25.6%)
Not Employed	93	(74.4%)
Employed when started ca tx	124	
Yes	67	(54%)
No	57	(46%)
Tx Affected Employment	122	
Yes	42	(34.4%)
No	80	(65.6%)
Income support	120	
Self	28	(24.0%)
Self/partner/others	92	(75.5%)
Gross income	117	
<\$100,000/year	82	(70.0%)
>\$100,000/year	35	(29.8%)
Received Pharma/Advocacy Help	123	
Yes	57	(46.3%)
No	66	(54.0%)
% Support from Pharma/Advocate Groups	125	
<20%	13	(10.4%)
20-50%	9	(7.2%)
50-100%	34	(27.2%)
Don't know	10	(.8%)
Skipped	59	(47.2%)
Monthly OOP costs	118	
<\$500/mon	78	(66.0%)
>\$500/mon	40	(34.0%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n = 12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n = 18 (13.2%).

Table 4-2a
Experience of Financial Toxicity
COST Individual Item Scores
Participant Perception Seven Days after Start of Cancer Treatment Given Orally
Score range: 0-44 [n = responses; (%)]

Overall COST Score (n = 119)	Range	Mean	SD
	10-39 (29)	25.13	5.154

	0 Not at all	1 A little bit	2 Somewhat	3 Quite a bit	4 Very Much
I know that I have enough money in savings, retirement or assets to cover the cost of my treatment. (n = 117)	27 (23.1%)	21(18.0%)	23 (19.7%)	17 (14.5%)	29 (24.8%)
My out-of-pocket medical expenses are more than I thought they would be. (n =111)	16 (14.4%)	7 (6.3%)	21 (19%)	29 (26.1%)	45 (41.0%)
I worry about the financial problems I will have in the future as a result of my illness or treatment. (n =97)	3 (3.1%)	15 (15.5%)	19 (19.6%)	25 (25.8%)	45 (46.4%)
I feel I have no choice about the amount of money I spend on care. (n= 118)	2 (2.2%)	8 (6.8%)	19 (16.1%)	24 (20.3%)	65 (55.1%)

Table 4-2a
Experience of Financial Toxicity
COST Individual Item Scores
Participant Perception Seven Days after Start of Cancer Treatment Given Orally
Score range: 0-44 [n = responses; (%)]
(continued)

I am frustrated that I cannot work or contribute as much as I usually do. (n=114)	30 (26.3%)	13 (11.4%)	22 (19.3%)	13 (11.4%)	36 (32.0%)
I am satisfied with my current financial situation. (n=117)	38 (32.4%)	16 (13.7%)	29 (24.8%)	20 (17.0%)	14 (12/0%)
I am able to meet my monthly expenses. (n =115)	14 (12.2%)	7 (6.1%)	34 (29.6%)	25 (21.7%)	35 (30.4%)
I feel financially stressed. (n = 116)	22 (18.9%)	12 (10.3%)	29 (25.0%)	21 (18.1%)	32 (27.6%)
I am concerned about keeping my job and income, including work at home. (n = 107)	26 (24.3%)	13 (12.1%)	20 (18.7%)	18 (16.8%)	30 (28.0%)
My cancer or treatment has reduced my satisfaction with my present financial situation. (n= 118)	9 (7.6%)	19 (16.1%)	21 (17.8%)	23 (19.5%)	46 (39.0%)
I feel in control of my financial situation. (n = 116)	24 (20.6%)	26 (22.4%)	33 (28.4%)	23 (19.8%)	10 (8.6%)

COST = Comprehensive Score Financial Toxicity

Table 4-2b
Experience of Financial Toxicity
COST Individual Item Scores
Participant Perception Six Months after Start of Cancer Treatment Given Orally
Score range: 0-44 [n = responses; (%)]

Total COST Score	Range	Mean	SD
(n = 119)	8-39 (31)	25.17	5.614

	0 Not at all	1 A little bit	2 Somewhat	3 Quite a bit	4 Very Much
I know that I have enough money in savings, retirement or assets to cover the cost of my treatment. (n = 116)	29 (25%)	19 (16.3%)	26 (22.4%)	21 (18.1%)	21 (18.1%)
My out-of-pocket medical expenses are more than I thought they would be. (n = 116)	9 (7.8%)	17 (14.6%)	21 (18.1%)	26 (22.4%)	43 (37.0%)
I worry about the financial problems I will have in the future as a result of my illness or treatment (n = 116)	6 (5.1%)	13 (11.2%)	17 (14.6%)	20 (17.2%)	60 (51.7%)
I feel I have no choice about the amount of money I spend on care. (n = 115)	2 (1.7%)	3 (2.6%)	18 (15.7%)	20 (17.4%)	72 (62.6%)

Table 4-2b
Experience of Financial Toxicity
COST Individual Item Scores
Participant Perception Six Months after Start of Cancer Treatment Given Orally
Score range: 0-44 [n = responses; (%)]
(continued)

I am frustrated that I cannot work or contribute as much as I usually do. (n = 116)	29 (25%)	18 (15.5%)	22 (18.9%)	14 (12.0%)	33 (28.4%)
I am satisfied with my current financial situation. (n = 118)	38 (32.2%)	9 (7.6%)	39 (33.1%)	18 (15.3%)	14 (11.9%)
I am able to meet my monthly expenses (n = 118)	9 (7.6%)	20 (17.0%)	30 (25.4%)	25 (21.2%)	34 (28.8%)
I feel financially stressed. (n = 117)	16 (13.7%)	16 (13.7%)	27 (23.0%)	18 (15.4%)	40 (34.1%)
I am concerned about keeping my job and income, including work at home. (n = 113)	40 (35.4%)	13 (14.4%)	17 (15.0%)	14 (12.4%)	29 (25.7%)
My cancer or treatment has reduced my satisfaction with my present financial situation. (n = 111)	14 (12.6%)	16 (14.4%)	18 (16.2%)	17 (15.3%)	46 (41.4%)
I feel in control of my financial situation. (n = 117)	25 (21.4%)	20 (17.0%)	31 (26.4%)	23 (19.7%)	18 (15.4%)

COST = Comprehensive Score Financial Toxicity

Table 4-3

**Out of Pocket (OOP) Expenses
Responses to Demographics Survey
(Participants responding: n = 117)**

	n	%
Transportation	101	86.3%
Hotel	35	29.9%
Lost wages	23	19.7%
Child care	3	2.6%
OTC meds	67	57.2%
<i>Other:</i>		
Pet care	1	<1%
Prescription meds	1	<1%
Medical Marijuana	1	<1%
Meals when travelling	1	<1%
Flights	1	<1%
Chiropractor/massage	1	<1%

**Table 4-4
Distress Thermometer
(0-10 score)**

Levels of Distress

	@ 1 week Post Start of Treatment		@ 6 months Post start of Treatment	
	n	%	n	%
	92		97	
Low distress (1-4)	32	(35%)	39	(40%)
Medium distress (5-7)	15	(16%)	20	(21%)
High distress (8-10)	39	(42%)	38	(39%)

Missing data: Distress Thermometer: 7 days post start of tx, n = 44 (32.3%); 6 mons post start of tx, n = 39 (29%).

Table 4-5
Perceived Stresses
Responses to Distress Thermometer Instrument
(Participants responding = 115)

	n	%		n	%		
Practical Problems			Physical Problems				
Child Care	1	<1%	Appearance	53	48.1%		
Housing	14	12.1%	Bathing/Dressing	8	7.0%		
Insurance/Financial	64	55.7%	Breathing	27	23.5%		
Transportation	18	15.7%	Changes in urination	17	14.8%		
Treatment Decisions	27	23.5%	Constipation	33	29.0%		
Family Problems			Diarrhea	41	35.7%		
Dealing with children	9	7.8%	Eating	34	30.0%		
Dealing with partner	28	24.3%	Fatigue	74	64.3%		
Ability to have children	4	3.5%	Feeling swollen	31	27.0%		
Family health issues	41	35.7%	Fevers	8	7.0%		
Treatment Decisions	44	38.3%	Getting around	37	32.1%		
Emotional Problems			Indigestion	37	32.1%		
Depression	53	46.1%	Memory/concentration	64	55.7%		
Fears	66	57.4%	Mouth sores	13	11.3%		
Nervousness	39	34.0%	Nausea	29	25.2%		
Sadness	54	47.0%	Nose dry/congested	35	30.4%		
Worry	82	71.3%	Pain	59	51.3%		
Loss of Interest in usual activities	58	50.4%	Sexual	28	24.3%		
Spiritual/Religion			11	9.6%	Skin dry/itchy	61	53.0%
					Sleep	66	57.4%
					Substance use	7	6.1%
					Tingling in hands/feet	47	40.1%
					<i>Other</i>		
					Leg cramps	6	5.2%
					Skin Cancer	1	<1%
					Caregiver for Family	1	<1%
					Infections	3	2.6%
					Hot/Cold	1	<1%
					Taste of Food	1	<1%
					Falling	1	<1%
					Skin Eruptions/Rash	4	3.5%
					Arthralgia	1	<1%

Table 4-6
Correlations between
Total COST Score (Financial Toxicity)
and Total Distress Thermometer Score

	COST Score @ 7 days post start of Treatment (n = 119)	COST Score @ 6 months post start of Treatment (n = 119)
Distress Thermometer Score		
n	92	97
p	.276	.405
r	-.115	-.085

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

p = significance @ < .05

NOTE: No correlations are significant

Missing data: COST scores 7 days post start of tx, $n = 17$ (8.8%); 6 mons post start of tx, $n = 17$ (8.8%)

Missing data: Distress Thermometer: 7 days post start of tx, $n = 44$ (32.3%); 6 mons post start of tx, $n = 39$ (29%)

Table 4-7
Correlations between
Demographic variables to COST (Financial Toxicity) Scores
(@ Seven Days After Start of Treatment)
(n =117)

	Gender	Age	Living status	Education
n	136	136	136	136
p	.335	.509	.599	.771
r	.083	.057	-.046	-.025

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: COST scores 7 days post start of tx, n = 17 (8.8%)

Table 4-8
Correlations between
Demographic variables and COST (Financial Toxicity) Scores
(@ Six Months After Start of Treatment)
(n =117)

	Gender	Age	Living status	Education
n	136	136	136	136
p	.207	.332	.829	.956
r	.109	.084	-.019	.005

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: COST scores 6 mons post start of tx, n = 17 (8.8%)

Table 4-9
Correlations
Clinical Variables to COST (Financial Toxicity) Scores
(@ Seven Days After Start of Treatment)
(n =117)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug plan
n	136	132	129	124	130	130
p	.249	.106	.504	.429	.366	.035
r	-.101	.142	-.059	-.072	-.080	-.185*

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

*Correlation is significant at the 0.05 level (2-tailed)

Missing data: COST scores 7 days post start of tx, n = 17 (8.8%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%).

Table 4-10
Correlations
Clinical Variables to COST (Financial Toxicity) Scores
(@ Six Months After Start of Treatment)
(n = 117)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug plan
n	136	132	129	124	130	130
p	.243	.379	.508	.804	.631	.022
r	-.102	.078	-.059	.023	-.043	-.201*

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

*Correlation is significant at the 0.05 level (2-tailed)

Missing data: COST scores 6 mon post start of tx, n = 17 (8.8%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%).

Table 4-11
Correlations between
Financial Variables to COST (Financial Toxicity) Scores
(@ Seven Days After Start of Treatment)
(n =117)

	Employ Now	Employed when start Tx	Tx affected employment	Income Support	Gross Income	Received pharma help	% help from Pharma	Monthly OOP
n	125	124	122	120	117	123	125	118
p	.827	.941	.002	.207	.918	.791.	.086	.216
r	-.020	.007	.282*	-.116	-.010	.024	-.148	.115
p								.005
rs								.259*

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

rs = Spearman's Rank Order Correlation

*Correlation is significant at the 0.01 level (2-tailed)

Missing data: COST scores 7 days post start of tx, n = 17 (8.8%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n =12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n =18 (13.2%).

Table 4-12
Correlations between
Financial Variables to COST (Financial Toxicity) Scores
(@ Six Months After Start of Treatment)
(n =117)

	Employ Now	Employed when start tx	Tx affected employment	Income Support	Gross Income	Received pharma help	% help from Pharma	Monthly OOP
n	125	124	122	120	117	123	125	118
p	.673	.902	.001	.060	.371	.578	.084	.102
r	-.038	-.011	.326*	-.172	.083	-.052	-.149	.151
p								<.001
rs								.340*

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

rs = Spearman's Rank Order Correlation

*Correlation is significant at the 0.01 level (2-tailed)

Missing data: COST scores 6 mons post start of tx, n = 17 (8.8%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n =12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n =18 (13.2%).

