Financial Toxicity and Cost-Related Non-Adherence in Patients with Chronic Blood Cancers

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To my parents, who believed in me from day one

and

To my husband, Matt, ever loving and patient

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INTRODUCTION

The aim of this Thesis is to elucidate a better understanding of the financial burdens that patients with chronic blood cancers face in paying for life-saving treatments. Many people are aware of the burden cancer places on an individual and may have personal experience with a family member or friend being diagnosed with the disease. Most citizens and policymakers are also living in a time of hyper-awareness of the growing issue of unsustainable drug prices in the United States. However, the majority of previous research and policies address societal level burdens of rising healthcare costs, rather than individual financial burdens. The rising societal-level costs to treat cancer and the introduction of novel prescription drug therapies, are having an even further adverse effect on an individual basis. There must be further investigation and exposure on how subjective financial burden affects individual cancer patients' health and quality of life.

The specific questions I seek to answer through this Thesis are:

1. **What factors are associated with financial difficulty among cancer patients?**
2. **How do these factors vary for people with cancer drugs, versus those who use other courses of treatment?**
3. **Among cancer drug users, what kinds of cost coping strategies do patients employ?**
4. **How do these strategies vary between cancer and non-cancer drugs?**
5. **How are mental and physical health-related quality of life related to financial burden in cancer patients?**
6. **Is quality of life different for patients with and without cancer drug use?**

I will begin by shedding light on how we reached this point in the United States by taking a macro view of historical drug-pricing related policies and focusing specifically on the current high price of life-saving oral-targeted cancer therapies. Additionally, I will provide background information on the

disease characteristics of chronic blood cancers to illustrate why the use of oral drugs is such a novel and important therapy. Once it is explained *why* patients are facing high cost-sharing responsibilities, I will delve into the negative consequences these patients face as a result of not being able to afford life-saving medications. These include not adhering to treatment regiments (i.e. "cost-related non-adherent behaviors"), cost-defraying techniques (i.e. what sacrifices patients make in order to pay for medication), and finally the consequences of having poorer mental and physical health outcomes also defined as "financial toxicity".

Using a survey distributed by Patient Power, an online support community for patients with cancer, data was collected on a variety of topics including sociodemographic characteristics, subjective financial burden, treatment behaviors and subjective quality of life. A total of 239 patients with either chronic lymphocytic leukemia or multiple myeloma responded for analysis.

Receiving a cancer diagnosis is a major, life-altering event with a proven impact on health-related quality of life alone and social identify (Park, 2009). Findings from this study support the notion that patients should not have suffer from the additional financial burdens of treatment due to the unaffordable costs. Intervention strategies for financial toxicity and policy initiatives at lowering costs for oral anticancer drugs are urgently needed.

BACKGROUND & LITERATURE REVIEW

The High Cost of Prescription Drugs in the United States

Total health expenditures in the United States have increased substantially over the past several decades. Additionally, the U.S. has higher prices for most health care services and prescription drugs, according to available internationally comparable data (Kamal and Cox, 2018). From the early 2000's to around 2010, overall prescription drug expenditure was at a modest, but insignificant, and unalarming growth rate (Kamal and Cox, 2018). With the introduction of Medicare Part D in 2010 and the Affordable

Care Act in 2012, prescription drug spending actually decreased. However, seen in **Figure 1** prescription drug spending began rising sharply in 2014, at over an 11% growth rate. This growth is attributed to the expenditures on specialty drugs, including medications to treat cancer and hepatitis C (Kamal and Cox, 2018). Furthermore, Medicare's spending on prescription drugs, despite the introduction of Part D, continues to rise. For example, from 2004 to 2014, Medicare's share of drug expenditures increased form 2% of $193 billion to 29% of $298 billion (Kamal and Cox, 2018). Since 2014, the trend in both medical and drug expenditures continues to rise at an unsustainable rate.

A way to measure spending trends is to see what percentage of the economy is devoted to health and healthcare spending. **Figure 2** illustrates the percentages that the U.S. spends out of its Gross Domestic Product (GDP) on health. In 1970, the U.S. only spent around 7% of its GDP on total health spending, both through public and private funds. By 2017, the amount has increased to almost 18% of GDP (Kamal and Cox, 2018).

Additionally, the U.S. is an outlier to the rest of the world on how much it spends out of its GDP on health. For example, in 2016, the U.S. spent 18% of its Gross Domestic Product (GDP) on healthcare, whereas the next highest country only spent 12%. The average amount spent on healthcare per person in comparable countries ($5,198) is half that of the U.S. ($10,348) (Kamal and Cox, 2018). Meanwhile, utilization of these services, including physician consultations and hospital stays, is lower than in many comparable countries. Despite having fewer office visits and shorter average hospital stays, the U.S. overall spends twice as much per person on healthcare than do comparable countries (Kamal, 2018).

The high cost of cancer drugs fits into a larger trend of high medical costs in the United States. Prescription drug prices in the United States have been increasing over the past decade and are becoming unsustainable and unaffordable for American patients. According to the Centers for Disease Control (CDC), half of all Americans have used at least one prescription drug in the past 30 days (CDC,

2017). National trends in prescription drug expenditures and projections published for 2017 summarizes "total U.S. prescription sales for the 2016 calendar year at $448.2 billion, a 5.8 percent increase" compared with 2015 (Schumock, 2017). Prescription expenditures in clinics totaled nearly $64 billion, a 12 percent increase from 2015. Hospital drug spending was almost $35 billion, up 3 percent from 2015 (NCSL, 2018).

There is not one specific reason why drug prices have reached unsustainable costs, but rather a culmination of factors. These include the discovery of innovative specialty drugs (Kamal and Cox, 2018) market exclusivity (Kesselheim, 2016) limited negotiation powers by federal and state agencies, multiple middlemen and lack of transparency in pricing (Cubanski and Neuman, 2018). The US is an outlier from other countries in part because it does not regulate or negotiate the prices of new prescription drugs when they come onto the market. Instead, drug makers are allowed to set their own prices for a given product and allows every drug that's proven to be safe come onto the market (Kliff, 2018). There are policy trade-offs for not allowing negotiation. One benefit of the US system is that certain drugs that sell in the United States may not be available in other countries. Thus, the United States may have the most innovative and life-saving treatments. However, if patients are unable to afford them, the availability of innovative treatments could be a moot point (Kliff, 2018). The major dilemma continues to be between this trade-off, and policymakers often question – should we exchange innovation for access? Currently, we do not have a policy solution to address this question. Science continues to progress with high costs of research and development of new drugs, and no limits to the prices that manufacturer's can set. Therefore, innovation may continue to progress, but access may become even more limited as prices continue to rise.

Despite major reforms to our healthcare system in 2010, many critics argue that the Affordable Care Act did very little to combat the rising costs of prescription drugs, and prices continue to rise. As an explanation for inaction, some point to a deal between President Obama and PhRMA in which Medicare

was prohibited from negotiating drug prices in return for PhRMA's support of the proposed legislation (Owens, 2016). Many members of Congress have been outspoken on the issue of high prescription drug prices. Bernie Sanders, for example, has his own six-point plan – called the "Sanders Plan" – aimed at cutting costs (Sanders, 2018). Individual states are also playing a role in the push for reform; the Maryland state legislature recently introduced a bill that would allow a commission to set maximum amounts pharmacies and state programs could pay for expensive, brand-name prescriptions (Hicks, 2018). President Trump himself has called for reforms that would reduce the cost of prescription drugs. In his State of the Union address in January 2018, he called bringing drug prices down "one of his greatest priorities" (Managan, 2018).

A new budget deal signed by President Trump in February 2018 included a provision aimed at reducing overall prescription drug costs in the United States. The plan requires pharmaceutical companies to give Medicare steeper discounts on expensive prescription drugs and includes a five-state pilot project that would allow states to negotiate drug prices. While experts predict that the plan could make a significant difference for Medicare patients that take very expensive drugs, critics argue that the changes will barely make a dent in the issue and do little to address the root causes of high prescription drug prices in the U.S. (Tribble, 2018).

The Price Tag of Cancer Drugs

Following national trends, orally prescribed cancer medications are priced significantly higher than almost any other prescription drugs in the United States. The median monthly cost for new cancer drugs increased from $1,770 in the period between 1995 and 1999 to $10,059 in the period between 2010 and 2014 (Szabo, 2017). Hence, a year's supply of new cancer drugs is commonly priced at over $100,000 and some new drugs even top $250,000 per year (Szabo, 2017).