Table 4-13
Correlations between
Total COST Scores (Financial Toxicity)
and Adherence

	COST Score @ 7 days post start of Treatment	COST Score @ 6 months post start of Treatment
Adherence		
n	119	119
p	.003	.005
r	-.260	-.245

COST = Comprehensive Score Financial Toxicity

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: Correlations are significant

Missing data: Adherence, n = 8 (5.9%)

Missing data: COST scores 7 days post start of tx, n = 17 (8.8%); 6 months post start of tx, n = 17 (8.8%)

Table 4-14
Pairwise Correlation Demographic Variables
(n = 136)

	Gender	Age	Living status	Education
Gender	1			
Age	.301* (<.001)	1		
Living status	.224* (.009)	1.56 (0.69)	1	
Education	-.047 (.584)	.058 (.504)	-.264* (.002)	1

* Correlation is significant at the 0.01 level (2-tailed)

Table 4-15
Pairwise Correlation Clinical Variables
(n = 136)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug Plan
Skipped Treatment	1					
Stopped Other meds	.067 (.451)	1				
Take some of other Meds	.600** (<.001)	.167 (.060)	1			
↓Dose of Other Meds	.145 (.107)	.158 (.083)	.386** (<.001)	1		
Type Insurance	-.088 (.322)	-.065 (.466)	.015 (.870)	.104 (.255)	1	
On Drug Plan	0.21 (.810)	-0.52 (.559)	-.052 (.558)	-.074 (.415)	.219* (.013)	1

* Correlation is significant at the 0.05 level (2-tailed)

** Correlation is significant at the 0.01 level (2-tailed)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%)

Table 4-16
Pairwise Pearson's Correlation: Financial Variables

	Employed Now	Employed when Start Tx	Tx Affected Employment	Income Support	Gross Income	Received Pharma Help	% Help from Pharma	Monthly OOP
<i>n</i> =	125	124	122	120	117	123	125	118
Employed Now	1							
Employed when Start Tx	.393** (<i><.001</i>)	1						
Tx Affected Employment	.122 (.181)	-.096 (.296)	1					
Income Support	-.047 (.610)	-.091 (.323)	.238** (.009)	1				
Gross Income	-.030 (.751)	.056 (.549)	-.200* (.031)	.283** (.002)	1			
Received Pharm Help	.077 (.402)	.023 (.801)	-.054 (.554)	.152 (.099)	.354** (<i><.001</i>)	1		
% Help from Pharma	.024 (.786)	.024 (.790)	.037 (.686)	.165 (.072)	.336** (<i><.001</i>)	.869** (<i><.001</i>)	1	
Monthly OOP	.068 (.468)	.012 (.896)	-.051 (.585)	.049 (.603)	.108 (.251)	.351** (.001)	.274** (.003)	1

* Correlation is significant at the 0.05 level (2-tailed)

** Correlation is significant at the 0.01 level (2-tailed)

Missing data: Employed now, *n* = 11 (8.1%); Employed when start tx, *n* = 12 (8.8%); Tx affected employment, *n* = 14 (10.3%); Income Support, *n* = 16 (11.8%); Gross Income, *n* = 18 (13.2%); Received pharma help, *n* = 13 (9.6%); % help pharma *n* = 11 (8.1%); Monthly OOP, *n* = 18 (13.2%).

Table 4-17
Correlations Between
Demographic Variables and Distress Thermometer Scores
(@ Seven Days after Start of Treatment)
(n = 92)

	Gender	Age	Living status	Education
n	136	136	136	136
p	.889	.913	.395	.389
r	-.015	-.012	-.090	.091

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Distress Thermometer: 7 days post start of tx, n = 44 (32.3%).

Table 4-18
Correlations Between
Demographic Variables to Distress Thermometer Scores
(@ Six Months After Start of Treatment)
(n = 97)

	Gender	Age	Living status	Education
n	136	136	136	136
p	.380	.484	.558	.317
r	.090	.072	-.060	.103

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Distress Thermometer: 6 mons post start of tx, n = 39 (29%).

Table 4-19
Correlations between
Clinical Variables and Distress Thermometer Scores
(@ Seven Days After Start of Treatment)
(n = 92)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug plan
n	136	132	129	124	130	130
p	.364	.306	.515	.189	.910	.897
r	.096	.109	.070	.144	-.012	.014

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Distress Thermometer: 7 days post start of tx, n = 44 (32.3%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%)

Table 4-20
Correlations between
Clinical Variables and Distress Thermometer Scores
(@ Six Months After Start of Treatment)
(*n* = 97)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug plan
n	136	132	129	124	130	130
p	.254	.269	.267	.717	.928	.452
r	.118	.115	.115	.039	.009	.078

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Distress Thermometer: 6 mons post start of tx, n = 39 (29%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%).

Table 4-21
Correlations between
Financial Variables to Distress Thermometer Scores
(@ Seven Days After Start of Treatment)
(*n* = 92)

	Employed Now	Employed when Start Tx	Tx Affected Employment	Income Support	Gross Income	Received Pharma Help	% Help from Pharma	Monthly OOP
n	125	124	122	120	117	123	125	118
p	.441	.611	.360	.168	.773	.052	.165	.612
r	.084	.055	-.100	.152	-.032	.210	.230	.057

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Distress Thermometer: 7 days post start of tx, n = 44 (32.3%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n = 12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n = 18 (13.2%).

Table 4-22
Correlations between
Financial Variables to Distress Thermometer Scores
(@ Six Months after Start of Treatment)
(n = 97)

	Employed Now	Employed when start Tx	Tx Affected Employment	Income Support	Gross Income	Received Pharma help	% Help from Pharma	Monthly OOP
n	125	124	122	120	117	123	125	118
p	.953	.909	.939	.305	.861	.069	<.001	.358
r	-.006	.012	.008	.111	.019	.193	.336*	-.100

r = Pearson's Correlation

* Correlation is significant at the 0.01 level (2-tailed)

Missing data: Distress Thermometer: 6 mons post start of tx, n = 39 (29%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n = 12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n = 18 (13.2%)

Table 4-23
Correlations between
Demographics Variables and Adherence
(n = 128)

	Gender	Age	Living status	Education
n	136	136	136	136
p	.905	.852	.257	.671
r	-.011	-.017	.101	.038

r = Pearson's Correlation

Correlation is significant at the 0.05 level (2-tailed)

NOTE: No correlations are significant

Missing data: Adherence: n = 8 (5.9%)

Table 4-24
Correlations Between
Clinical Variables and Adherence
(n = 128)

	Skipped Treatment	Stopped other Medications	Take some of other medications	↓ Dose of Other Medications	Insurance: Medicare or Private	On Drug plan
n	136	132	129	124	130	130
p	.006	.756	<.001	.794	.934	<.001
r	.243*	.028	.368*	-.024	.007	.345*

r = Pearson's Correlation

* Correlation is significant at the 0.01 level (2-tailed)

Missing data: Adherence: n = 8 (5.9%)

Missing data: Stopped other meds, n = 4 (2.9%), took some of other meds, 7 = (5.1%); reduced dose other meds, 12 = (8.8%); insurance, n = 6 (4.4%); on drug plan, n = 6 (4.4%).

Table 4-25
Correlations Between
Financial Variables and Adherence
(n = 128)

	Employ Now	Employed when start tx	Tx affected employment	Income Support	Gross Income	Received pharma help	% Help from Pharma	Monthly OOP
n	125	124	122	120	117	123	125	118
p	.583	.153	.786	<.001	.045	.161	.051	.351
r	-.050	.131	.025	-.055**	.188*	.080	.173	-.088

r = Pearson's Correlation

* Correlation is significant at the 0.05 level (2-tailed)

** Correlation is significant at the 0.05 level (2-tailed)

Missing data: Adherence: n = 8 (5.9%)

Missing data: Employed now, n = 11 (8.1%); Employed when start tx, n = 12 (8.8%); Tx affected employment, n = 14 (10.3%); Income Support, n = 16 (11.8%); Gross Income, n = 18 (13.2%); Received pharma help, n = 13 (9.6%); % help pharma n = 11 (8.1%); Monthly OOP, n = 18 (13.2%).

CHAPTER 5 DISCUSSION

Introduction

This chapter presents a discussion of a descriptive, cross-sectional study about cancer patients and their financial toxicity (FT) experience and whether that experience affected their level of distress or adherence to treatment. This chapter provides a scholarly context about the study's results, describing the participants, their FT experience and relationships among FT-associated variables, perception of distress and adherence to prescribed cancer treatment given orally.

The study's data were collected on-line from 136 participants, who were members of the patient education/advocacy community, Patient Power[®]. Participants were self-identified as diagnosed with a malignancy and prescribed a cancer treatment given orally. Participants completed three study instruments to better describe themselves and their FT experience: a Demographics Questionnaire, the Comprehensive Score for Financial Toxicity (COST) and the Comprehensive Cancer Network (NCCN) Distress Thermometer (DT).

Healthcare Costs

The participants in this study confirm what is known in clinical practice--that the challenges associated with FT affect whether patients can maintain their health care

coverage (Conway, 2019; Carrera, Kantarjian & Blinder, 2018; Warsame et al., 2018; Goldstein, 2017; KFF, 2017).

The burden of FT includes--but is not limited to--access to care, coverage for care, maintaining sources of income and the impact of FT on interpersonal relationships (Collado & Brownell, 2019; Salsman, Bingen, Barr & Freyer, 2019; Thom & Benedict, 2019; Honda et al., 2018; Knight et al., 2018; Peppercorn, 2017).

The experience of FT is especially burdensome for individuals diagnosed and treated for cancer (NCI, 2019; Mohammed & El-sol, 2018; Winkfield et al., 2018; Shen, Zhao, Liu & Shih, 2017). As experienced by cancer patients, the focus about FT may be due to the disruptive impact of cancer on the patient (Allcott et al., 2019; Yabroff, et al., 2019), the high cost of treatments (Cole, Jazowski & Dusetzina, 2019; Farano, & Kandah, 2019; Giuliani & Bonetti, 2019; Tran & Zafar, 2018; Truong et al., 2019; Prasad, de Jesus & Mailankody, 2017) and the long-term impact that FT has on cancer patients and their caregivers (Banegas et al., 2019; Bradley, 2019; Cole et al., 2019; Goldstein, 2017).

FT and Study Results

Demographics

This study explored the impact of FT on a sample group of cancer patients, prescribed treatments given orally. The majority of participants had cancer diagnoses associated with standard-of-care treatments that were especially high in cost; the majority of participants were diagnosed with the chronic hematologic malignancies myelogenous

leukemia (CLL) and malignant myeloma (MM) (Hilal, Betcher & Leis, 2018; Schneider, Steinbrecher & Stilgenbauer, 2019). For three-months of treatment for these diagnoses, the range of cost (without insurance coverage, co-payments, deductibles, discounts or other factors affecting the cost of treatment) is \$15,000-\$50,000 (B. Chan, personal communication, October 10, 2019).

As documented in other studies about patients diagnosed with chronic hematologic malignancies, these study participants received relatively new treatments, representing treatment breakthroughs (Farano & Kandah, 2019; Hilal et al., 2018). For these study participants as with others diagnosed with these hematologic malignancies, their disease is considered a chronic condition, so they can be on treatment for a long time (Schneider et al., 2019; Peppercorn, 2017). Considered standard treatments for study participants' malignancies, the most frequently reported treatments were imbrutinib (Imbruvica®), lenalidomide (Revlimid®) and ruxolitinib (Jakafi®) (Schneider et al., 2019; Hilal et al., 2018).

Moreover, over time, when one treatment becomes ineffective, providers may choose to switch treatments, once again with the option of prescribing treatments with relatively new FDA approvals (Farano & Kandah, 2019; Giuliani & Bonetti, 2019). Therefore, additional new treatments for these chronic hematologic malignancies can be costly (Cole et al., 2019; Truong et al., 2019). In addition, new treatments (in oral formulations) are early in their FDA approval period so are at high cost, since pharmaceutical companies want to recoup the cost of drug development (Banegas et al.,

2019; Califf & Slavitt, 2019; Collado & Brownell, 2019; Giuliani & Bonetti, 2019; Tay-Teo, Ilbawi, & Hill, 2019; Truong et al., 2019; Yabroff et al., 2018; Prasad et al., 2017).

In this study, the sample population of participants was older, well educated, with stable social supports and means or strategies to pay for their treatments. The majority of participants in this study were covered by adequate insurance or had supplemental health care insurance policies. This study's overall participant profile matches a significant cohort of the CLL and MM patient population, who have found ways to continue on their long-term treatments (Allcott et al., 2019; Yabroff et al., 2018; Schneider et al., 2019).

More women than men were represented in the study sample (women: n = 75, 51.1%; men: n = 61, 44.9%). With actuarial tables confirming that women live longer than men, women's FT experience may be perceived as more acute or at a higher level. This more profound female FT experience may be due to more prolonged financial stress; that stress can build due to age and be exacerbated by less than adequate or no health insurance coverage (Shen, et al., 2017; Gordon et al., 2017).

The overwhelming majority of the study's sample population did not skip cancer treatments given orally due to FT. In addition, participants reported that they rarely adjusted prescribed non-cancer medications to maintain and pay for their cancer treatment. This was in keeping with what has been published about FT experienced by cancer patients and whether they adjusted their cancer therapy so they could stay on treatment (Renner, Burotto & Rojas, 2019; Knight et al., 2018; Murphy et al., 2018; Schiffer, 2018).

Two thirds of the study's participants reported gross income of <\$100,000/year with the remaining third reporting gross income >\$100,000/year. (In 2017, the average median household income in the U.S. was projected at \$57,652 (US Census Bureau, 2019).

For the general population of cancer participants receiving treatments given orally, not all cancer patients have the option of receiving treatment given orally or the means to pay for new cancer treatments in oral form (Hilal et al., 2018). Thus, this study population benefitted from higher gross incomes, insurance coverage that, in general, paid for the cost of their treatments and/or pharmaceutical company-funded programs, which helped cover their treatment expense. These results suggest that this study's sample population may not be representative of the experience of other cancer participants treated with high-cost cancer treatments (Farano & Kandah, 2019). But this study's results do suggest that the factors of adequate insurance, access to treatment support (from pharmaceutical companies and foundations) and an adequate or temporarily interrupted income stream (employment) mitigate the impact of FT when patients are prescribed high-cost treatments (Macmillan, 2019, Shen et al., 2017)

FT Experience

This study's participants experienced various levels of FT and at various times, as documented by the COST instrument scores and specific responses to the COST instrument questions. In this study, approximately one third of participants reported their perception of FT was quite a bit or very much, based on COST scores at both seven days post start of treatment and six month post start of treatment.

These results concur with other studies of cancer patients and FT. For studies that used the COST instrument to further describe and clarify the FT experience, those studies reported that certain cancer patients experienced higher levels of FT during some period of their cancer treatment (Bouberhan et al., 2019; Ezeife et al., 2019; Ferrell et al., 2018; Honda et al., 2018).

Of note in this study, study participants were asked about their perceptions of FT at two timepoints, which other studies have not explored in their study designs. For this study, the level of total FT scores was slightly higher six-months after treatment began compared to seven days after treatment began. These findings concur with other studies, which report that cancer patient FT can increase over time, especially with the stress of continuing, high-cost therapies, as well as the chronic impact of a cancer diagnosis on daily life (Thom & Benedict, 2019; Carrera et al., 2018; Shen et al., 2017).

In this study from the COST instrument, these specific FT responses were scored higher at both the seven day and six month post start of treatment timepoints: “Feel no choice about cost of care”, “worry about future financial problems due to illness”, “higher than anticipated out of pocket medical expenses”, “reduced satisfaction in current financial situation due to cancer treatment”, “ability to meet monthly expenses” and “overall financial stress”. These responses were in keeping with findings from other studies about FT and the cancer patient experience (Ezeife et al., 2019; Carrera et al., 2018; Honda et al., 2018).

Out of Pocket Expenses for Treatment

About two thirds of study participants reported OOP costs < \$500/month with the remaining third of participants reporting OOP costs >\$500/month. Studies have reported that OOP health insurance co-pays and deductibles are rising (KFF, 2017). For cancer patients, OOP costs can be extensive and unpredictable (Conway, 2019).

Participants in this study also concur that transportation costs (gas and parking) are the most often cited OOP costs related to cancer treatment (Leopold et al., 2019; Rosenzweig et al., 2019). Study participants also noted they experienced higher copays and deductibles associated with their insurance coverage and treatment (Conway, 2019; KFF, 2017). Other OOP costs from this study's participants (loss of income, child care, over-the-counter medications), are similar to OOP costs reported in other FT studies (Leopold et al., 2019; NCI, 2019; Buttner et al., 2018).

Financial Support for Treatment

For study participants responding about receiving financial support for treatment from pharmaceutical, foundation or other non-insurance sources, they were generally split between those who received support (n = 57, 46.3%) and those who did not receive support (68, 54.0%). Cancer patients' source of additional financial support and how much financial support goes to the cost of treatment have not been rigorously studied (MacMillian, 2019). In this study, approximately half of study participants did not respond to the question about the percentage of financial support received from non-insurance sources. Still in clinical practice, pharmaceutical, foundation or other non-

insurance sources significantly augment the OOP expenses of cancer treatment when patients' insurance coverage does not cover the cost of treatment (MacMillan, 2019).

In this study for participant perception of distress related to demographic, clinical and financial variables, the only statistically significant relationship was perception of distress at six months post start of treatment and the percentage expense supported by pharmaceutical companies or foundations ($r = .336$, $p = .001$). This suggests that over time, the level of distress can be affected by the level of pharmaceutical or foundation financial support (MacMillan, 2019).

Distress Experience

More than a third of study participants reported high distress due to FT at both one week post start of treatment and at six months post start of treatment. Distress due to just FT is difficult to measure, when the cancer experience in its entirety is stressful.

For this study at the two timepoints, there was no statistically significant relationship established between FT and participants' perception of distress. Still other studies concur that FT is a prevalent source of distress for cancer patients so FT has clinical significance (Ezeife et al., 2019; Thom & Benedict, 2019; Carrera et al., 2018).

Worth noting in this study at both timepoints, almost a third of participants did not respond to the study's distress instrument. This, once again, suggests that identifying FT as a distinct source of stress to cancer patients is difficult (Thom & Benedict, 2019). In this study, the non response to the distress instrument may be due to the participant's own difficulty in separating FT-related stress from the participant's general distress about the cancer experience (Rosenzweig et al., 2019; Thom & Benedict, 2019). It may

also be due to not wanting to respond to an instrument measuring distress (Vanhoose et al., 2015; Mitchell, 2007).

Adherence to Treatment

Most study participants reported that they adhered to their prescribed cancer treatment given orally and did not stop, interrupt or alter their prescribed treatment regimen because of FT. These findings are in keeping with studies that show despite the stress brought on by FT, treatment adherence is high (Gupta et al., 2019). In this study, COST instrument scores, representing FT, had a weak negative correlation related to adherence at seven days post start of treatment ($r = -.260, p = .003$) and at six months post start of treatment ($r = -.245, p = .005$). But in this study due to the sample size, FT could not be statistically established as a predictor of adherence.

As identified in other studies to maintain treatment adherence, participants in this study mobilized a multitude of strategies to support adherence: intact and robust health insurance coverage; coverage from supplemental health insurance policies; drug coverage plans that cover specialty medications (i.e. new cancer treatments given orally); financial support from pharmaceutical, foundation or other non-insurance sources to cover treatment costs; and the ability to adequately cover OOP costs of treatment (sufficient gross income, sources of regular income) (Cole et al., 2019; Gupta et al., 2019; Taylor, 2019; Rosenzweig et al., 2019, Honda et al., 2018; Knight et al., 2018).

In this study, adherence to treatment was weakly correlated to income support ($r = .005, p = >.001$) and gross income ($r = .045, p = .188$).

FT Relationships

In the context of FT, this study's findings suggested weak relationships at both seven days and six months post start of treatment, based on COST scores and whether participants had a drug plan, whether they were employed and whether they adhered to treatment. Several studies of cancer patients have identified similar FT-associated relationships (Schneider et al., 2019; Taylor, 2019; Gilligan, Alberts, Roe & Skrepnek, 2018).

In this study describing participants' experience of FT and demographic variables, there were weak relationships associated between gender and age; gender and living status; and education to living status. These relationships may not be consistent for all cancer patients and their experience with FT (Thomas et al., 2019).

From participants' experience with FT and clinical variables, this study suggests weak relationships between

- lowering the dose of non-cancer medications and taking some prescribed non-cancer medications, as prescribed
- being covered by insurance and being covered by a drug plan
- adherence to treatment and having a drug plan
- employed now and employed when started treatment
- treatment affected employment and income support
- income support and gross income
- gross income and receiving help from pharmaceutical companies/foundations

- gross income and percentage of help received from pharmaceutical companies/foundations
- received help from pharmaceutical companies/foundations and OOP monthly costs

and

- percentage help from pharmaceutical companies/foundations and OOP monthly costs.

In this study, a moderate correlation was established between skipping cancer treatment and taking some prescribed non-cancer medications ($r = .600$, $p = < .001$). This study also indicated a high correlation between pharmaceutical/foundation support and percentage help offered participants from those sources ($r = .869$, $p = .001$);

For all the study's intra-variable relationships listed above, these relationships confirm that FT issues are entwined and affect the overall FT experience (Ezeife et al., 2019; Gupta et al., 2019; MacMillan, 2019; Renner, Burotto & Rojas, 2019; Thomas et al., 2019; Prasad et al., 2017; Shen et al., 2017).

Summary: FT and Study Results

This descriptive, cross-sectional study included participants diagnosed with chronic hematologic malignancies, treated with treatments given orally. Therefore, for their long-term cancer treatment, these study participants received high-cost cancer treatments, which affected their experience with FT, distress associated with FT and adherence to prescribed treatments.

Confirming previous study findings in the literature, this study's patient population experienced various levels of FT and at various times. In this study, approximately one third of the participants reported that FT was quite a bit or very much both at seven days post start of treatment and six month post start of treatment.

Distress associated with FT can be an issue although FT as a distinct source of distress was not confirmed in this study. To accommodate issues of FT, study participants received support from pharmaceutical, foundation or other non-insurance sources. They also were able to cover the cost of their treatment due to having robust insurance coverage, adequate income streams and the ability to cover OOP costs.

In this study, despite the patient's perception of FT at both one week post start of treatment and at six months post start of cancer treatment given orally, adherence to cancer treatment was largely not affected.

Finally, this study's findings concur that the FT experience for cancer patients is associated with many variables, which have intertwined relationships (Ezeife et al., 2019; Gupta et al., 2019; Thomas et al., 2019; Carrera et al., 2018; Prasad et al., 2017).

Limitations

This study's findings have several limitations; these limitations affect whether the findings are applicable or generalizable to the FT experience of all cancer patients.

Study Design

Study limitations included the study design. The study was a descriptive, cross-sectional design study, seeking participants via a convenience sample from one on-line cancer patient education/advocacy group site. The participants were self-described as diagnosed with cancer and prescribed treatment given orally. Because of the study design, the profile of each participant could not be verified so the study's data, representing the experience of cancer patients and FT, also could not be verified.

The study requested that participants respond to the study's three measurement instruments, relaying their perceptions about FT at two timepoints. Choosing these particular timepoints was arbitrary. In addition, study data relied on participants determining perceptions from their past, which could have been inexact, exaggerated and/or reliant on interpretations from vague memories.

Sample Population

In general, the participant sample was small in number, older, highly educated, adequately insured, benefitted from stable social supports, had adequate income streams and diagnosed with a chronic cancer diagnosis. The participants were asked to respond to their experience associated only with their cancer treatment prescribed orally. Because of their cancer diagnosis and their cancer treatments prescribed orally, those treatments had higher costs.

Study participants were English speaking, had access to the internet and were asked to respond to study questionnaires posing questions about complex concepts—FT and distress. Although the sample population was recruited anonymously, the participant responses could have been biased toward what they assumed would be the outcomes of the study (i.e. everyone suffers from FT; everyone has had an extreme FT experience.)

Participants in the study were not asked about their culture, ethnicity or sexuality. Therefore, those characteristics were unknown and so could not be reported. Because this information was not captured, the interpretations of study findings are limited.

Instruments in Study

The Comprehensive Score for Financial Toxicity (COST) instrument is a relatively new instrument to measure FT and has been tested valid with advanced cancer patients (deSouza et al., 2017, 2014). Its reliability and validity as a measurement instrument has not been studied in many populations with various diagnoses, stages of disease, treatment side effect profiles and experiences of FT (Bouberhan et al., 2019; Ezeife et al., 2019; Honda et al., 2018).

The National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT) has been widely studied and used to evaluate distress in cancer patients. However, its reliability and validity as an instrument when administered online has not been thoroughly tested (NCCN, 2018).

The study's Demographics Questionnaire, administered on-line and focused on categorical responses to questions, was developed so it would be easy for participants to

complete. There was no reliability or validity testing of the questionnaire. Because the questionnaire requested broad responses to sensitive topics (gross income, specifics about the experience of FT, financial support to cover the costs of treatment), captured study data may be too broad to determine FT distinctions related to the FT experience, demographic and clinical variables, FT association with distress and FT association with adherence to treatment. In addition, this study's instruments did not capture the patient's self-assessment of severity or stage of illness, which would impact responses for FT, distress and adherence.

In relation to the study's three instruments, participants may have been reluctant to complete all or part of the instruments' questions since some questions were about sensitive topics. Among those sensitive topics was the experience with FT, the ability to pay for treatment, the need to secure financial resources to supplement the expense of treatment and distress during cancer treatment.

Clinical Practice Implications

This study results suggest several implications for practice.

Despite FT as a relatively newly-recognized stress in the cancer patient's experience, FT as a form of stress can occur in varying degrees, depending on the patient and caregiver circumstances (Thomas et al., 2019; Carrera et al., 2018). The ability for the cancer patient and caregivers to function depends on a combination of physical, psychosocial and spiritual factors (Knight et al., 2018). When and whether FT affects patients is due to the dynamic, complex experience of cancer as a disease, as well as the experience of being treated for cancer (Thomas et al., 2019). With FT contributing to

patient and caregivers stress, FT affecting care may be anticipated (Rosenzweig et al., 2019; Thom & Benedict, 2019; Carrera et al. 2018). It may also be addressed with the expertise of those who can problem-solve the patient's healthcare financial status (Carr & Rosato, 2019; Sherman & Fessele, 2019; Berry et al., 2018). And just as with other stresses, FT can be managed as part of the plan of care (NCCN, 2018).

As with all stresses associated with the care of cancer patients and caregivers, the nurse-- as a member of the interdisciplinary care team--can make a significant impact to address FT.

Nursing Care

Assessment. As a standard of care, FT is becoming a component of the nurse's clinical assessment (Carr & Rosato, 2019).

As a part of a clinical assessment initiated or continued by the clinical nurse, FT assessment does not need to be overly intrusive or involved. The assessment can include a few questions to start a conversation about FT issues or continue that conversation as treatment proceeds. Then the conversation can continue as the plan of care continues or changes (Carr & Rosato, 2019).

The foundation for a FT-associated clinical assessment begins with questions similar to those listed in the COST instrument (deSouza et al., 2017, 2014). At its foundation, a nurse-initiated FT assessment generates information from the patient about the patient's health insurance, sources of income, OOP costs and the physical and psychological effects of FT (Katz, 2018).

Referrals. Any effective care of patients experiencing FT requires support and counsel from those who have expertise about healthcare coverage and financial issues (Sherman & Fessele, 2019; Berry et al., 2018). In academic healthcare centers, comprehensive cancer centers and large health care systems, that expertise has become available to patients through financial counselors and/or specially-trained nurse navigators, social workers and lay patient navigators (Carr & Rosato, 2019).

Nurses who provide direct care to patients can be the conduit to financial counselors (Nipp, Sonet & Guy, 2018). As members of the interdisciplinary team, nurses can best care for patients by knowing available resources, connecting the patient with effective financial-support resources and ensuring that patients receive information, support and direction so that FT is addressed (Sherman & Fessele, 2019).

Support. In relation to the cancer patient's care plan, the nurse remains a reliable source of support, providing patient education, psychosocial support and strategies for problem solving (Carr & Rosato, 2019; Thomas et al., 2019; Ferrell et al., 2018) As this study's findings suggest, providers who are aware of the patient's FT issues can better intervene to provide effective support (Bradley, 2019).

Decision Making

As the study's results confirm, FT contributes to patients' uncertainty related to the cancer diagnosis, treatment plan and life expectancy. Since studies have raised the visibility of FT as a stress for cancer patients, several decision-making models have been proposed to open up the discussion about treatment and financially-based pros and cons about treatment options (Chino et al., 2019; Leopold et al., 2018; Gidwani-Marszowski et

al., 2018; Bien et al., 2017). These proposed frameworks may support transparency between providers and patients about treatment options toward shared decisions about treatment (Nipp et al., 2018).

The role of the provider, opening up the process of decision making, has been studied, focusing on changing the hierarchy of information, traditionally in the sole control of the provider. These revised models attempt to shift decision-making to both the provider and patient, based on the patient's preferences (Warsame et al., 2019). These evolving decision-making frameworks intend to broaden treatment discussions—including issues of the cost of care (Dine, Masi & Smith 2019; Doshi et al., 2019; Hong, Matusiak & Schumock, 2018).

However, these decision-making frameworks are limited since providers often do not know the cost of the therapies they recommend (Farano & Kandah, 2019). And providers typically do not have access to basic information about the patient's finances related to treatment decisions. In general, providers do not know the patient's individual insurance coverage benefits or options for supplemental financial support for care (Dine et al., 2019). Moreover, there is no guarantee that the patient understands his or her health care financial information or status (Nipp et al., 2018).