In a global context, the U.S. is an outlier with respect to the costs of cancer drugs around the world (Bollycky, 2013). Seen in **Figure 3**, the median monthly price of 23 cancer drugs in the U.S. is $8,700; the same drugs cost $2,600 in the UK, $2,700 in Australia, and $3,200 in China (Crow, 2016) Gleevec, a drug used to treat leukemia and other cancers, costs $70,000 per year in the U.S. but only $2,500 in India.

For cancer drugs specifically, the introduction of targeted oral therapies, the monopoly market, and the inelastic nature all contribute to high prices. Targeted cancer drugs are for a smaller subset of cancer patients and cost more to develop, test, and bring to the market. With the introduction of targeted cancer drugs, cheaper one-size-fits-all options are no longer the most effective type of drug. Therefore, the price of cancer drugs has risen with the advent of targeted oral therapies (Precision Medicine, 2017). Second, there is a monopoly market for cancer drugs. With over the counter medication, a patient can pick and choose between brands, causing different brand medications to compete for prices. However, with cancer drugs, a virtual monopoly is created because each is administered sequentially or in combination. Therefore, it is difficult to pick and choose between brands, allowing pharmaceutical companies to charge a higher price (Rajkumar and Siddiqui, 2018). Finally, cancer drugs are incredibly inelastic, meaning their demand is insensitive to a change in price. Patients and insurers are willing to pay high prices for even a modest improvement in outcome because of their life-saving abilities (Rajkumar and Siddiqui, 2018).

If patients did not have to rely on these cancer drugs as part of treatment, or if the demand was low and price was elastic based on the market, cost would not be an issue or potential barrier to care. Understanding the life-saving abilities and inelastic demand of cancer drugs requires understanding the disease itself, such as the patient population characteristics, disease characteristics, usual courses of diagnosis and prognosis, and other possible treatment options for patients with chronic blood cancers.

Chronic Blood Cancer Disease Characteristics & Treatments

Chronic lymphocytic leukemia (CLL)

CLL is the most common leukemia in adults and is a specific type of cancer of the blood and bone marrow, which is the spongy tissue inside bones where blood cells are made (Mayo Clinic, 2018). This type of blood cancer is considered "chronic" due to the fact that it typically progresses more slowly, than other "acute" forms of cancers (faster onset and disease progression) (Mayo Clinic, 2018). Medical professionals have not been able to identify the "trigger" or cause that starts the process of cell multiplication and production of abnormal, and ineffective lymphocytes (Mayo Clinic, 2018). Risk factors that have been identified by researchers for developing CLL include: age, race, family history and exposure to chemicals. On average, people diagnosed with CLL are in their 70's, and whites are more likely to develop CLL than other races (Mayo Clinic, 2018). CLL is diagnosed in different stages, typically early, intermediate or advanced. The stage of the cancer determines the treatment route. In general, patients diagnosed within the early stage do not require immediate treatment but may later on. Treatment types are also based on associated symptoms, overall health and preferences. Treatment options in the later or advanced stages include: chemotherapy, immunotherapy, bone marrow transplant, and our treatment of interest within this paper – targeted drug therapy.

In targeted therapies, prescription drugs are used to specifically target the changes inside cells that cause them to become cancerous. Unlike standard chemotherapy which are used to attack *all* cells, these drugs attack the more specific CLL cells, without damaging health cells. Oral drugs usually prescribed for CLL include Imbruvica (ibrutinib), Venclexta (venetoclax) and Zydelig (idelalisib) (Chronic Lymphocytic Leukemia, 2018).

Multiple myeloma (MM)

Multiple myeloma (MM) is also a cancer of bone marrow, but specifically within plasma cells (rather than lymphocytes like in CLL) (Multiple Myeloma, 2018). When plasma cells become cancerous and grow uncontrollably, they crowd out the healthy blood cells. Treatment discourses are similar to CLL, in that it is dependent on the severity and prognosis of the disease when it is diagnosed. Risk factors that have been identified by researchers for developing multiple myeloma include: age, sex, race and family history. Most people are diagnosed in their mid-60's, and risk increases with age. Men are more likely to develop multiple myeloma than women, and African American's are about twice as likely to develop the disease than white people (in contrast to CLL). Standard treatments for multiple myeloma include chemotherapy, corticosteroids, bone marrow transplant, radiation therapy, and out treatment of interested – targeted drug therapy. Oral drugs usually prescribed for multiple myeloma include Thalomid (thalidomide), Revlimid (lenalidomide), Pomalyst (pomalidomide), Velcade (bortezomib), Farydak (Panobinostat) and Nilarno (ixazomib) (Mayo Clinic, 2018).

Previously, these cancers had no cure and were treated with courses of surgery cell transplantation, chemotherapy, radiation and other more invasive measures as the only option. Oral drugs to fight cancer, also known as "TKI inhibitors", were discovered as a novel and lifesaving treatment and are considered by some to be the most successful class of therapies developed in cancer (Zafar, 2015). Prior to the use of oral-targeted therapies, median survival of those with blood cancers was only 5 to 6 years. Research has shown that maintenance therapy (the ongoing use of targeted drugs) increases patient survival rates for blood cancers (Mayo Clinic, 2018). However, survival rates are dependent upon stage of cancer when it is diagnosed and can vary from patient to patient.

Although much less invasive and more effective, the price tag of the treatment would influence patients having the ability to afford and use these drugs. For example, when imatinib (a TKI inhibitor for

chronic myeloid leukemia) was introduced in 2001, is was one of the highest price drugs available, costing $30,000 per year, and by 2012 the cost had tripled to $92,000 (Szabo, 2017).

Cost-Related Non-Adherence & Cost-Defraying Techniques

The introduction of TKI inhibitors and oral-targeted therapies has greatly increased survival for those with chronic blood cancers. However, despite the significant clinical benefits, previous research has found that at least 30% of patients are nonadherent in taking TKI inhibitors due to cost-sharing and inability to afford the medication, even after prescription drug coverage (Dusetzina, 2013). It is advised by medical professionals that patients should not skip doses and take their medications as prescribed to get the best response. Poor adherence to medications is the main reason for inadequate response and poor health outcomes, thus stressing the importance of adhering to treatment regiments (Leukemia and Lymphoma Society, 2018).

This exorbitantly high price of cancer drugs has adverse effects, causing patients to skip treatments and experience financial turmoil. Previous research has coined this term "cost-related non-adherence" (CRN), which refers to individuals who report restricting use of prescription medication because of cost. Examples of CRN practices include skipping medications, cutting medication doses in half, delaying filling a prescription, using alternative therapies, etc. It has been shown that individuals who report CRN have significantly worse health outcomes (Noens, 2009).

Many studies have evaluated CRN in different subsets of the patient population and for different cancers. A meta-analysis of studies which examined the associations between prescription drug plan cost-containment measures found that increased cost sharing (i.e. patients taking more of the burden of the payments for medications) is associated with worse adherence among existing users, and more frequent discontinuation of previously prescribed therapies (Goldman, 2007). In another example, one study found that among patients with breast cancer, higher co-payments were associated with

higher rates of non-adherence (Neuget, 2011) Another study found that insurance plans which required high cost sharing of oral chemotherapy drugs are associated with a higher risk of prescription abandonment (Streeter, 2011). However, given the exclusively high prices, disease onset and progression, as well as the critical importance of prescription medications in managing chronic blood cancers, the extent to which CRN effects health outcomes and experience other barriers in this population needs further studying.

Financial Toxicity & Health-Related Quality of Life

A growing body of evidence has coined a new term – "Financial Toxicity" – in relation to the high out-of-pocket costs and cost-sharing insinuated on cancer patients. This term is primarily used in oncology research and practice to describe the distress of paying for treatments and the impacts on quality of life and healthcare. Financial toxicity has even gone as far as to compare to actual biological treatment toxicities such as nausea, vomiting, insomnia or depression. These toxicities can lead to poorer patient outcomes at times of treatment delays or discontinuation (Gordon, 2017). The current literature supports both objective financial burden and subjective financial distress as key markers for financial toxicity (Zafar, 2015). However, most research and policies are directed at societal level burdens rather than individual financial burdens. The rising costs of healthcare and costs to treat cancer on a societal level are also having adverse effects on individuals. This is evident in the fact that even insured patients are facing increasing out-of-pocket costs and increased cost-sharing. As insurance companies continue to bear the unsustainable growing cost burden of medicine, portions of these costs have now shifted to patients more than ever before (Zafar, 2015)

Gordon et al. performed a systematic review of literature on financial toxicity among cancer survivors in order to identify the determinants and how it is measured (Gordon, 2017). After reviewing 25 studies, the most commonly reported factors associated with financial toxicity included being female,

younger age, lower income, and a more recent diagnosis. The most relevant and important finding to add to this discussion is that cancer survivors experienced significantly higher financial toxicity relative to non-cancer comparison groups. Ultimately the findings suggest that the financial burdens for cancer patients is in excess and can be debilitating to households, quality of life and optimal cancer care (Gordon, 2017). Similar studies support this evidence, in particular the financial burdens for blood cancer. A study done by Huntington et al. surveyed 100 individuals with ongoing treatment for Multiple Myeloma. This group found that 71% had at least minor financial burden and 46% of MM patients used savings to pay for treatment.

Receiving a diagnosis alone of CLL or MM, aside from financial burden, has been shown to have an impact on quality of life and mental health (Zebrack, 2001). Unlike most cancers, the treatment discourse of "watch and wait" and long-term survival status can by psychologically difficult for patients who know they have a serious health problem. Additionally, because the diagnoses of these two diseases tend to occur later in life, patients face these burdens while concurrently coping with other health problems due to older age. A study by Shanafelt et al. found that the emotional well-being and health related quality of life scores in CLL patients were profoundly lower than those of the general population, at all stages of the disease.

Ultimately, the previous literature elucidates the dual-threat combination of both receiving a cancer diagnosis and high cost-sharing responsibilities of treatment that is potentially leading to increased levels of financial toxicity in patients with blood cancers. Oral-targeted therapies have been proven to increase life-expectancy in these patients, thus reducing burdens on the biological end. However, both societal level costs of cancer and individual cost-sharing for cancer treatments continues to grow. Therefore, there is no current solution for aiding in mental health and improving quality of life for patients if cost-sharing at the individual level cannot be reduced. This study contributes to the current discussion of financial toxicity in cancer patients by examining which factors are associated with

financial difficulty, what cost-coping strategies patients use, and how financial difficulty and cost-coping strategies affect patients' quality of life. It will require further research to explain this dual threat but addressing financial burdens and distress is ultimately a piece of the puzzle for reduced mental health burdens and enhanced health-related quality of life.

METHOD OF INVESTIGATION

Study Design

This was an observational, cross-sectional survey assessing patient-reported prescription medication adherence, financial coping strategies, subjective financial burden and self-reported health among patients with chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). The survey instrument was developed, and pilot tested at Vanderbilt University and was self-administered through REDCap online.

Participants

Participants were enrolled via referral from Patient Power, an online community aimed at enabling and connecting cancer patients across the world to medical experts, and patient advocates through a variety of resources. The survey was first promoted on Patient Power's social media platforms (Facebook, Instagram and Twitter) and patient newsletters on October 12, 2018. The survey was promoted a two weeks later via the same platforms, and closed November 4 (open for 23 days). Eligible patients were members of Patient Power who had one of three chronic blood cancers (chronic lymphocytic leukemia, chronic myeloid leukemia and multiple myeloma). The Vanderbilt University Institutional Review Board approved this study. Outlined in **Figure 4**, there were 342 total responses recorded, with 283 starting the survey, and 59 who opened but left incomplete or no responses. Of the 283 completed surveys, 259 participants indicated that they had blood cancer, while 24 had another type of cancer. Since our interest is focused on participants with blood cancers, the other group was excluded Additionally, we excluded those with chronic myeloid leukemia because there was not a

sufficient number of responses (N=20) for analysis. Thus, we ended up with 239 survey responses for analyses (N=148 with chronic lymphocytic leukemia, N=91 with multiple myeloma).

According to the American Cancer Society, the identified demographic risk factors for CLL average age at time of diagnosis is 70 years old and white. This is consistent with our cohort of patients, in that 98.7% identified as white, and 59.2% reported being over 65 years old (94.6% reported being over 55 years old). Risk factors identified for MM include being diagnosed over 60 years old, male and African American. This is consistent with our cohort, in that 86.9% report being over 55 years old. However, it is consistent in the fact that our cohort represented a minority of males (38.5%) and only 6.6% African American for patients with multiple myeloma, which could produce potential bias in analysis.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize participants' sociodemographic characteristics, disease and treatment characteristics, self-reported health, financial burden and use of cost-coping strategies. All analyses were conducted in collaboration with Dr. Stacie Dusetzina, associate professor in the department of Health Policy at Vanderbilt University. Bivariate and multivariate regression models were used to assess the association between patient sociodemographic characteristics and financial burden. I estimated the relationship between self-reported financial burden and health-related quality of life (PROMIS Global Mental & Physical Health Scores), and self-reported financial burden and cost-related non-adherent behavior. Variables including gender, income, insurance type and use of prescription drug coverage were controlled for as possible covariates in adjusted analyses. A p value of <.05 in the final model was considered statistically significant. All models were calculated using SAS statistical software programming.

RESULTS

Sociodemographic Characteristics

The final sample included 239 eligible participants were analyzed for overall sociodemographic characteristics. **Table 1** illustrates these characteristics stratified by disease type (CLL vs MM). The majority reported being diagnosed with chronic lymphocytic leukemia, were female, non-Hispanic white, 65-74 years old, and had a median income of $80,000-$99,999. Patients reported a median disease duration of between 2 to 5 years and over half (54.8%) report taking oral drugs as part of their current cancer-directed treatment. Most patients were either privately insured through their employer (46%) or had Medicare (54.1%). Overall, 96.6% reported having prescription drug coverage.

Factors Associated with Financial Burdens

Of respondents, 39.5% reported that having cancer caused financial hardship. Of those who reported financial hardship, One fifth report this being very difficult (**Table 2**). Additionally, almost one third of patients report significant or catastrophic financial burden as a result of having cancer. This differed among patients based on their use of orally-administered anticancer drugs with those who reported taking oral drugs as part of their cancer treatment being 40% more likely to report any financial hardship.

For our models, we recoded our outcome variable of subjective financial burden from the 5-point Likert scale categories of 1 “not a financial burden at all”, 2 “minor financial burden”, 3 “moderate financial burden”, 4 “significant financial burden”, and 5 “catastrophic financial burden” to a binary variable of either 1 “financial burden” or 2 “no financial burden”. Patients who reported “not a financial burden at all” or “minor financial burden” were recoded as “no financial burden”. Patients who reported “moderate”, “significant” or “catastrophic” financial burdens were recoded as having financial burden.

We included gender, race, age, income, disease duration, and health insurance as possible covariates in our multivariate adjusted analysis. We did not include ethnicity or whether a patient had prescription drug coverage because there was little variability among the sample (95.4% non-Hispanic and 96.6% had prescription drug coverage). We recoded age from 6 categories into a binary variable as either younger than 65 years older 65 years and older to have even comparison categories. We recoded insurance from 6 categories to 3 new categories as either having Medicare, private insurance or unknown. The majority of respondents were over 65 and on Medicare, which is disproportionate to the general population – our sample reported 54.1% on Medicare, and general population in 2017 was 14% (Health Insurance Coverage 2017). This was to be expected, since the average disease onset of chronic blood cancers occurs after 65 years of age, which is when citizens become eligible for Medicare. Based on frequency data (found in **Table 1)** We combined disease duration categories of being diagnosed for "<6 months" and "7 months to <2 years" to just "<2 years".

Table 3 shows the results of both our bivariate and multivariate our regression analysis. In unadjusted analyses, female patients and patients under 65 years old were more likely to report financial burden than male patients and patients over 65 years old. Those who were diagnosed for 6-<10 years reported greater financial burden than other disease duration groups. Regarding income, those with higher income ($80,000 - $100,000+) were less likely to experience financial burden. Lastly, patients with CLL were less likely to experience financial burdens than those with MM. In adjusted analyses, controlling for possible covariates, only oral drug use and disease duration were significantly associated with subjective financial burden (alpha of .05).