Frameworks and decision-making tools focus on patient choice (Seidman, Masi, Gomez-Rexrode, 2019; Bien et al., 2017), value of treatment (Doshi et al., 2019; Leopold et al., 2019; Gidwani-Marszowski et al., 2018), cost of care (Dine et al., 2019, Truong et al., 2019; Yu, Eton & Garrison, 2019), patient expectations (Hong et al., 2018)

information provided (Warsame et al., 2019), or a combination of the above (Doshi et al., 2019, Gidwani-Marszowski et al., 2018, Hong et al., 2018).

Future Research

This study's findings suggest directions for future research to better understand the FT experience, formulate FT standards of care and to establish clinical FT policies related to the care plan (Thomas et al., 2019). Questions remain about FT and cancer patients—when it occurs, how best to address it, what resources can be mobilized over time and how to mitigate the high cost of cancer medications and treatment. What are the most effective and sensitive clinical interventions that provide patients and their caregivers with information, support and ways to problem solve? (Berry, Deming & Danaher, 2018).

Opportunities for FT Research

Among opportunities for FT research are cancer patients at risk for FT (Rupper, 2018), FT challenges they face (Winkfield et al., 2018), patients with limited or interrupted incomes due to their diagnoses (Allcott et al., 2019; Collado & Brownell, 2019), intense FT flashpoints during the continuum of care (Yu et al., 2019), treatment protocols that increase FT (Cole et al., 2019) and advocacy strategies (Thomas et al., 2019).

To address FT experienced by patients and caregivers, nurse researchers—as members of interprofessional teams—can identify, then investigate interventions that result in better patient outcomes (Thomas et al., 2019; Mohammed et al., 2018). These outcomes suggest that the standard of care requires FT expertise in the plan of care (Bradley, 2019; Sherman & Fessele, 2019). Studies are needed about the merit of the

designated financial navigator role (Sherman & Fessele, 2019; Thom & Benedict, 2019; Berry et al., 2018), financial experts for patients at FT risk (Sherman & Fessele, 2019), financial expertise to address FT at specific timepoints (Berry et al., 2018), the need for comprehensive healthcare coverage (Conway, 2019) and strategies to pay for the cost of care (Cole, et al., 2019; Yu et al., 2019).

Survivorship

Cancer survivors present distinct FT implications (Benagas et al., 2019, Coughlin & Dean, 2019, Yabroff et al., 2019). Survivors face FT issues related to extended treatment costs and sacrifices to pay for long-term or recurrent disease (Chino et al., 2019; Peppercorn 2017; Prasad et al., 2017). They are challenged to secure adequate healthcare insurance coverage and pay higher insurance premiums (Coughlin & Dean, 2017; KFF, 2017). They are concerned about their ability to keep working and maintain an income stream (Pearce et al., 2019). And they need ongoing support and new resources to access care (Benagas et al., 2019, Pearce et al., 2019, Salsman et al., 2019, Yabroff, et al., 2019; Zahnd et al., 2019).

Federal Policy and Drug Costs

Despite market forces that affect the cost of drugs in the U.S., the federal government's influence over drug prices is significant, related to its ability to establish price controls or to negotiate prices for a large swath of patients covered by government-supported health care (Blumenthal, 2016).

With access to affordable, quality health care remaining a #1 priority of consumers in the U.S., the high cost of prescription drugs is just one of many health care

issues requiring a solution (Speaker, 2019). Since the price of drugs in the U.S. can be twice the cost of drugs in other wealthy countries (Blumenthal, 2016), the public's call for legislative remedies is persistent even while effective strategies to navigate barriers remain elusive (Stone, 2019; Sweeney, 2019; Walter, 2019)

Federal policies that affect drug prices are very complex. The challenge to decipher policies and determine who or what is influencing the cost of drugs contributes to the complexity. Specific issues associated with federal policy include questions regarding how drug prices are determined, which drug prices can be negotiated, the extent of rate hikes, the transparency of billing and limitations or restrictions on pharmacy formularies (Horvath, 2018; KFF, 2019; Stone, 2019).

Moreover, momentum to support any given legislative or policy proposal is fluid, affected by coalitions representing a wide array of players and agendas: health care facilities, health care providers, consumer advocacy groups, political parties, pharmaceutical companies and the government itself (Kodjak, 2018; Stone, 2019; Walter, 2019).

Legislative and Regulatory Initiatives

Legislation to impact the cost of drugs is generated by Congress. Legislation establishes broad, general laws that direct policy. Regulations are generally written and promulgated by the executive branch to implement and enforce legislation (ISB, 2019).

Legislation

An example of drug cost legislation proposed in the 116th Congress session of Congress (2019-2020) is HR-3, The Lower Drug Costs Now Act (Speaker, 2019). Among the provisions of HR-3 is a requirement to change laws that currently prohibit the Centers for Medicare & Medicaid Services (CMS) from negotiating prescription drug prices for its Medicare beneficiaries (Feke, 2019; McCaughan, 2017). For Medicare beneficiaries, HR-3 proposes that CMS negotiate the price of certain drugs, including insulin and selected drugs that do not have generic equivalents since the government already can negotiate prices for federally supported Medicaid programs and the Veterans Administration (Feke, 2019; McCaughan, 2017). Many of the targeted drugs in HR-3 are for drugs most commonly prescribed for Medicare beneficiaries.

Another component of HR-3 calls for setting maximum drug price ceilings for certain drugs and to allow a new framework for cost sharing when drug prices hit a pre-determined threshold (Speaker, 2019).

Although HR-3 does not target specialized cancer drugs in the legislation, efforts to curb specialized cancer drug prices start with winning the battle about sensible drug pricing for common prescription drugs (Stone, 2019; Sweeny, 2019).

Regulations

In general, regulations that address drug prices are the purview of the U.S. Department of Health and Human Services (DHHS), specifically through its agencies, the Centers for Medicare and Medicaid Services (CMS) and the Food and Drug Administration (FDA) (CMS.gov, 2019; Waxman et al., 2019).

FDA rules that explicitly impact cancer drugs include those addressing the development and approval of new drugs, and more specifically patents and exclusivity rights. The American Association of Clinical Oncology (ASCO), the professional society of clinical oncologists, has opposed regulations “extending market or data exclusivity periods” for a wide array of new cancer treatments, classified as small-molecule, generic, orphan, and biologic drugs (ASCO, 2019). ASCO also has joined other patient advocacy groups, opposing Pharmacy Benefit Management (PBM) companies (third party prescription drug administrators), whose initiatives attempt to control cancer treatment costs but limit the ability of providers to prescribe appropriate and effective treatments for patients (ASCO, 2019). (In 2017, PBM companies managed prescription benefits for an estimated 85% of health insurance benefits for those with public and private health insurance plans (NASEM, 2017).)

The DHHS has also proposed revising regulations associated with improving transparency of drug costs, so that visibility of those costs would encourage negotiation and produce fewer surprises to consumers. Those regulations would eliminate bills for the costs of care that were never discussed or determined before care was rendered.

These efforts have been initiated to establish more rational “Balanced Billing”. “Balance Billing” usually is defined as billing a patient for the difference between the total cost of services being charged and the amount the insurance pays. In reference to high cancer drug costs, revisions in “Balanced Billing” regulations would protect the patient from exorbitant bills when patients must go out of their insurance network for care and pay for that non-covered care. For oncology patients, these situations occur

when their standard of care requires treatment that includes specialized cancer drugs not covered by their insurance. However once again, progress toward support of revised regulations has been thwarted by the Courts, who have, to date, agreed with the pharmaceutical industry argument that revised regulations represent regulatory overreach (Stone, 2019; Sweeney, 2019).

Federal Policy and Values

So, in the long run, to pass legislation that has any effect on the cost of drugs, lawmakers--representing the electorate—must deal with what society values. That focus on values includes what the electorate determines as fair—or even acceptable—as larger questions loom about a broken, inefficient health care system (Sweeney, 2019). These questions pit all sides in economic, legal and moral power struggles. And from these struggles, it remains to be seen what drug cost changes can occur in a partisan political climate.

Conclusion

The experience of FT is an additional stress to cancer patients and their caregivers, especially during treatment, but also throughout the continuum of care. The FT experience has many components, and is distinct for each individual, depending on the patient's diagnosis, treatment plan, cost of treatment and clinical and financial factors. For any given patient when treatment begins and as it continues, FT may affect the patient's perception of distress and adherence to treatment.

This study's findings characterized the FT experience, its timing and possible FT management strategies. These findings contribute to the ongoing clinical foundation

about FT, suggesting ways to improve the complex care of cancer patients and their caregivers.

References

- Allcott, N., Dunham, L., Levy, D. Carr, J. & Stitzenberg (2019). Financial burden amongst cancer patients treated with curative intent surgery alone. *American Journal of Surgery*, 218(3):452-456.
- Altice, C., Banegas, M., Tucker-Seeley, R. & Yabroff, K. (2017). Financial hardships experienced by cancer survivors: A systematic review. *Journal of the National Cancer Institute*, 109(2): 1-17.
- American Society of Clinical Oncology (ASCO) (2018). ASCO Position Statement on Addressing the Affordability of Cancer Drugs. Retrieved on July 13, 2018 from asco.org/advocacy-policy/asco-inaction/asco-offers-path-addressing-affordability-cancer-drugs-new-position.
- American Association of Clinical Oncology (ASCO). (2019). Congress Must Address Drug Costs, Disparities, and Transparency to Lower Out-of-Pocket Cancer Spending, June 11, 2019. ASCO in Action. Retrieved Nov. 11, 2019 congress from <https://www.asco.org/advocacy-policy/asco-in-action/-must-address-drug-costs-disparities-and-transparency-lower>
- Baken, D. & Wooley, C. (2011). Validation of the Distress Thermometer, Impact thermometer and combinations of these in screening for distress. *Psycho-Oncology*, 20: 609–614.
- Banegas, M, Guy, G. deMoor, J., Ekwueme, D., Virgo, K., Kent, E...Yabroff, K. (2016). For working-age cancer survivors, medical debt and bankruptcy create financial hardships. *Health Affairs (Millwood)* 35(1): 54-61.
- Bayer, B., Amaya, B., Baniewicz, D., Callahan, C., Marsh, L. & McCoy, A. (2017). Cancer immunotherapy. *Clinical Journal of Oncology Nursing*, Supp, 21(2):13-21.

- Bernard, D. S., Farr, S. L., & Fang, Z. (2011). National estimates of out-of-pocket health care expenditure burdens among nonelderly adults with cancer: 2001 to 2008. *Journal of Clinical Oncology*, 29(20), 2821-2826.
- Berry, L., Deming, K. & Danaher, T. (2018). Improving Nonclinical and Clinical-Support Services: *Lessons from Oncology Mayo Clinical Proceedings, Innovations & Quality Outcomes*, 2(3):207-217.
- Bestvina, C., Zullig, L., Rushing, C., Chino, F., Samsa, G., Altomare. L.,...Zafar, S. (2014). Patient-oncologist cost communication, financial distress, and medication adherence. *Journal of Oncology Practice*, 10(3):162–7.
- Bien, D., Danner, M., Venedey, V., Civello, D, Evers, S., & Hiligsman, M. (2017). Patients' preferences for outcome, process and cost attributes in cancer treatment: A Systematic review of discrete choice experiments. *Patient*, 10:553–565.
- Blumenthal, D. & Squires, D. (2016). Drug Price Control: How Some Government Programs Do It. To the Point. The Commonwealth Fund. May 10, 2016. Retrieved Dec. 2, 2019 from <https://www.commonwealthfund.org/blog/2016/drug-price-control-how-some-government-programs-do-it>
- Bouberhan, S., Shea, M., Kennedy, A., Erlinger, A., Stack-Dunbier, H., Buss, M....Esselen, K. (2019). Financial toxicity in gynecologic oncology. *Gynecologic Oncology*, 154: 8–12.
- Bradley, (2019). Economic burden associated with cancer caregiving, *Seminars in Oncology Nursing*, 35:333-336.
- Bradley, C., Yabroff, K., Warren J., Zeruto, C., Chawla, N. & Lamont, E. (2016). Trends in the treatment of metastatic colon and rectal cancer in elderly patients. *Medical Care*, 54 (5): 490-7.

- Brassil, K. & Ginex, P. (2018). History of immunotherapy. In S. Walker & E. Dunphy (Eds.) *Cancer Immunotherapy*. Pittsburgh: Oncology Nursing Society. pp. 1-18.
- Business Group Health (2018). Specialty Pharmacies. Retrieved from
from: <https://www.businessgrouphealth.org/topics/cost-solutions-benefits-design/specialty-pharmacy/>
- Buttner, M., Konig, H. Lobner, M., Briest, S. Konnopka, A., Dietz, A. Riedel-Heller, S. & Singer, S. (2018). Out-of-pocket-payments and the financial burden of 502 cancer patients of working age in Germany: results from a longitudinal study. *Supportive Care in Cancer*, 27(6):2221-2228.
- Califf, R. & Slavitt, A. (2019). Lowering cost and increasing access to drugs without jeopardizing innovation. *JAMA*, 321 (16): 1571-1573.
- Carr, E. & Rosato, E. (2019). Making the case: Clinical assessment of financial toxicity. *Clinical Journal of Oncology Nursing*, 23 (Supp.2) 19-26.
- Carrera, P. (2017) The financial hazard of personalized medicine and supportive care. Paper presented at: Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) 2017 Annual Meeting; June 22-24, 2017; Washington, DC.
- Carrera, P. M., Kantarjian, H. M., & Blinder, V. S. (2018). The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. *CA: A Cancer Journal for Clinicians*, 68(2), 153-165.
- Charmaz, K. (1991). *Good days, bad days: The elf in chronic illness and time*. New Brunswick, NJ: Rutgers University Press.