Cost-Related Non-Adherence & Cost-Defray Techniques

After collecting demographic data and subjective financial burden data, we asked participants if they were "currently taking oral prescription medications for treatment for cancer." Of the 239

participants who reported having either CLL or MM, 131 patients said "yes" they are currently taking orally prescribed drugs as part of their cancer treatment (n=66 for MM and n=65 for CLL). 131 respondents that did respond yes to taking orally prescribed drugs were evaluated for the presence of cost-related non-adherence and other cost-defraying strategies. These behaviors include "skipping medication doses", "taking less medicine", "delay filling a prescription", "asking doctor for lower cost", "buying prescription drugs from another country" and "using alternative therapies". Detailed in **Table 4,** Only 17.6% (n=23) of respondents who were prescribed oral drugs as part of treatment engaged in one or more cost-related non-adherent behavior. 73.3% (n=96) did not participate in any CRN behaviors, meaning they took their oral drugs used to treat cancer as prescribed by their physician. Additionally, cost-related non-adherent behaviors were broken down by either behavior related to cancer medication, behavior related to another medicine (not cancer related) or both. These findings are summarized in the graph below.

While the cost-related non-adherence behaviors were less common among the cohort than has been observed in other studies, we found a much higher percentage of patients who reported using "cost-defraying" techniques to compensate for the high-cost of cancer drugs. These techniques include "obtaining samples from a doctor", "cutting back on leisure activities", "reducing spending on basics", "using savings set aside for other purposes", etc. In total, 63.4% (n=83) of the sample reported using at least one or more of these "cost-defraying" techniques.

Financial Burden and Health-Related Quality of Life

Our final outcome of interest was the association between health-related quality of life and financial burden. We were further interested in the distinction of whether this differed between patients who reported using oral anticancer drugs, and patients who did not take oral anticancer drugs as part of treatment. **Table 5** summarizes Self-Reported Health using the PROMIS Global-10 Mental and

Physical Scale & Scoring and stratified by oral anticancer drug use. This is a publicly available and validated global health assessment tool that allows measurements of symptoms, functioning, and healthcare-related quality of life (HRQoL) for a wide variety of chronic diseases and conditions. The scoring system of the PROMIS Global-10 allows each of the individual items to be examined separately to provide specific information about perceptions of physical function, pain, fatigue, emotional distress, social health and general perceptions of health.

Score interpretations are described in **Figure 4** and help infer quantitative scores to qualitative ranges of health-related quality of life, ranging from "poor" to "excellent", across a spectrum. The average mental health scores for the cohort (212 respondents, 20 did not report all scores for associated measure) were 46.5 (+/- 9.26) and the average physical health scores were 47.6 (+/- 9.59) which are both interpreted as "Good". The difference for global mental health was only 1.2 points, and the difference for global physical health was only 0.9.

We used a multivariate adjusted regression model to better understand the relationship between financial burden and its effect on both mental and physical health-related quality of life scores. We ran two different models – one using mental health PROMIS scores, and one using physical health PROMIS scores as our outcome variable. In our unadjusted analysis, seen in **Table 6** we found a 6.62 point decrease in mental-health scores and a 6.01 decrease in physical health scores. In **Table 7** we controlled for possible covariates including age, gender, insurance, cancer type, disease duration and income, and still found a significant decrease of 4.86 in mental-health scores and 4.16 decrease in physical health scores.

We were further interested in whether there was a difference in health-related quality of life between patients who used oral anticancer drugs, and patients who did not use oral anticancer drugs as part of treatment. In our multivariate adjusted regression model, controlling for the same possible co-

variates previously mentioned, we did not find a significant difference between health-related quality of life scores and anticancer drug use.

DISCUSSION

1. What factors are associated with financial difficulty in cancer patients?

Previous research has detailed the burden of health care-related cost-sharing expense. Additionally, recent studies have specified the financial burdens associated with cancer treatments (Altice, 2016). However, this study is among the first to evaluate the subjective financial burden in a special cohort of patients who have a high proportion of oral anticancer drug users. These oral anticancer drugs or "TKI Inhibitors" are recent innovations to treatments, and although improving disease outcomes, their unaffordability and price tags of over $10,000 create subsequent financial difficulties.

A systematic review of financial toxicity among cancer populations reported the most common factors linked to financial toxicity were "being female, younger age, having a low income, receiving adjuvant therapies and having a recent diagnosis" and "high financial burden for cancer patients is in excess of that for persons not experiencing cancer" (Gordon, 2017). Consistent with recent evidence among other cancer patients, in our analysis we did find that patients who are female, younger, and lower income to have a greater risk for financial burdens. Additionally, patients with a disease duration of 6-<10 years report the highest level of financial burden, which could suggest the time when oral-targeted treatments are usually administered or potential depletion of resources over time, but that cannot be validated by the data captured. Most treatment discourses, as mentioned before, are at a "watch and wait" stage if caught early on and patients do not begin treatment until the disease has progressed (American Cancer Society, 2018).

The impact of financial burdens can be debilitating to households, and identifying which patients are more at risk will help with any future intervention strategies. Although financial toxicity is a complex problem, a greater awareness and acknowledgement of burdens and associated risk factors can lead to solutions towards optimal patient outcomes by physicians, policymakers, patients, and families.

2. How does this vary for people with cancer drugs, versus those who use other courses of treatment?

Due to the previously mentioned fact that CLL and MM are treated with a high proportion anticancer drugs compared to other types of cancers, we were interested in whether the hefty price tag of these drugs created a significant amount of financial difficulty, as compared to those who were not treated with anticancer drugs.

Cancer treatments are generally expensive, however anti-cancer drugs are more expensive than typical discourses of chemotherapy, surgery or "watch and wait" strategies (American Cancer Society, 2018). This is consistent with our findings that patients who did take oral anticancer drugs reported 40% more financial difficulty than those who didn't and a significant association between subjective financial burden and oral prescription drug use. This suggests a greater urgency in controlling prescription drug pricing, since it is an obvious predictor for subjective financial burdens. As research and development of oral anticancer drugs continue to progress, prices must be contained so patients have both accessible and affordable treatment options for better survivorship.

3. Among cancer drug users, what are the cost coping strategies?

Various cost-coping strategies to combat the high prices of drug treatments have been studied and classified into the 6 most common ways: skipping medication doses, taking less medicine, delaying filling a prescription, asking a doctor for a lower cost medication, buying prescription drugs from another country and using alternative therapies. Previous studies have evaluated how different diseases which are treated with oral medications, such as diabetes, hypertension, cardiovascular and other

chronic diseases (Qato, 2016). Due to the recent innovations in anticancer drugs, few studies have evaluated cost-related nonadherence among this patient population.

The most common types of cost-related non-adherent behavior among our sample for cancer medications were delaying filling a prescription to save money and asking a doctor for a lower cost medication, although relatively low proportions of respondents engaged in these behaviors. More common strategies were not cost-related non-adherent behaviors, but rather "cost-defraying" strategies. 63.4% of patients reported using cost-defray strategies as compared to only 17.6% who participated in one or more CRN behavior. Although a complex issue, with various factors at play, our results indicate patients are more likely to follow treatments due to their life-saving capabilities but having to subsidize costs through other mechanisms. These most common mechanisms for defraying the cost-sharing of the cost of cancer care include cutting back on leisure activities, using savings and seeking pharmaceutical company assistance. Possible factors associated with these patient decisions could be that patients are still choosing to fill their medications but engaging in other cost-savings strategies as a result. Furthermore, patients may be receiving assistance to manage prescription drug costs as many reported seeing such assistance. For example, national cancer societies such as the Leukemia and Lymphoma Society offer various co-pay assistance and patient financial assistance programs. These, along with other cost-related coping strategies could help limit the impact of out-of-pocket costs patients pay for cancer drugs.

Approximately 17% of patients are using non-adherence strategies and the majority of these are not taking both their cancer medications or medications for another disease. To better understand what is occurring among these non-adherent groups of patients it may be useful to identify whether there are "clusters" of strategies that are occurring and for which patient groups. For example, are those in higher socioeconomic groups, who have savings set aside, more likely to participate in "using savings" and "cutting back on leisure activities", compared to those in lower socioeconomic groups who may not

have savings set aside and are more likely to participate in strategies such as “seeking pharmaceutical assistance” and “reduce spending on basics”. A qualitative analysis to better understand the group of patients who use non-adherence strategies to reduce costs could also reveal a more robust insight into why patients make treatment decisions. It is vital to understand this subset of patients who use non-adherence strategies because they could be at very high risk of negative health outcomes.

4. How do cost-coping strategies vary between cancer and non-cancer drugs?

When asking about cost-related non-adherent behaviors, we wanted to ask about medications outside of cancer as well, to see if there was any variability in whether patients were adherent to cancer drugs as compared to non-cancer drugs. We assumed this sample would have possible comorbidities that required prescription medication due to age and risk factors of this patient population. A survey of 2206 community-dwelling adults aged 62 to 85 years old found that 87% reported at least one prescription medication and 36% used five or more prescription medications (Qato, 2016). We found patients were more likely to skip medication doses, take less medicine, and buy prescription drugs from another country for non-cancer related medications. Alternatively, we found behaviors such as asking doctor for a lower cost medication and using alternative therapies equal or more common for cancer medications. Treatment discourses and disease type help illuminate why there may be differences between cancer and non-cancer drug adherence. Although we did not ask specific types of other medications and medical conditions were classified in the “other medications” category, chronic diseases and common medications among people over 65 years old would explain some of the differences observed. For example, prescription medications to manage chronic diseases such as hypertension are common among elderly individuals, and nonadherence to medications impacts more than two thirds of hypertensive individuals (Tibebu, 2017). Additionally, patients may not find the benefit of managing their blood pressure as vital and imperative to their health as managing a more

severe disease like cancer. Thus, they may be more willing to adhere to cancer treatments, and sacrifice spending money on other medications for non life-threatening diseases.

5. How is health-related quality of life related to financial burden in cancer patients?

We found a significant difference in both mental and physical health scores between patients who reported a financial burden versus those who did not. We found that patients reporting financial burden are more likely to have almost 5 points lower on mental health scores, and similarly over 4 points lower on physical health scores. Reviewing the spectrum of scores in **Figure 4**, this is important because subjective mental health is on approximately a 10-point scale, meaning for every 10-point increase in scores, category increases (i.e. from "fair" to "good" or "very good" to "excellent"). Additionally, a national dataset measuring healthy non-cancer adults found the average PROMIS physical health score to be 53.2 and average PROMIS mental health score to be 53.9 (Weaver, 2012). Thus, there is a clear distinction in non-cancer patient's overall quality of life, as compared to our cohort of CLL and MM patients. This is critical information for practitioners to understand the burden of cancer and associated costs on overall quality of life.

If financial burden is associated with diminishing mental and physical health, there is evidence to suggest high financial toxicity among this patient population. As previously mentioned, financial toxicity has been compared to similar treatment toxicities such as nausea, vomiting, insomnia or depression that can lead to poorer patient outcomes at times of treatment delays or discontinuation (Gordon, 2017). Thus, physicians should be aware of patients who are at risk of non-biological factors such as financial toxicity, which could lead to poorer health outcomes.

6. Is quality of life different for patients with and without anticancer oral drug use?

Although we found significance among overall reporting of financial burden and its relationship with health-related quality of life, we did not find a significant difference between mental and physical

health scores in patients who used orally prescribed drugs, versus those who did not. This could be due to a variety of factors, including the fact that more patients who take oral cancer drugs also report higher financial burden. Thus the "financial burden" category captures an accurate reflection of oral cancer drug users. Additionally, mental health and physical health have a large number of factors such as age, other co-morbidities, life events, and social networks that may have more important roles than oral drug use. Despite there not being a difference in oral anticancer drug users versus non-oral anticancer drug users, the findings that financial burden is significantly associated with both lower mental and physical health among chronic blood cancer patients, regardless of treatment type, should create a sense of urgency to seek ways to lower cost-sharing to improve health-related quality of life.

LIMITATIONS

The findings from this study are subject to limitations and have several sources of bias that may impact the generalizability. First, we recruited patients specifically through Patient Power, a community for patient advocacy. Patients involved within these groups are more likely to be engaged in their cancer care since they are connected to resources with medical professionals and oncology specialists. Additionally, they may be more knowledgeable of the resources available to them to seek financial assistance to ease the burden of cost-sharing, since one of Patient Power's mission is to provide financial, insurance and family resources.

Similarly, these patients were selected as a convenience sample and recruited through media platforms such as email, Facebook, Twitter and Instagram via an online survey. If a patient does not have access to a computer, phone or other device, they would not have been able to take the online survey. This is reflected in our results, in that this patient sample tends to be of higher socioeconomic status (median income $80,000-$99,999). Additionally, patients report high private insurance rates (only 2.0% uninsured) may be leaving out patients with lower socioeconomic status and uninsured patients.

Patients in these groups have been found by previous research to have even higher rates of financial burden and toxicity (Zafar, 2015) and tend to be more difficult to recruit by the low response rates of other survey studies focused on these populations.

Previous studies have looked at patients who are seeking financial assistance because they are unable to afford out of pocket copays or in patients with high uninsurance rates (Zafar, 2015). The uniqueness of this study is that it reveals essentially a "best-case scenario" of patients who are highly insured (96.6%) and of higher socioeconomic status (average household income greater than $80,000). This reveals that, despite having proper treatment coverage and financial flexibility to cover extraneous medical costs, we still see significant levels of financial burden in paying for cancer. Furthermore, If the "best case scenario" patients are unable to afford treatment, it is extremely concerning how these high costs will affect those in lower socioeconomic groups and those with less financial flexibility to pay for treatment. It would be expected that poorer, less well-connected patients are going to experience more hardship and likely even greater negative effects on health.

Another limitation of our study includes our measures associated with financial burden and cost-related non-adherence were all self-reported and subjective data, which were not validated. However, several previous studies evaluating similar patient populations have used the same 5-point Likert scale of "Not a financial burden at all" to "Catastrophic financial burden" as a tool to gage accurate levels of financial burden (Zafar, 2015) (Gordon, 107). Additionally, based on previous research, we used the indicator of cost-related non-adherence as participating in only one or more behaviors from a defined list. Further investigation into these behaviors could include evaluating those with 2 or less versus those with 3 or more, to have a better representation of true non-adherence to treatment, as well as potential for patients to write in other forms that could be considered "non-adherent" that were not on the list.

Given the limitations, this study still provides novel insight and takes a deeper dive into the financial burdens experienced by a unique cohort of cancer patients. Different from previous studies, this study was able to study financial burdens and reduced quality of life within a well-insured and financially secure cohort of patients. Additionally, CLL and MM may be subjected to higher levels of financial burdens due to their unique treatment characteristics of taking orally-targeted drugs, as opposed to traditional cancer treatments such as chemotherapy or surgery.

Suggestions for future research to offset some of these limitations include drawing from a larger sample size with universal data sets to be more generalizable to a larger population. Additionally, it would be interesting to compare financial toxicities across different cancer types, and other chronic diseases as well as capture other co-morbidities through electronic medical records.

Future directions towards change could include the development of intervention strategies outside of cost-sharing subsidies (e.g. non-profits) to reduce prices for patients. It would also be interesting to take a deeper dive into patients who reported cost-related non-adherence behaviors to understand the key differences among these patients and those who do not skip medications, and what subsequent health risks non-adherent patients may be exposed to as a result of cost-cutting strategies. Additional directions include further acknowledgement and addressing of social determinants of health by practitioners as part of usual care, and lastly, policy directives and solutions to combat high prescription drug prices.

CONCLUSION

This study comes within a timely window for greater insight into a recent and growing issue in health policy. As healthcare costs are increasingly shifted to patients through premiums and out-of-pocket costs, the ongoing surveillance of the multiple domains of financial hardship will be vital for cancer patients to navigate treatment options and survivorship. Additionally, increased knowledge

about financial coping behaviors such as cost-related non-adherence that patients use to manage cancer care will be critical in developing interventions to improve adherence to treatment and better survivorship.

Patients with chronic blood cancers and who take oral anticancer drugs experience a considerable amount of subjective financial burden due to cost-sharing and other factors. Certain factors such as gender, age, income and disease duration are associated with higher financial burden, should be explored further to better understand how social determinants impact health and financial toxicity. These patients who experience financial burdens go to extreme lengths to manage paying for life-saving treatments such as depleting savings, borrowing money or reduce spending on basic needs. Additionally, some patients may not even take medications as prescribed due to high costs. This is extremely worrisome, in that if patients do not take medications as prescribed, they are at higher risks for poor health outcomes.

Quality of life is also being diminished as patients must face battling cancer and financial distress congruently. Receiving a cancer diagnosis alone is subjective to higher rates of mental distress and lower rates of quality of life. The additional burden of financial barriers and high cost-sharing responsibilities to obtain proper care and treatments is likely to reduce health-related quality of life even further. Understanding how and among whom to best measure financial distress is critical to the design of future interventional studies towards improved health outcomes and quality of life among cancer patients.