- Chino, F. Lu, Y., Samsa, G., Abernethy, A. & Zafar, Y. (2014). Self-Reported Financial Burden and Satisfaction with care among patients with cancer. *The Oncologist*, 19:414–420.
- Chino, F., Peppercorn, J., Rushing, C. Nicolla, J., Kamal, A., Altomare, I, Samsa, G. Zafar, S. (2019). Going for broke: A longitudinal study of patient-reported financial sacrifice in cancer care. *Journal of Oncology Practice*, 14(9): e533-e546.
- Claxton, G., Rae, M., & Panchal, N. (2015). Consumer assets and patient cost sharing. Retrieved from <https://www.kff.org/health-costs/issue-brief/consumer-assets-and-patient-cost-sharing/>
- CMS.gov. (2019). CMS Takes Action to Lower Prescription Drug Prices and Increase Transparency. May, 16, 2019. Retrieved from <https://www.cms.gov/newsroom/press-releases/cms-takes-action-lower-prescription-drug-prices-and-increase-transparency>
- Collado, L., & Brownell, I. (2019). The crippling financial toxicity of cancer in the United States. *Cancer Biology & Therapy*, 20:10, 1301-1303.
- Cole, A. Jazowski, S. & Dusetzina, T. (2019). Initiation of generic imatinib may improve medication adherence for patients with chronic myeloid leukemia. *Pharmacoepidemiology Drug Safety*, 1–5.
- Conway, L. (2019). Reduce financial toxicity. The Advisory Board. Washington D.C.
- Coughlin, S., & Dean, L. (2019). Cancer survivorship care plans, financial toxicity, and financial planning alleviating financial distress among cancer survivors. *Supportive Care in Cancer*, 27:1969–1971.
- Cubanski, J., Neuman, T., & Damico, A. (2018). Closing the Medicare Part D coverage gap: Trends, recent changes, and what’s ahead. Retrieved from <https://www.kff.org/medicare/issue-brief/closing-the-medicare-part-d-coverage-gap-trends-recent-changes-and-whats-ahead/>

- Davidoff, A., Erten, M., Shaffer, T., Shoemaker, J., Zuckerman, I., Pandya, N., . . . Stuart, B. (2013). Out-of-pocket health care expenditure burden for Medicare beneficiaries with cancer. *Cancer*, 119(6), 1257-126
- Dine, C., Masi, D & Smith, C. (2019). Tools to help overcome barriers to cost-of-care conversations. *Annals of Internal Medicine*, 170:S36-S38.
- Delgado-Guay M., Ferrer, J., Rieber, A., Rhondali, W., Tayjasanant, S., Ochoa, J...Bruera, E., (2015). Financial distress and its associations with physical and emotional symptoms and quality of life among advanced cancer patients. *Oncologist*, 20:1092-8.
- deSouza, J., Yap, B., Hlubocky, F., Wroblewski, K., Ratain, M., Cella, D., Daugherty, C. (2014). The development of a financial toxicity patient-reported outcome in cancer: the COST measure. *Cancer*, 120, 3245–3253.
- deSouza, J., Yap, B., Wroblewski, K., Blinder, V., Araujo, F., Hlubocky, F...Cella, D. (2017). Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the comprehensive score for financial toxicity. *Cancer*, 123:476-84.
- Donovan, K., Grassi, L., McGinty, H., & Jacobsen P. (2014). Validation of the Distress Thermometer worldwide: state of the science. *Psycho-Oncology*, 23: 241–250.
- Doshi, J., Miller-Sonet, E., Puckett, J. & Glick, H. (2019). Advocating for new patient-centered tools for value-based treatment choices in oncology. *Journal of Clinical Pathways*, 5(2):44-47.
- Doyle, D. (2017). Oncologists must begin to discuss financial toxicity with patients. *American Health & Drug Benefits*. August, 2017: 36-37.

- Dusetzina, S. B., Winn, A. N., Abel, G. A., Huskamp, H. A., & Keating, N. L. (2014). Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia. *Journal of Clinical Oncology*, 32(4), 306-311.
- Ekwueme, D., Yabroff, K., Guy, G., Banegas, M., deMorr, A., Li, C....Virgo, K. (2014). Medical costs and productivity issues of cancer survivors—United States, 2008-2011. *MMWR Morbidity and Mortality and Weekly Report*, 63 (23):505-510.
- Ell K., Xie B., Wells A., Nedjat-Haiem, F., Lee, P., & Vourlekis, B. (2008). Economic stress among low-income women with cancer: effects on quality of life. *Cancer*, 112(3): 616-25.
- Ezeife, D., Morganstein, B., Lau, S., Law, J., Le, L, Bredle, J....Leigh, N. (2019). Financial burden among patients with lung cancer in a publicly funded health care system. *Clinical Lung Cancer*, 20(4): 231-6 .
- Farano, J. & Kandah, H. (2019). Targeting financial toxicity in oncology specialty pharmacy. *Journal of Managed Care & Specialty Pharmacy*, 25 (7): 765-769.
- Federal Drug Administration (FDA). (2018). Drugs@FDA: FDA approved drug products. Retrieved from: <https://www.accessdata.fda.gov/scripts/cder/daf/>
- Feke, T. (2019). Medicare pays more for drugs than Medicaid or the VA: Can government negotiations with pharmaceutical companies cut costs? Retrieved Dec. 2, 2019 from <https://www.verywellhealth.com/drugs-cost-more-than-from-medicaid-or-the-va-4047440>

- Fenn, K., Evans, S., McCorkle, R., DiGiovanna, M., Puzstai, L Sanft, T....Chagpar, A. (2014). Impact of Financial Burden of Cancer on Survivors' Quality of Life. *Journal of Oncology Practice*, 10(5): 332-339.
- Ferrell, B., Kravitz, K., Borneman, T., Taratoot-Friedmann, E. (2018). Family caregivers: A qualitative study to better understand the quality-of-life concerns and needs of this population. *Clinical Journal of Oncology Nursing*, 22(3):286-294.
- Galbraith, A., Ross-Degnan, D., Soumerai, S., Rosenthal, M., & Gay, C. & Leiu, T. (2011). Nearly half of families in high-deductible health plans whose members have chronic conditions face substantial financial burden. *Health Affairs*, 30(2): 322-331.
- Garraway, L., Verweij, J. & Ballman, K. (2013). Precision oncology: an overview. *Journal of Clinical Oncology*, 31(15):1803-1805.
- Gidwani-Marszowski, R., Nevedal, A., Blayney, D., Patel, M., Kelly, P. Timko, C.... Asch, S. (2018). Oncologists' views on using value to guide cancer treatment decisions. *Value in Health*, 21: 931–937.
- Gilligan, A., Alberts, D., Roe, D. & Skrepnek, G. (2018). Death or debt? National estimates of financial toxicity in persons with newly-diagnosed cancer. *American Journal of Medicine*, 131(10):1187–1199.
- Ginex, P., Brassil, K. & Ely, B. (2017). Immunotherapy: Exploring the state of science. *Clinical Journal of Oncology Nursing*, Supp,21(2): 9-12.
- Giuliani, J. & Bonetti, A. (2019). Financial toxicity and non-small cell lung cancer treatment: The optimization in the choice of immune check point inhibitors. (2019). *Anticancer Research*, 39: 3961-3965.

- Glaser, B. & Strauss, A. (1967). *The Discovery of Grounded Theory: Strategies for Qualitative Research*, Chicago, Aldine Publishing Company.
- Goldstein, D. (2017). Financial toxicity in cancer care—Edging toward solutions. *Cancer*, April 17, 2017, 1301-1302.
- Gordon L., Merollini, K., Lowe, A. & Chan, R. (2017). A systematic review of financial toxicity among cancer survivors: We can't pay the co-pay. *Patient*. 10(3):295-309.
- Graves, D., Arnold, S., Love, C., Kirsch K., Moore, P., & Passik S. (2007). Distress screening in a multidisciplinary lung cancer clinic: prevalence and predictors of clinically significant distress. *Lung Cancer*, 55(2):215-24.
- Gupta, S., Abouzaid, S. Libert, R., Parikh, K., Ung, B., Rosenberg, A., (2019). Assessing the effect of adherence on patient-reported outcomes and out of pocket costs among patients with multiple myeloma clinical lymphoma. *Myeloma & Leukemia*, 18 (3): 210-8.
- Guy, G., Ekwueme, D., Yabroff, K., Dowling, E., Rodriguez, J., deMoor, S., & Virgo, K. (2013). Economic burden of cancer survivorship among adults in the United States. *Journal of Clinical Oncology*, 31 (30): 3749-57.
- Guy, G., Yabroff, K., Ekwueme, D., Smith, A., Dowling, E., Rechis, R...Richardson, L. (2014). Estimating the health and economic burden of cancer among those diagnosed as adolescents and young adults. *Health Affairs (Millwood)* 33 (6): 1024-31.
- Guy, G., Yabroff, K., Ekwueme, D, et al. (2015). Healthcare expenditure burden among non-elderly cancer survivors, 2008-2012. *American Journal of Preventive Medicine*, 49 (6 Suppl 5): S489-97.

- Haslem, D, Chakaraty, I & Fulde, G. (2018) Precision medicine in advanced cancer patients improves overall survival and lowers weekly healthcare costs. *Oncotarget*, 9(15): 12315-12322.
- Haslem, D., Chakravarty, I., Fulde, G., Gilbert, H., Tudor, B. Lin, K...Nadauld, L. (2018). Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs. *Oncotarget*, 9(15): 12316-12322.
- Health and Human Services, U.S. (2018). National Health Expenditure (NHE) Fact Sheet: Estimates for healthcare, 2026. Retrieved Sept. 15, 2018 from <https://www.hhs.gov/healthcare/index.html>
- Henrikson, N. & Shankaran V. (2015). Improving price transparency in cancer care. *Journal of Oncology Practice*, 12(1):44-47.
- Hilal, T., Betcher, J. & Leis, J. (2018). Economic impact of oral therapies for Chronic Lymphocytic Leukemia—the burden of novelty. *Current Hematologic Malignancy Reports*, 13:237–243.
- Hoadley, J, Cubanski, J. & Neuman, T. (2015a) It pays to shop: Variation in out of pocket costs for Medicare Part D enrollees 2016. Kaiser Family Foundation issue brief, Dec. 2015. Retrieved from: <http://files.kff.org/attachment/Issue-Brief-It-Pays-to-Shop-Variation-in-Out-of-Pocket-Costs-for-Medicare-Part-D-Enrollees-in-2016>
- Hoadley, J., Cubanski, J. & Neuman, T. (2015b). Medicare Part D at Ten Years: The 2015 Marketplace and Key Trends, 2006-2015. Retrieved from <https://www.kff.org/medicare/report/medicare-part-d-at-ten-years-the-2015-marketplace-and-key-trends-2006-2015/>

- Honda, K., Gyawali, B., Ando, M., Sugiyama, K., Mitani, S., Masuishi, T., & Narita, Y. (2018). A prospective survey of comprehensive score for financial toxicity in Japanese cancer patients: report on a pilot study. *Cancer*, 12:847
- Hong, S., Li, E., Matusiak, L. & Schumock, G. (2018). Spending on antineoplastic agents in the United States, 2011 to 2016. *Journal of Oncology Practice*, 14 (11), e685-e691.
- Howard, D., Bach, P. Berndt E., & Conti, R. (2015). Pricing in the market for anticancer drugs. NBER Working Paper No. 20867. Cambridge, MA; National Bureau of Economic Research. NBER Program: 2015.
- Horvath, J. (2018). Prescription Drug Importation: New Federal Initiatives and the Case for State Action. *Health Affairs*, Nov. 14, 2018. Retrieved Nov. 11, 2019 from <https://www.healthaffairs.org/doi/10.1377/hblog20181113.552343/full/>
- Huntington, S. (2016). Cancer-related financial toxicity: Beyond the realm of drug pricing and out-of-pocket costs. *Annals of Oncology*, 27(12): 2143–2145 doi:10.1093/annonc/mdw540
- Huntington, S., Weiss, B., Vogl, D., Cohen, A. Garfall, A. Mangan, P....Stadtmauer E. (2015). Financial toxicity in insured patients with multiple myeloma: a cross-sectional pilot study. *Lancet Haematology*, 2: e408–16.
- Institute of Medicine (IOM). (2013). Delivering high-quality cancer care: Charting a new course for a system in crisis. [cited 2013 Sept 10]. Available from: <http://nationalacademies.org/HMD/Reports/2013/Delivering-High-Quality-Cancer-Care-Charting-a-New-Course-for-a-System-in-Crisis.aspx>
- Irwin, M. & Johnson L. (2015). Factors influencing oral adherence: Qualitative metasummary and triangulation with quantitative evidence. *Clinical Journal of Oncology Nursing*, 19(3): 6-30.

- ISB (2017). Laws vs. Regulations ... and Why the Difference Matters. Retrieved from <https://indivisiblesb.org/laws-vs-regulations-and-why-the-difference-matters/>
- Jacobson, J. (2019). Managing cancer patients' expectations amid hope and hype. *Health Affairs*, 38(2): 320-323.
- Jacobsen P., Donovan K., Trask P., Fleishman S., Zabora, J., Baker. F., & Holland, J. (2005). Screening for psychologic distress in ambulatory cancer patients: A multicenter evaluation of the Distress Thermometer. *Cancer*, 103:1494–1502.
- Jagsi, R., Pottow, J., Griffith, K., Bradley, C., Hamilton, A., Graff, J....Hawley, S. (2014). Long-term financial burden of breast cancer: experiences of a diverse cohort of survivors identified through population-based registries. *Journal of Clinical Oncology*, 32(12):1269-76.
- Kaiser Family Foundation (KFF). (2017). 2017 Employer Health Benefits Survey. Retrieved July 11, 2018 from <https://www.kff.org/report-section/ehbs-2017-summary-of-findings/>.
- Kaiser Family Foundation (KFF). (2018). The Medicare Part D Prescription Drug Benefit. Retrieved from July, 11, 2018 from files.kff.org/attachment/Fact-Sheet-The-Medicare-pt-D-Prescription-Drug-Benefit.
- Kaiser Family Foundation (2019). Prescription Drugs. Retrieved Nov. 12, 2019 from https://www.kff.org/tag/prescription-drugs/?utm_source=web&utm_medium=trending&utm_campaign=prescription-drugs/
- Kale, H. & Carroll, N. (2016). Self-reported financial burden of cancer care and its effect on physical and mental health-related quality of life among US cancer survivors. *Cancer*, 122(8):283–9.

- Kantarjian, J., Steensma, D. Sanjuan, J. Elshaug, A & Light, D. (2014). High cancer drug prices in the United States: Reasons and proposed solutions. *Journal of Oncology Practice*, 10(4): e208-e211.
- Katz, A. (2018). Let's talk about financial toxicities. *Oncology Nursing Forum*, 45(3), 281–282.
- Knight, T., Deal, A., Dusetzina, S., Muss, H., Choi, S., Bensen, J. & Williams, G. (2018). Financial toxicity in adults with cancer: Adverse outcomes and noncompliance. *Journal of Oncology Practice*, 14(11): e665-e673.
- Kodjak, A. (2018). How Drug Companies Control How Their Drugs Are Covered By Medicaid, July 18, 2018. All Things Considered, National Public Radio. Retrieved Nov. 11, 2019 from <https://www.npr.org/2018/07/18/630246488/how-drug-companies-are-controlling-how-their-drugs-are-covered-by-medicaid>
- Light, D. & Kantarjian, H. (2013). Market spiral pricing of cancer drugs. *Cancer*, 119(22); 3900-3902.
- Leopold, C., Araujo-Lane, C., Rosenberg, C., Gilkey, M. & Wagner, A. (2019). Out-of-Pocket cancer care costs and value frameworks: A case study in a community oncology practice with a financial navigator program. *PharmacoEconomics*, July 19, 2019.
- Maeda, H. & Khatami, M. (2018). Analyses of repeated failures in cancer therapy for solid tumors: poor tumor-selective drug delivery, low therapeutic efficacy and unsustainable costs. *Clinical Translational Medicine*, 7:11.
- Mariotto, A., Yabroff, K., Shao, Y., Feuer E., & Brown M. (2011). Projections of the cost of cancer care in the United States: 2010-2020. *Journal of the National Cancer Institute*, 103:117-128.

- Massa, S., Rohde, R., McKinstry, C., Gresham, M, Osazuwa-Peters, N. Ward, G. & Walker, R. (2018). An assessment of patient burdens from head and neck cancer survivorship care. *Oral Oncology*, 82: 115-121.
- McCaughan, M. (2017). Veterans Health Administration: The Veterans Health Administration can often obtain very favorable prices for drugs and may be a model for Medicare and others. Prescription Drug Pricing. *Health Affairs*. Retrieved Dec. 2, 2019 from https://www.healthaffairs.org/doi/10.1377/hpb20171008.000174/full/healthpolicybrief_174.pdf
- McNulty J. & Khera, N. (2015). Financial Hardship—an unwanted consequence of cancer treatment. *Current Hematology Malignancy Report*, 10:205–212.
- Medicare (2018). Costs in the coverage gap. Retrieved from <https://www.medicare.gov/drug-coverage-part-d/costs-for-medicare-drug-coverage/costs-in-the-coverage-gap>
- Meeker, C., Geynisman, D., Egleston, B., Hall, M., Mechanic, K., Bilusic, M., Pilmack, E.....Wong, Y. (2016). Relationships among financial distress, emotional distress, and overall distress in insured patients with cancer. *Journal of Oncology Practice*, 12(7): e775-e764.
- Meisenberg, B. (2015). The financial burden of cancer patients: time to stop averting our eyes. *Support Care in Cancer*, 23:1201–1203.
- Mitchell, A. (2007). Pooled results form 38 analyses of the accuracy of distress thermometer and other ultra-short methods of detecting cancer-related mood disorders. *Journal of Clinical Oncology*, 25(29): 4670-4681.

- Mohammed, R. & El-sol, A. (2018). Nursing: 7 key cancer trends. *International Journal of Nursing Didactics*, 8: (04) April: 21-24.
- Morrison, C. (2015). Financial toxicity' looms as cancer combinations proliferate. *Nature Biotechnology*, 33(8): 783-784. MacMillan, L. (2019). Patient assistance programs. *Clinical Journal of Oncology Nursing*, 23 (Supp.2) 36-40.
- Murphy, C., Fullington, H., Alvarez, C., Betts, A., Craddock Lee, S... Halm, E. (2018). Polypharmacy and patterns of prescription medication use among cancer survivors. *Cancer*, 124:2850-7.
- Nair, S. & Kong, A. (2018). Emerging roles for clinical pharmacometrics in cancer precision medicine. *Current Pharmacology Reports*, 4:276–283.
- National Academy of Sciences, Engineering and Medicine (NASEM). (2017). Making Medicines Affordable: A National Imperative. Washington, DC: The National Academies Press. Available at <https://doi.org/10.17226/24946>.
- National Cancer Institute (NCI). (2019). Financial toxicity and cancer treatment (PDQ®)—Health Professional Version. Retrieved Sept. 15, 2019 from <https://www.cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-hp-pdq>
- National Comprehensive Cancer Network (NCCN) (2018). Distress management clinical practice guidelines: Retrieved Sept. 15, 2019 from https://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf
- National Comprehensive Cancer Network (NCCN). (2018). Distress thermometer. Retrieved from https://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf

- National Institutes of Health (NIH). (2018). NIH Human Subjects Policies and Guidance. Retrieved from: <https://humansubjects.nih.gov/nih-human-subjects-policies-guidance>
- Newton, J., Johnson, C., Hohnen, H., Bulsar, M, Ives, A., McKiernan, S....Saunders, C. (2018). Out-of-pocket expenses experienced by rural Western Australians diagnosed with cancer. *Supportive Care in Cancer*, 26:3543–3552.
- Nipp, R., Sonet, E. & Guy G. (2018). Communicating the financial burden of treatment with patients. ASCO Education Book. Retrieved Sept. 15, 2019 from asco.org/edbook.
- Patient Power (2018). Retrieved from <https://www.patientpower.info/>
- Pearce, A., Tomalin, B., Billingsley, K., Horevoorts, N., Duijts, S. Floortje, M....Koczwara, B. (2019). Financial toxicity is more than costs of care: the relationship between employment and financial toxicity in long-term cancer survivors. *Journal of Cancer Survivorship*, 13:10–20.
- Peppercorn, J. (2017). Financial toxicity and societal costs of cancer care: Distinct problems require distinct solutions. *The Oncologist*, 22:123–125.
- Pelletier, W. & Bona, K. (2015). Assessment of financial burden as a standard of care in pediatric oncology. *Pediatric Blood Cancer*, 62:S619–S631.

- Perrone, F., Jammi, C., DiMaio, M., Gimigliano, A., Gridelli, C. Pignata, S....Gall, C. (2016). The association of financial difficulties with clinical outcomes in cancer patients: secondary analysis of 16 academic prospective clinical trials conducted in Italy. *Annals of Oncology*, 27(12): 2224-2229.
- Ploos van Amstel, F., Tol, J., Sessink, K., van der Graaf, W., Prins, J. & Ottevanger, P. (2017). A specific distress cutoff score shortly after breast cancer diagnosis. *Cancer Nursing*, 40(3):E35-E40.
- Prasad, V. De Jesus, K., & Mailankody, S. (2017). The high price of anticancer drugs: Origins, implications, barriers, solutions. *Nature Reviews: Clinical Oncology*, 14: 381-390.
- Printz, C. (2014). Drug parity legislation: states, organizations seek to make oral cancer drugs more affordable. *Cancer*, 120-313-314.
- Ramsey, S., Blough, D., Kirchoff, A., Kriezenbeck, K, Fedorenko, C. Snell, K....Overstreet, K. (2013). Washington state cancer patients found to be at greater risk for bankruptcy than people without a cancer diagnosis. *Health Affairs*, 32(6): 1143-1152.
- Renner, A., Burotto, M. & Rojas, C. (2019). Immune checkpoint inhibitor dosing: Can we go lower without compromising clinical efficacy? *Journal of Global Oncology*, 1-3.
- Rosenzweig, M., West, M., Matthews, J., Stokan, M., Kook, Y., Gallups, S. Diergaarde, B. (2019). Financial toxicity among women with metastatic breast cancer. *Oncology Nursing Forum*, 46 (1): 83-91.
- Rotenstein, L, Dusetzina, S, Keating, N. (2018). Out of pocket spending not associated with oral oncolytic survival benefit. *Journal of Managed Care & Specialty Pharmacy*, 24(6): 494-502.

- Rupper, R. (2018). Historical and current advances that incorporate competing risk for benefit and mortality in older patients with cancer. *Clinical Therapeutics*, 40 (4): 504-511.
- Salsman, J., Bingen, K., Barr, R. & Freyer, D. (2019). Understanding, measuring, and addressing the financial impact of cancer on adolescents and young adults. *Pediatric Blood Cancer*, 66:e27660.
- Santacroce, S., Tan, K. & Killea, M. (2018). A systematic scoping review of the recent literature (2011–2017) about the costs of illness to parents of children diagnosed with cancer. *European Journal of Oncology Nursing*, 35: 22–32.
- Schiffer, C. (2018). The evolution of Dasatinib dosage over the years and its relevance to other anticancer medications. *Cancer*, July 1, 2018, 2687-2689.
- Schneider, C., Steinbrecher, D. & Stilgenbauer, S. (2019). Targeted therapy in CLL: changing the treatment paradigm. *Oncotarget*, 10,(40): 4002-4003.
- Schnipper, L., Davidson, N., Wollins, D., Blayney, D., Dicker, A., Ganz, P...Schilsky, R. (2016). Updating the American Society of Clinical Oncology Value Framework: Revisions and reflections in response to comments received. *Journal of Clinical Oncology*, 34(24), 2925-2934.
- Schnipper, L., Davidson, N., Wollins, D., Tyne, C., Blayney, D. & Blum, D. (2015). American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. *Journal of Clinical Oncology*, 33(23), 2563-2577.
- Seidman, J., Masi, D., Gomez-Rexrode, A. (2019). Personalizing value in cancer care: The case for incorporating patient preferences into routine clinical decision making. *Journal of Participatory Medicine*, 11(3):e13800.

- Shanafelt, T., Borah, B., Finnes, H., Chaffee, K., Ding, W., Leis, J...Call T. (2015). Impact of ibrutinib and idelalisib on the pharmaceutical cost of treating chronic lymphocytic leukemia at the individual and societal levels. *Journal of Oncology Practice*, 11:252-258.
- Shankaran, V., Leahy, T., Steelquist, J., Watabayashi, K., Linden, H., Ramsey, S....Overstreet, K. (2018). Pilot Feasibility Study of an Oncology Financial Navigation Program. *Journal of Oncology Practice*, 14:2, e122-e129.
- Shen, C. Zhao, B. Liu, L & Shih, Y. (2017). Financial burden for patients with Chronic Myeloid Leukemia enrolled in Medicare Part D taking targeted oral anticancer medications, *Journal of Oncology Practice*, 13(2): e152-e162.
- Sherman, D. & Fessele, K. (2019). Financial support models, *Clinical Journal of Oncology Nursing*, 23 (Supp.2) 14-18.
- Shih, Y., Smieliauskas, F., Geynisman, D., Kelly, R. & Smith, T. (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): 2190-6.
- Soni A (2015). Trends in the Five Most Costly Conditions among the U.S. Civilian Institutionalized Population, 2002 and 2012. Statistical Brief 470. Rockville, Md: Agency for Healthcare Research and Quality.
- Speaker. (2019). For the People: HR 3, the Lower Drugs Costs Now Act. Retrieved Dec. 2, 2019 from <https://www.speaker.gov/sites/speaker.house.gov/files/HR3%20Backgrounder%2010.2.19.pdf>
- Stone, A. (2019). The battle against drug pricing rages on. The Voice. Aug. 5, 2019. Retrieved Nov. 11, 2019 from <https://voice.ons.org/advocacy/the-battle-against-drug-pricing-wages-on>

- Sweeney, D. (2019). Experts hold conversations about access and affordability at ONS Policy Summit. *OSN Voice*, Feb. 2019, 22-23.
- Taylor, L. (2019). Financial toxicity and cost-related non-adherence in patients with chronic blood cancers. Retrieved from Vanderbilt University. Accession number 203-007.
- Tay-Teo, K., Ilbawi, A. & Hill, S. (2019). Comparison of sales income and research and development costs for FDA-approved cancer drugs sold by originator drug companies. *JAMA Network Open*, 2:1-11.
- Thom, B. & Benedict, C. (2019). The impact of financial toxicity on psychological well-being, coping self-efficacy, and cost-coping behaviors in young adults with cancer. *Journal of Adolescent and Young Adult Oncology*, 8 (3): 236-242.
- Thomas, T., Hughes, T., Mady, L. & Belcher, S (2019). Financial toxicity: A state of the science and nursing opportunities. *Clinical Journal of Oncology Nursing*, 23 (Supp.2) 5-13.
- Tran, G. & Zafar, Y. (2018). Financial toxicity and implications for cancer care in the era of molecular and immune therapies. *Annals of Translational Medicine*, 6(9):166.
- Truong, J., Chan, K., Mai, H., Chambers, A. Sabharwal, M. Trudeau, M. & Cheung, M. (2019). The impact of pricing strategy on the costs of oral anti-cancer drugs. *Cancer Medicine*, 8:3770–3781.
- Tucker-Seeley, R. & Yabroff, K. (2016). Minimizing the “financial toxicity” associated with cancer care: advancing the research agenda. *Journal of the National Cancer Institute*, 108(5):1-3.
- Tuinman, M., Gazendam-Donofrio, S., Hoekstra-Weebers, J. (2008). Screening and referral for psychosocial distress in oncologic practice: use of the Distress Thermometer. *Cancer*, 113(4):870-8.