The results of this study come within a timely window where America is at a crossroads in determining the future of cancer treatment in our country. America is known for being the greatest innovator of scientific discoveries and leading cancer treatments. On the contrary, the U.S. also has the highest cost of healthcare spending per GDP, and the highest cost of pharmaceutical drugs. If these ground-breaking treatments are unaffordable, inaccessibility essentially makes innovation useless. Will

legislators stand by as the exorbitant costs of cancer drugs continue to rise, or will they act to implement policy that will ease the financial burden of the millions of Americans battling cancer?

REFERENCES

1. Park, C.L., Zlateva, I., Blank, T.O. (2009) Self-identity After Cancer: "Survivor", "Victim", "Patient", and "Person with Cancer". *J Gen Intern Med*, **24**, 430-435.

2. Kamal, R., Cox, C., McDemott, D. (2018) What are the Recent and Forecasted Trend in Prescription Drug Spending. *Kaiser Family Foundation*. https://www.healthsystemtracker.org/chart-collection/recent-forecasted-trends-prescription-drug-spending/#item-start

3. Center for Disease Control and Prevention. (2017) Therapeutic Drug Use. https://www.cdc.gov/nchs/fastats/drug-use-therapeutic.htm

4. Schumock, G.T. et al. (2017) National Trends in Prescription Drug Expenditures and Projections for 2017. *Am J Health-Syst Pharm*. **74** (339-59).

5. NCSL Prescription Drug Policy Resource Center (2018) *NCSL*. http://www.ncsl.org/research/health/ncsl-prescription-drug-policy-resources-center.aspx

6. Kesselheim, A.S., Avorn, J., Sarpatwari, A. (2016) The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform. *JAMA*. **316** (858-871).

7. Cubanski, J., Neuman, T. (2018) Searching for Savings in Medicare Drug Price Negotiations. *Kaiser Family Foundation*. https://www.kff.org/medicare/issue-brief/searching-for-savings-in-medicare-drug-price-negotiations/

8. Kliff, S. (2018) The true story of America's sky-high prescription drug prices. *Vox*. https://www.vox.com/science-and-health/2016/11/30/12945756/prescription-drug-prices-explained

9. Hicks, J. (2018) Maryland Weighs New Approach to Curbing Prescription Drug Costs. *The Washington Post*. https://www.washingtonpost.com/local/md-politics/maryland-weighs-new-approach-to-curbing-prescription-drug-costs/2018/02/16/781493ea-104b-11e8-9065-e55346f6de81_story.html?utm_term=.5542edb6e0ea.

10. Owens, C. (2016) Why Prescription Drugs Aren't Part of Obamacare." *Morning Consult.* https://morningconsult.com/2016/03/24/why-prescription-drugs-arent-part-of-obamacare/

11. Mangan, D. (2018) Trump declares cutting drug prices is a top priority, wants to allow patients quick access to experimental treatments. *CNBC.* https://www.cnbc.com/2018/01/30/donald-trump-obamacare-state-of-the-union-insurance-health-care.html

12. Tribble, S.J. (2018) Trump's Budget Proposal Swings At Drug Prices But May Land Only A Glancing Blow. *NPR* https://www.npr.org/sections/health-shots/2018/02/13/585183996/trumps-budget-proposal-swings-at-drug-prices-but-may-land-only-a-glancing-blow

13. Szabo, L. (2017) As Drug Costs Soar, People Delay Or Skip Cancer Treatments. *NPR*. https://www.npr.org/sections/health-shots/2017/03/15/520110742/as-drug-costs-soar-people-delay-or-skip-cancer-treatments
14. Bollyky, T. (2013) Why Chemotherapy That Costs $70,000 in the U.S. Costs $2,500 in India. *The Atlantic*. https://www.theatlantic.com/health/archive/2013/04/why-chemotherapy-that-costs-70-000-in-the-us-costs-2-500-in-india/274847/.

15. Crow, D. (2016) Price of Cancer Drugs Vastly Higher in US, According to Study." *Financial Times,* 6 Jun. 2016, https://www.npr.org/sections/health-shots/2018/02/13/585183996/trumps-budget-proposal-swings-at-drug-prices-but-may-land-only-a-glancing-blow

16. Precision Medicine in Cancer Treatment (2017). *National Cancer Institute.* www.cancer.gov/about-cancer/treatment/types/precision-medicine.

17. Rajkumar, V., and Siddiqui, M.A. (2018) Reasons and Solutions for High Cost of Cancer Drugs. *Mayo Clinic.* www.mayo.edu/research/forefront/reasons-solutions-high-cost-cancer-drugs.

18. Chronic Lymphocytic Leukemia (2018). *Mayo Clinic* https://www.mayoclinic.org/diseases-conditions/chronic-lymphocytic-leukemia/symptoms-causes/syc-20352428

19. Chronic Lymphocytic Leukemia (CLL) (2018). *American Cancer Society.* https://www.cancer.org/cancer/chronic-lymphocytic-leukemia.html

20. Multiple Myeloma (MM) (2018). *American Cancer Society.* *https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html*

21. Dusetzina, S., Winn, A., Abel, G., Huskamp, H., and Keating, N. (2013). Cost Sharing and Adherence to Tyrosine Kinase Inhibitors for Patients With Chronic Myeloid Leukemia. *Journal of clinical oncology.* 32. 10.1200/JCO.2013.52.9123.

22. Noens et al. (2009). Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: the ADAGIO study. *Blood*. doi:10.1182/blood-2008-12-196543

23. Gordon, L.G., Merollini, K., Lowe, A., and Chan, R.J. (2017). A Systematic Review of Financial Toxicity Among Cancer Survivors: We Can't Pay the Co-Pay. *Patient*. **(10)** 295.

24. Zebrack, B.J. (2001) Cancer Surivor Identity and Quality of Life. **(8)** 5.

25. Health Insurance Coverage of the Total Population. (2017). *Kaiser Family Foundation.* https://www.kff.org/other/state-indicator/total-population/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D.

26. Altice CK, Banegas MP, Tucker-Seeley RD et al (2016). Financial hardships experienced by cancer survivors: a systematic review. J Natl Cancer Inst 109:djw205

27. Quato, D.M., Wilder, J., Schumm, L.P., Gillet V., Alexander G.C. (2016) Changes in Prescription and Over-the-Counter Medication and Dietary Supplement Use Among Older Adults in the United States, 2005 vs 2011. *JAMA Intern Med.* **176**, 473-82.

28. Tibebu, A., Mengistu, D., and Bulto, L.N. (2017). Adherence to prescribed antihypertensive medications and associated factors for hypertensive patients attending chronic follow-up units of selected public hospitals in Addis Ababa, Ethiopia. *International Journal of Health Sciences.* **11**(4).

29. Weaver, K.E. et al (2012). Mental and Physical Health-Related Quality of Life among US Cancer Survivors: Population Estimates from the 2010 National Health Inverview Survey. *Cancer Epidemiology, Biomarkers & Prevention*. **21**(11).