- Ubel, P., Aberneth, A, Zarar, S. (2013). Full disclosure-out of pocket costs as side effects. *New England Journal of Medicine*, 369-1484-1486.
- U.S. Census Bureau (2019). Quick Facts. Retrieved Nov. 1, 2019 from <https://www.census.gov/quickfacts/fact/table/US/SEX255218>
- VanHoose, L., Black, L., Doty, K., Sabata, D., Twumasi-Ankrah, P. Taylor, S. & Johnson, R. (2015). An analysis of the Distress Thermometer problem list and distress in patients with cancer. *Supportive Care in Cancer*, 23:1225.
- Walter, A. (2019). Politics with Amy Walter: Prescription Drug Costs and 2020. The Takeaway: Nov. 1, 2019. Public Radio International Retrieved Nov. 12, 2019 from https://www.wnycstudios.org/podcasts/takeaway/amy_walter
- Warsame, R., Kennedy, C., Kumbamu, A., Branda, M., Fernandez, C., Kimball, B., Leppin, A., O'Byrne, T., Jatoi, A., Lenz, H. & Tilburt, J. (2019). Conversations about financial issues in routine oncology practices: A multicenter study. *Journal of Oncology Practice*, 15(8): e690-e697.
- Waxman, H., Corr, B., Martin, K, Sharp, J. & Duong, S. (2019). The FDA's Drug Pricing Strategy: What's New?, Jan. 28, 2019. The Commonwealth Fund. Retrieved from <https://www.commonwealthfund.org/blog/2019/fdas-drug-pricing-strategy-whats-new>
- Winkfield, K., Phillips, J., Joffe, S. Halpern, M., Wollins, D., Moy, B. (2018). Addressing financial barriers to patient participation in clinical trials: ASCO Policy Statement, *Journal of Clinical Oncology*, 36(33): 3331-3340.
- Wheeler, S., Spencer, J., Pinheiro, L., (2018). Financial impact of breast cancer in black versus white women. *Journal of Clinical Oncology*, 36(7): 1695-1701.

Winn, A., Keating, N., & Dusetzina, S. (2016). Factors associated with tyrosine kinase inhibitor initiation and adherence among Medicare beneficiaries with chronic myeloid leukemia.

Journal of Clinical Oncology, 34(36): 4323-4328

Yabroff, K., Dowling C., Guy G., Baneagas, M., Davidoff, A., Xuesong, H...Ekwueme, D. (2016).

Financial hardship associated with cancer in the United States: Finding from a population-based sample of adult cancer survivors. *Journal of Clinical Oncology*, 34:259-267.

Yabroff, K., Gansler, T., Wender, R., Cullen, K. & Brawley, O. (2019). Minimizing the burden of

cancer in the United States: Goals for a high-performing health care system. *CA: Cancer Journal for Clinicians*, 69:166-183.

Yabroff, K., Zhao, J., Zheng, Z., Rai, A., & Han, X. (2018). Medical financial hardship among cancer survivors in the United States: What do we know? What do we need to know?.

Cancer Epidemiology and Prevention Biomarkers, 27(12), 1389-1397.

Yu, P., Eton, O., & Garrison, L. (2019). Challenges in assessing the clinical utility and economic

value of immune checkpoint inhibitor therapies of Cancer. *Journal for Immunotherapy of Cancer*, 7:235.

Zafar, S. (2016). Financial toxicity of cancer care: It's time to intervene. *JNCI: Journal of the*

National Cancer Institute, 108(5).

Zafar, S. & Abernethy, A. (2013a). Financial toxicity, part II: How can we help with the burden of

treatment-related costs? *Oncology*, 27(4), 253.

Zafar, S. & Abernethy, A. (2013b). Financial toxicity, part I: A new name for a growing problem.

Oncology (Williston Park, N.Y.), 27(2), 80-1, 149.

- Zafar, S., Peppercorn, J., Schrag, D., Taylor, D., Goetzinger, A., Zhong, X., & Abernethy, A. (2013). The financial toxicity of cancer treatment: A pilot study assessing out-of-pocket expenses and the insured cancer patient's experience. *Oncologist*, 18, 381–390
<https://doi.org/10.1634/theoncologist.2012-0279>.
- Zahnd, W., Davis, M., Rotter, J., Vanderpool, R., Perry, C., Shannon, J...Eberth, J. (2019). Rural-urban differences in financial burden among cancer survivors: An analysis of a nationally representative survey. *Supportive Care in Cancer*. Retrieved April 10, 2019 from <https://doi.org/10.1007/s00520-019-04742-z>
- Zhang, Y., Hueser, H., & Hernandez, I. (2017). Comparing the approval and coverage decisions of new oncology drugs in the United States and other selected countries. *Journal of Managed Care & Specialty Pharmacy*, 23:247-254.
- Zheng, Z., Yabroff, R., Guy, G., Han, X., Li, C., Banegas, M....Jemal A. (2016). Annual medical Expenditure and productivity loss among colorectal, female breast, and prostate cancer survivors in the United States. *Journal of National Cancer Institute*, 108(5): djv382
- Zullig, L., Peppercorn, J., & Schrag, D. (2013). Financial distress, use of cost-coping strategies and adherence to prescription medication among patients with cancer. *Journal of Oncology Practice*, 9:60-s-63s.

Appendix A



Feb 5, 2019 12:07 PM PST

Ellen Carr, Hahn School of Nursing & Health Science

Re: Expedited - Initial - IRB-2019-261, Treatments for Cancer Given Orally: Patients' Perception of Distress Due to Financial Toxicity

Dear Ellen Carr:

The Institutional Review Board has rendered the decision below for IRB-2019-261, Treatments for Cancer Given Orally: Patients' Perception of Distress Due to Financial Toxicity.

Decision: Approved

Selected Category: 7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Findings: None

Research Notes:

Internal Notes:

Note: We send IRB correspondence regarding student research to the faculty advisor, who bears the ultimate responsibility for the conduct of the research. We request that the faculty advisor share this correspondence with the student researcher.

The next deadline for submitting project proposals to the Provost's Office for full review is N/A. You may submit a project proposal for expedited or exempt review at any time.

Sincerely,

Dr. Thomas R. Herrinton, Administrator, Institutional Review Board

Office of the Vice President and Provost

Hughes Administration Center, Room 214

5998 Alcalá Park, San Diego, CA 92110-2492

Phone (619) 260-4553 • Fax (619) 260-2210 • www.sandiego.edu

Appendix B

Study Blurb

You are invited to be a participant in a research study conducted by Ellen Carr, RN. Ellen is a clinical oncology nurse. She is also a doctoral student at the Hahn School of Nursing and Health Science at the University of San Diego (USD).

The Study

The study is about the concept of financial toxicity, which is a term that refers to the financial consequences of cancer treatment, which may include significant out of pocket (OOP) costs, loss of income and caregiver burden. The study will help doctors, nurses and other health care providers better understand financial toxicity when experienced by cancer patients. The study will include patients like you, who have completed or are taking cancer therapy given orally.

The study involves you completing three surveys a) a demographics survey, b) a survey about your experience with financial toxicity during or after your cancer treatment, c) a survey about distress related to your cancer treatment. It will take about 10-15 minutes for you to complete the surveys on-line.

Inclusion/Exclusion Criteria

The inclusion criteria for participants will be adult patients (21 years or older) who are Spanish or English speaking, have the ability to read English and have an initial diagnosis of these malignancies: Breast cancer, head and neck cancer, Hodgkin's Lymphoma, lung cancer leukemia, lymphoma, melanoma, multiple myeloma, myeloproliferative neoplasms, pancreatic cancer, prostate cancer. Participants will need to have been prescribed by their oncologist a cancer treatment given orally as a component of their cancer treatment regimen. The treatment given orally will be been

prescribed with the patient receiving treatment for at least 4 weeks. The participants' health insurance coverage can include private health insurance or coverage by Medicare (Medicare Fee for Service (FFS), Medigap or Medicare Part C (Advantage)).

The exclusion criteria for study participants includes patients who have not been prescribed cancer treatment given orally (i.e. infusion only; radiation and/or surgery only) and those receiving in-patient cancer treatment. In addition, excluded study participants will be those covered by Medicaid or are those without health insurance coverage.

Interested in joining this Study?

If you would like more information about the study, here is a link to more information about the study: (Web Site #1) You can also contact Ellen Carr, the study investigator, directly at e-mail: xxxxxxxx; phone: xxxxxx.

If you are interested in participating in the study, here is a link to the informed consent for the study, then links to the surveys for you to complete: (Web Site #2)

Appendix C

Web Site #1 Content

Study Synopsis

Financial toxicity is an additional stress for patients being treated for cancer. The study is about the concept of financial toxicity, which is a term that refers to the financial consequences of cancer treatment, which may include significant out of pocket (OOP) costs, loss of income and caregiver burden that occur when patients are undergoing treatment. The study will help doctors, nurses and other health care providers better understand financial toxicity when experienced by cancer patients.

Oral medications for cancer are particularly expensive. It is expected that more pricey oral medications will be approved as cancer treatments so there will be more patients who will deal with the financial toxicity of treatment.

Therefore, Ellen Carr, an oncology nurse and doctoral student at the University of San Diego is studying financial toxicity and cancer patients who have been treated or are still in treatment with therapies given orally.

The study will include patients like you, who have completed or are taking cancer therapy given orally. The Study Purpose and Aims of the study follow:

Study Purpose:

For adult participants who have received or are receiving treatment for hematologic and solid tumor malignancies given orally, to determine the relationship between participants' experience of financial toxicity (FT), the participants' perception of distress, and participants' self-identified adherence to prescribed treatments

Study Aims:

1. To describe sociodemographic, clinical and financial characteristics, the experience of FT, perception of the level of distress, and adherence to treatment in a sample of adult participants who have received or are receiving treatment given orally for hematologic or solid tumor malignancies.
2. To examine relationships between participant sociodemographic, clinical and financial characteristics, participants' experience of FT, participants' perception of distress, and participants' adherence to treatment.
3. To explore the likelihood that participant experience of FT predicts participant perception of distress and non-adherence to treatment given orally.

FAQs about the Study

- 1) What will I need to do to participate in the study?

The study involves you completing three surveys a) a demographics survey, b) a survey about your experience with financial toxicity during or after your cancer treatment, c) a survey about distress related to your cancer treatment. It will take about 10-15 minutes for you to complete the surveys on-line.

- 2) Do I need to answer all questions on the surveys?

No. You can only give responses to questions that you choose to answer.

- 3) Will I be paid to participate in the study?

There is no payment for completing the study surveys

4) How will I hear about the results of the study?

When the study results are complete and ready to be announced and published, Ellen can let you know. (You will need to provide your contact information on your informed consent form so she can contact you.)

Study Investigator's contact information

If you would like more information about the study, here is a link to more information about the study: (Web Site #1) You can also contact Ellen Carr, the study investigator, directly at e-mail: xxxxxxxx; phone: xxxxxx.

Instructions to join the Study

If you are interested in participating in the study, here is a link to the informed consent for the study, then after confirm acceptance of the informed consent, Ellen will contact you via your e-mail with a link to the surveys for you to complete: (Web Site #2)

Appendix D

Web Site #2 Content

Study Synopsis (repeat from Web site #1)

Financial toxicity is an additional stress for patients being treated for cancer. The study is about the concept of financial toxicity, which is a term that refers to the financial consequences of cancer treatment, which may include significant out of pocket (OOP) costs, loss of income and caregiver burden that occur when patients are undergoing treatment. The study will help doctors, nurses and other health care providers better understand financial toxicity when experienced by cancer patients.

Oral medications for cancer are particularly expensive. It is expected that more pricey oral medications will be approved as cancer treatments so there will be more patients who will deal with the financial toxicity of treatment.

Therefore, Ellen Carr, an oncology nurse and doctoral student at the University of San Diego is studying financial toxicity and cancer patients who have been treated or are still in treatment with therapies given orally.

The study will include patients like you, who have completed or are taking cancer therapy given orally. The Study Purpose and Aims of the study follow:

Study Purpose:

For adult participants who have received or are receiving treatment for hematologic and solid tumor malignancies given orally, to determine the relationship between participants' experience of financial toxicity (FT), the participants' perception of distress, and participants' self-identified adherence to prescribed treatments

Study Aims:

1. To describe sociodemographic, clinical and financial characteristics, the experience of FT, perception of the level of distress, and adherence to treatment in a sample of adult participants who have received or are receiving treatment given orally for hematologic or solid tumor malignancies.
2. To examine relationships between participant sociodemographic, clinical and financial characteristics, participants' experience of FT, participants' perception of distress, and participants' adherence to treatment.
3. To explore the likelihood that participant experience of FT predicts participant perception of distress and non-adherence to treatment given orally.

Instructions to complete the Informed Consent

Please follow the link to the Informed Consent form:

Informed Consent:

Introduction: You are invited to be a participant in a research study conducted by Ellen Carr, RN. Ellen is a clinical oncology nurse. She is also a doctoral student at the Hahn School of Nursing and Health Science at the University of San Diego (USD).

The study is about the concept of Financial Toxicity. Financial Toxicity refers to the financial consequences of cancer treatment, which may include significant out of pocket (OOP) costs to you and your family, loss of income and patient and caregiver burden. The study will help doctors, nurses and other health care providers better understand financial toxicity when experienced by cancer patients. This study will include patients like you, who have completed or are taking cancer therapy given orally.

Purpose of the study:

For patients receiving treatment for hematologic and solid tumor malignancies given orally, the purpose of this study is to determine the relationship between the patient's experience of financial toxicity, the patients' perception of their level of distress and whether patients went ahead and took or completed their prescribed therapy given orally.

Procedures:

From an on-line survey that you can complete at your convenience, you will be asked about your experience with financial toxicity during the period when you were (or still are) taking your cancer therapy given orally. Specifically, you will be asked to complete three brief surveys about the financial burden while you are on the therapy, any distress related to the financial burden when you were on the therapy and if the financial burden caused you to stop taking your therapy or take part of your therapy. Completing all the questions on the three surveys will take about 10-15 minutes. You can choose to not answer some of the questions.

Potential Risks and Discomforts:

The questions on the survey may cause you to feel sad or mad. You can choose not to answer any questions. You also may stop answering questions at any time.

Anticipated Benefits to You:

You will not receive any direct benefit from participating in the study. There is no compensation for participating in this study. However, after completing the survey, you may feel good about relaying your experiences about the financial burden when you received your therapy.

Anticipated Benefits to Others:

The study results will help doctors, nurses and other health care providers better understand financial toxicity when experienced by cancer patients. With that knowledge, ways to lessen the financial burden for patients and their caregivers can be developed.

Privacy/Confidentiality:

Your responses to the surveys will be kept confidential. This informed consent and any other identifying information will be kept separate from the survey results. All study information will be kept in a locked, secured location. Your survey results will be assigned a unique identification number. Any study identification number assigned to you will only be known by Ellen, the study investigator, and her dissertation committee; they are the only people who will have access to your study identification number. Any report of the study results will not identify you by name or your identification number.