APPENDIX

Figure 1: History of Prescription Drug Spending in the United States

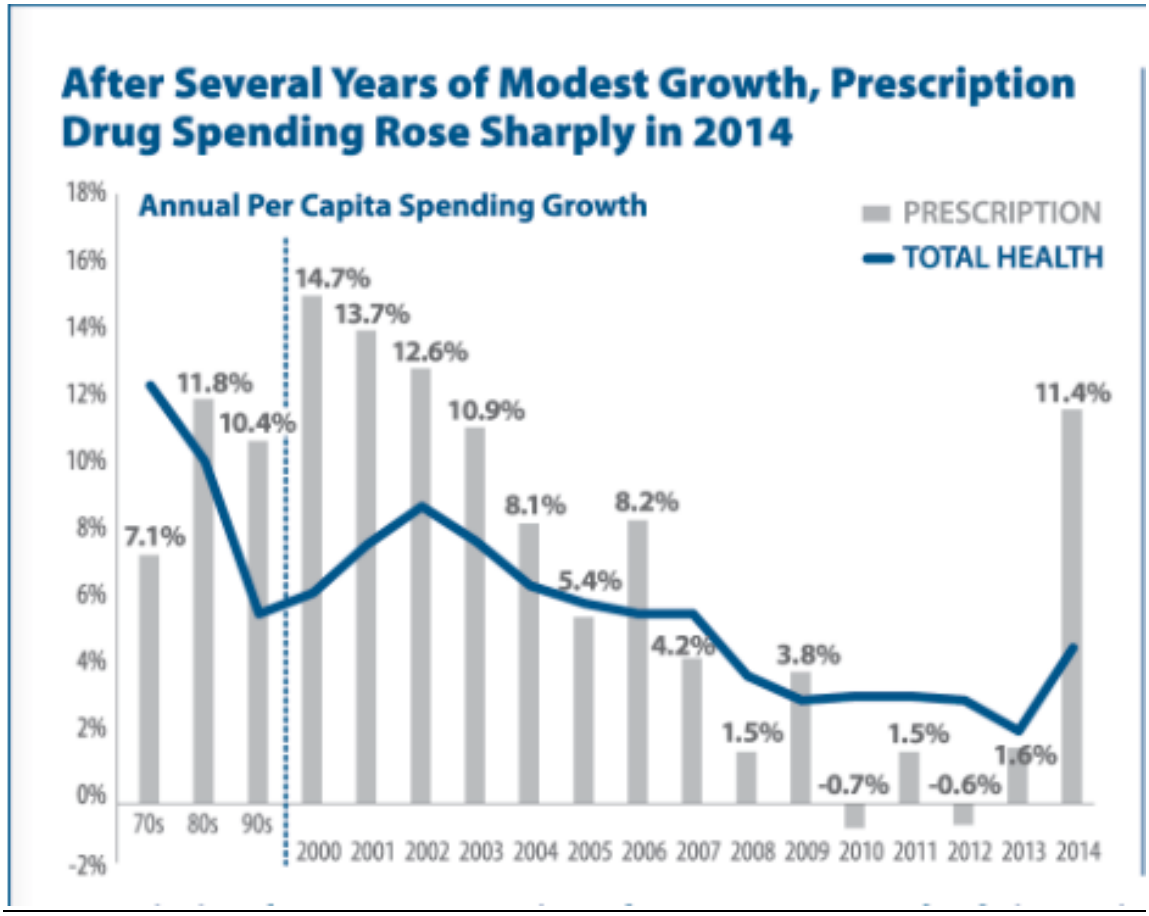


Figure 2: Total Health Expenditures as Gross Domestic Product

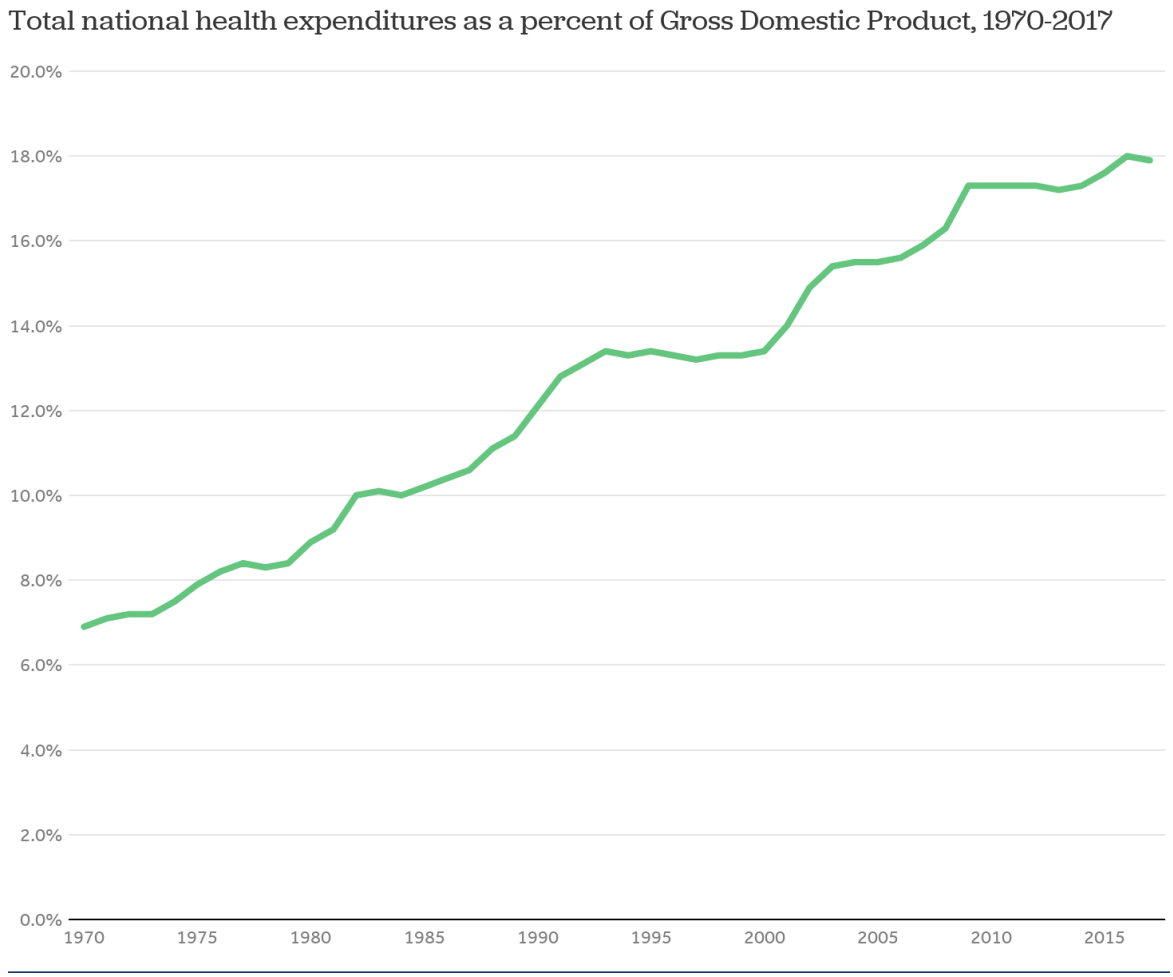


Figure 3: High Cost of Patented Cancer Medicines in US