Withdrawal from Study:

Your participation in the study is entirely voluntary. If you participate in the study, your participation will not affect your current or future cancer care. You can withdraw from the study at any time, either during or after your participation in the study, with no negative consequences. If you withdraw from the study, your survey results will be destroyed.

Your Rights:

You can choose to participate in the study. If you do participate, you can withdraw from the study at any time without consequences. You are not waiving any legal rights if you choose to participate in the study. If you have questions about your rights as a participant of this study or if you have concerns about the study and want to discuss those with someone other than Ellen Carr,

you can contact the University of California Office of Research Protection, phone: xxxx address: xxxxx

You may request a copy of the study’s final results by indicating your interest at the end of this consent. And after this study if you are interested in being contacting by the investigator again about a follow-up study about financial toxicity and cancer patients, please check the box below.

Investigator Identification:

Ellen Carr, RN, is the study investigator. If you have questions for Ellen, you can contact her via this e-mail link: xxxxxx. You can also contact her at 619-922-3903.

+++++

Participant Signature:

By clicking the accept key below, you are confirming that you have read this document, you understand the purpose of the study and you have had the opportunity to ask questions about proceeding to participate in the study.

Name

Signature (key click) Date stamp:

e-mail address:

NOTE: Based on your clicking the accept key, Ellen Carr, the study’s investigator, will now contact you by your e-mail above with a link to the study’s questionnaires. By completing the study’s questionnaires, you have provided consent to participate in this study.

+++++



Investigator Signature:

By clicking the key below, I confirm that I have provided an explanation of the study to the participant and have answered his/her questions. By the participant confirming that he/she has read this document, the participant understands the purpose of the study and has had the opportunity to ask questions, thereby giving asset/consent to proceed to participate in the study.

Name

Signature (key click) Date stamp:

++++++

Further contact from Ellen Carr about study results or follow-up study:

- Please send a summary of the study results to:

Name

e-mail address

- I am not requesting a summary of the study results
- I am willing to be contacted by Ellen Carr, the study investigator, about a follow-up study about financial toxicity and cancer.

Name

e-mail address

Appendix E

Instrument # 1: Demographic Questionnaire

General

- 1) I am
 - Female
 - Male

- 2) I am
 - < 50 years old
 - 50-64 years old
 - >65 years old

- 3) My living status is
 - Married
 - Live with a domestic partner in the same household
 - Live as a single
 - Live in a community setting (i.e. with roommates)

- 4) Highest level of education
 - < 12th Grade
 - 12th Grade
 - Some college
 - Completed college
 - Some or complete graduate school

Cancer Diagnosis

- 1) I am diagnosed with cancer or malignancy
 - Yes
 - No
 - Don't know

- 2) If yes to #1 above, my cancer diagnosis is
(Open text; optional response)

- 3) Stage at Diagnosis
 - Stage 1
 - Stage 2
 - Stage 3
 - Stage 4

- 4) Prescribed oral cancer therapy (drugs, dose, frequency)
(Open text)
- 5) Are you receiving your treatment given orally now?
 Yes
 No
- 6) Because of issues of cost or expense of the cancer therapy (given orally), when prescribed the therapy I:
 Stayed on or completed the therapy
 Temporarily stopped taking the therapy
 Never started the therapy
- 7) Because of the cost or expense of the cancer therapy (given orally), did you decide to stop taking any other prescribed medications or treatments for your other conditions? (i.e. examples of other conditions, which you are receiving treatments: high blood pressure, diabetes, high cholesterol, upset stomach, heart disease, arthritis, chronic pain, mental health conditions, etc.)
 Yes
 No
- 8) For other prescribed medications you are taking (see #7), did you decide to take some of those prescribed medications at their prescribed doses rather than your cancer therapy (given orally) because of the cost or expense to take all your prescribed non-cancer and cancer medications?
 Yes
 No
- 9) For other prescribed medications you are taking (see #7), did you decide to take lower or less doses of medications rather than your cancer therapy (given orally) because of the cost or expense to take all your prescribed non-cancer and cancer medications?
 Yes
 No

Insurance

- 1) Do you have health insurance coverage?
 - Yes
 - No

- 2) If yes to #1, please check your current insurance coverage?
 - Private Insurance (not Medicare)
 - Medicare
 - Medigap
 - Medicare Part C (Advantage)

- 3) Do you have a Prescription Drug Plan?
 - Yes
 - No

- 4) If yes to #3, which plan?
 - Private insurance prescription plan
 - Medicare Part D

Finances

- 1) I am employed
 - Fulltime
 - Part-time (<20 hours/week)
 - Not employed

- 2) Were you employed at the start of your treatment?
 - Yes
 - No

- 3) Does being in treatment for your cancer affect your ability to be employed?
 - Yes
 - No

- 4) My income supports
- Myself only
 - Myself and committed partner
 - Myself, committed partner and others
- 5) During the last tax year, my gross income was
- < \$50,000/year
 - \$50,000-\$100,000/year
 - \$100,000-\$200,000/year
 - >\$200,000/year
- 6) To cover the cost of my cancer treatment given orally, I am responsible to pay for:
- <20% of the cost
 - 20-50% of the cost
 - 50-100% of the cost
- 7) To cover the cost of my treatments, I received monetary help from pharmaceutical companies, advocacy groups
- Yes
 - No
- 8) If yes to #7, the monetary help I received per treatment was approximately:
- < 20%
 - 20-50%
 - 50-100%
 - Don't know
- 9) During my cancer treatment, other treatment-related expenses that I paid for out-of-pocket include or included:
- transportation
 - hotel costs
 - lost wages
 - child care
 - over the counter medication
 - Other (open text)
- 10) The monthly estimated out of pocket costs that I identified in #9 are:
- <\$100/month
 - \$100-500/month
 - 500-1000/month
 - >\$1000/month

Appendix F

Instrument #2: Comprehensive Score for Financial Toxicity (COST)

COST – FACIT (Version 1)

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

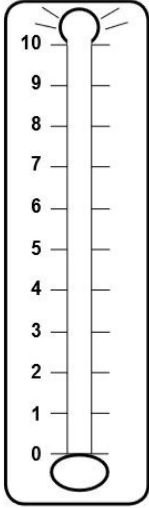
	Not at all	A little bit	Some- what	Quite a bit	Very much
FT1 I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment.....	0	1	2	3	4
FT2 My out-of-pocket medical expenses are more than I thought they would be	0	1	2	3	4
FT3 I worry about the financial problems I will have in the future as a result of my illness or treatment	0	1	2	3	4
FT4 I feel I have no choice about the amount of money I spend on care.....	0	1	2	3	4
FT5 I am frustrated that I cannot work or contribute as much as I usually do.....	0	1	2	3	4
FT6 I am satisfied with my current financial situation	0	1	2	3	4
FT7 I am able to meet my monthly expenses	0	1	2	3	4
FT8 I feel financially stressed.....	0	1	2	3	4
FT9 I am concerned about keeping my job and income, including work at home.....	0	1	2	3	4
FT10 My cancer or treatment has reduced my satisfaction with my present financial situation	0	1	2	3	4
FT11 I feel in control of my financial situation.....	0	1	2	3	4

Figure 1. . Comprehensive Score for financial Toxicity (COST)-Functional Assessment of Chronic Illness Therapy (FACIT). Items 2, 3, 4, 5, 8, 9, and 10 were reverse scored. The lower the score, the worse the financial toxicity.

Source: deSouza J, Yap B, Wroblewski K, Blinder V, Araujo F, Hlubocky F, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the comprehensive score for financial toxicity (COST). *Cancer*. 2017;123:476-84. (Used with permission.)

Appendix G

Instrument #3: National Comprehensive Cancer Network (NCCN) Distress Thermometer
(version 2.2018)

<p>NCCN DISTRESS THERMOMETER</p> <p>Instructions: Please circle the number (0–10) that best describes how much distress you have been experiencing in the past week including today.</p> <div style="display: flex; justify-content: space-between; align-items: center;"> <div style="text-align: center;"> <p>Extreme distress</p>  </div> <div style="text-align: center;"> <p>No distress</p> </div> </div>	<p>PROBLEM LIST Please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.</p> <table border="0"> <tr> <td style="text-align: center;">YES</td> <td style="text-align: center;">NO</td> <td style="text-align: center;">Practical Problems</td> <td style="text-align: center;">YES</td> <td style="text-align: center;">NO</td> <td style="text-align: center;">Physical Problems</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Child care</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Appearance</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Housing</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Bathing/dressing</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Insurance/financial</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Breathing</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Transportation</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Changes in urination</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Work/school</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Constipation</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Treatment decisions</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Diarrhea</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Eating</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Fatigue</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Feeling swollen</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Dealing with children</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Fevers</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Dealing with partner</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Getting around</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Ability to have children</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Indigestion</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Family health issues</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Memory/concentration</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Mouth sores</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Nausea</td> </tr> <tr> <td></td> <td></td> <td></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Nose dry/congested</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Depression</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Pain</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Fears</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Sexual</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Nervousness</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Skin dry/itchy</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Sadness</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Sleep</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Worry</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Substance use</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Loss of interest in usual activities</td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Tingling in hands/feet</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td>Spiritual/religious concerns</td> <td></td> <td></td> <td></td> </tr> </table> <p>Other Problems: _____</p>	YES	NO	Practical Problems	YES	NO	Physical Problems	<input type="checkbox"/>	<input type="checkbox"/>	Child care	<input type="checkbox"/>	<input type="checkbox"/>	Appearance	<input type="checkbox"/>	<input type="checkbox"/>	Housing	<input type="checkbox"/>	<input type="checkbox"/>	Bathing/dressing	<input type="checkbox"/>	<input type="checkbox"/>	Insurance/financial	<input type="checkbox"/>	<input type="checkbox"/>	Breathing	<input type="checkbox"/>	<input type="checkbox"/>	Transportation	<input type="checkbox"/>	<input type="checkbox"/>	Changes in urination	<input type="checkbox"/>	<input type="checkbox"/>	Work/school	<input type="checkbox"/>	<input type="checkbox"/>	Constipation	<input type="checkbox"/>	<input type="checkbox"/>	Treatment decisions	<input type="checkbox"/>	<input type="checkbox"/>	Diarrhea				<input type="checkbox"/>	<input type="checkbox"/>	Eating				<input type="checkbox"/>	<input type="checkbox"/>	Fatigue				<input type="checkbox"/>	<input type="checkbox"/>	Feeling swollen	<input type="checkbox"/>	<input type="checkbox"/>	Dealing with children	<input type="checkbox"/>	<input type="checkbox"/>	Fevers	<input type="checkbox"/>	<input type="checkbox"/>	Dealing with partner	<input type="checkbox"/>	<input type="checkbox"/>	Getting around	<input type="checkbox"/>	<input type="checkbox"/>	Ability to have children	<input type="checkbox"/>	<input type="checkbox"/>	Indigestion	<input type="checkbox"/>	<input type="checkbox"/>	Family health issues	<input type="checkbox"/>	<input type="checkbox"/>	Memory/concentration				<input type="checkbox"/>	<input type="checkbox"/>	Mouth sores				<input type="checkbox"/>	<input type="checkbox"/>	Nausea				<input type="checkbox"/>	<input type="checkbox"/>	Nose dry/congested	<input type="checkbox"/>	<input type="checkbox"/>	Depression	<input type="checkbox"/>	<input type="checkbox"/>	Pain	<input type="checkbox"/>	<input type="checkbox"/>	Fears	<input type="checkbox"/>	<input type="checkbox"/>	Sexual	<input type="checkbox"/>	<input type="checkbox"/>	Nervousness	<input type="checkbox"/>	<input type="checkbox"/>	Skin dry/itchy	<input type="checkbox"/>	<input type="checkbox"/>	Sadness	<input type="checkbox"/>	<input type="checkbox"/>	Sleep	<input type="checkbox"/>	<input type="checkbox"/>	Worry	<input type="checkbox"/>	<input type="checkbox"/>	Substance use	<input type="checkbox"/>	<input type="checkbox"/>	Loss of interest in usual activities	<input type="checkbox"/>	<input type="checkbox"/>	Tingling in hands/feet	<input type="checkbox"/>	<input type="checkbox"/>	Spiritual/religious concerns			
YES	NO	Practical Problems	YES	NO	Physical Problems																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Child care	<input type="checkbox"/>	<input type="checkbox"/>	Appearance																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Housing	<input type="checkbox"/>	<input type="checkbox"/>	Bathing/dressing																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Insurance/financial	<input type="checkbox"/>	<input type="checkbox"/>	Breathing																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Transportation	<input type="checkbox"/>	<input type="checkbox"/>	Changes in urination																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Work/school	<input type="checkbox"/>	<input type="checkbox"/>	Constipation																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Treatment decisions	<input type="checkbox"/>	<input type="checkbox"/>	Diarrhea																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Eating																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Fatigue																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Feeling swollen																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Dealing with children	<input type="checkbox"/>	<input type="checkbox"/>	Fevers																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Dealing with partner	<input type="checkbox"/>	<input type="checkbox"/>	Getting around																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Ability to have children	<input type="checkbox"/>	<input type="checkbox"/>	Indigestion																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Family health issues	<input type="checkbox"/>	<input type="checkbox"/>	Memory/concentration																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Mouth sores																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Nausea																																																																																																																																												
			<input type="checkbox"/>	<input type="checkbox"/>	Nose dry/congested																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Depression	<input type="checkbox"/>	<input type="checkbox"/>	Pain																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Fears	<input type="checkbox"/>	<input type="checkbox"/>	Sexual																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Nervousness	<input type="checkbox"/>	<input type="checkbox"/>	Skin dry/itchy																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Sadness	<input type="checkbox"/>	<input type="checkbox"/>	Sleep																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Worry	<input type="checkbox"/>	<input type="checkbox"/>	Substance use																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Loss of interest in usual activities	<input type="checkbox"/>	<input type="checkbox"/>	Tingling in hands/feet																																																																																																																																												
<input type="checkbox"/>	<input type="checkbox"/>	Spiritual/religious concerns																																																																																																																																															

Source: NCCN: Retrieved from

https://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf

(Used with permission: NCCN)