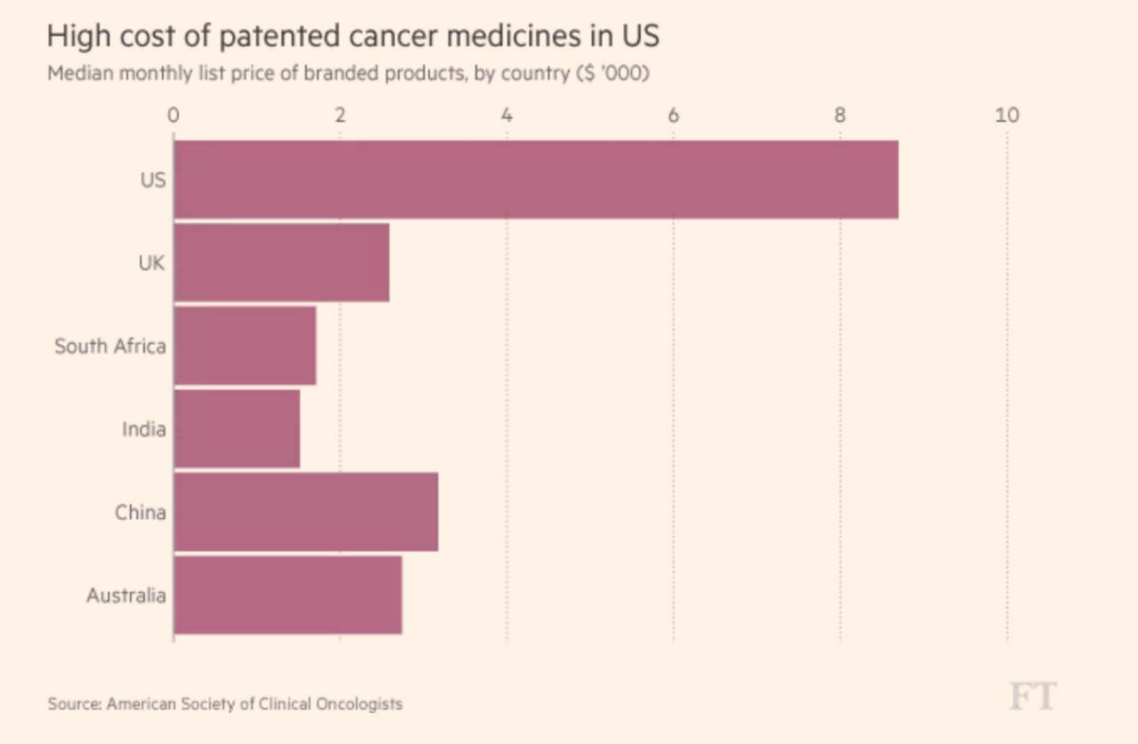


Figure 4: Patient Recruitment Flowchart

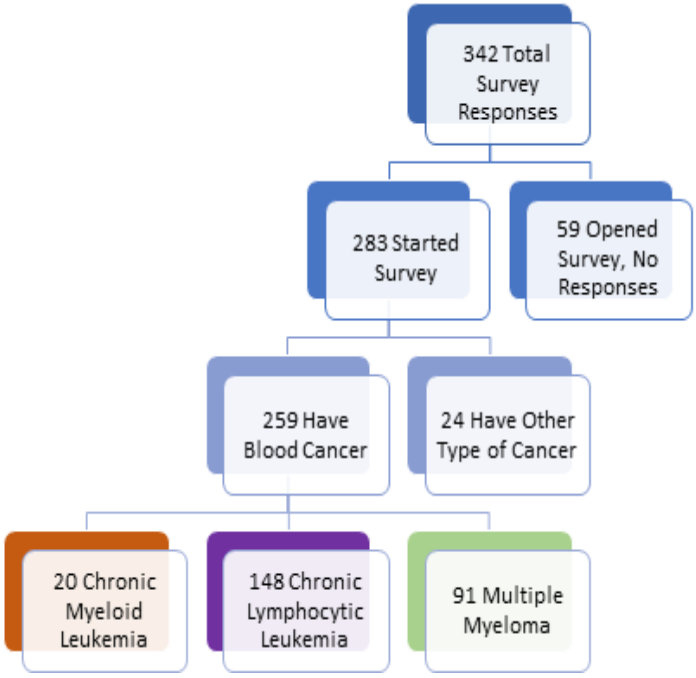


Figure 5: Cost-Related Non-Adherence

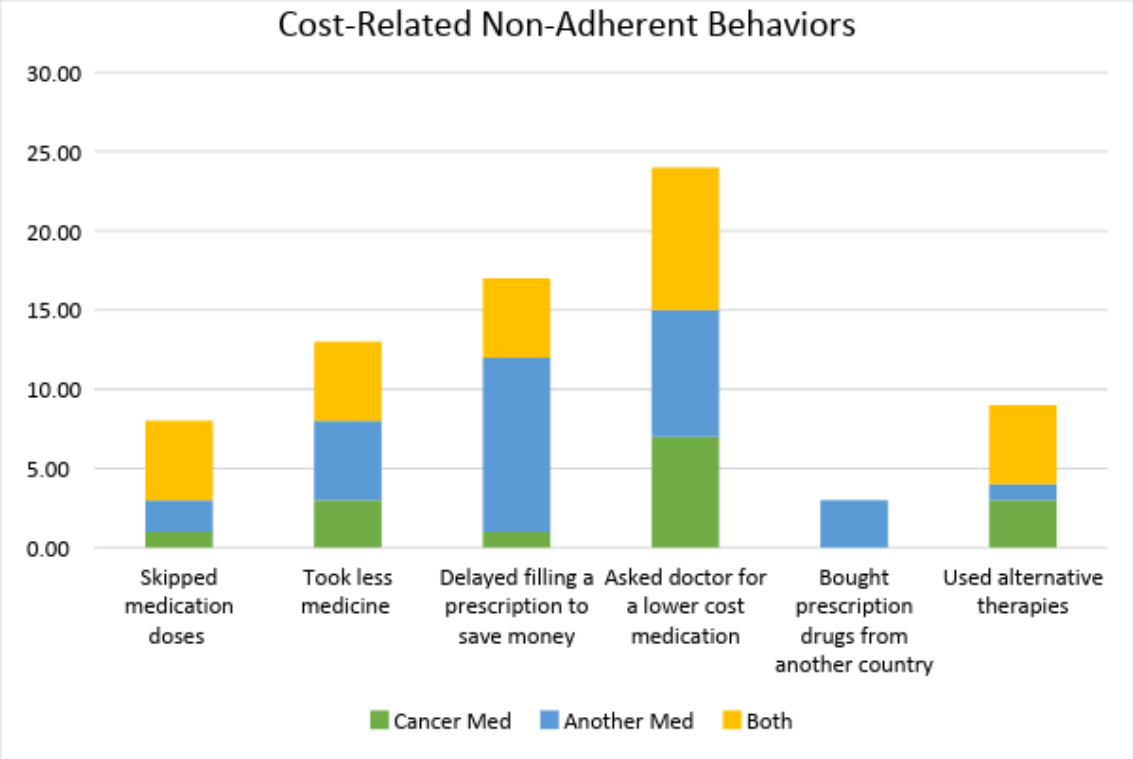


Figure 6: Cost Defray Strategies

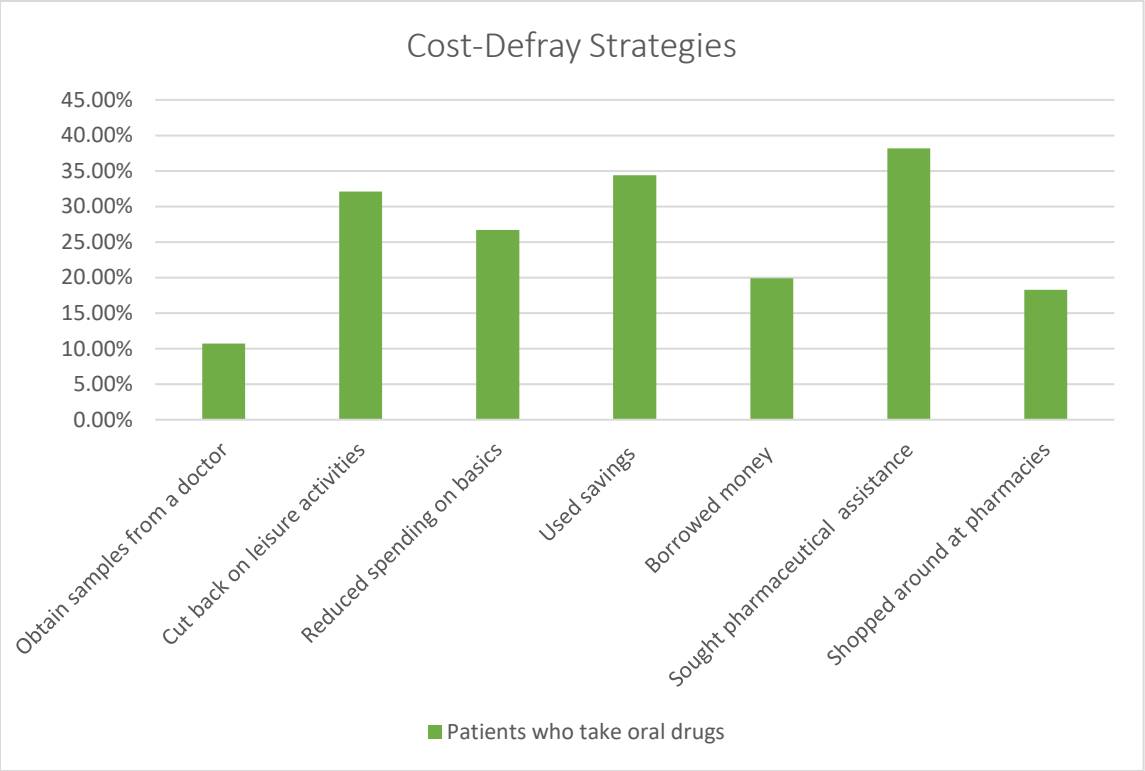
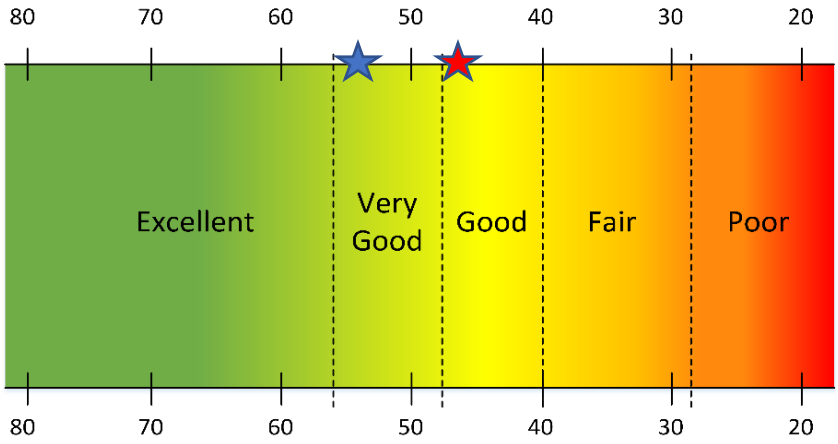


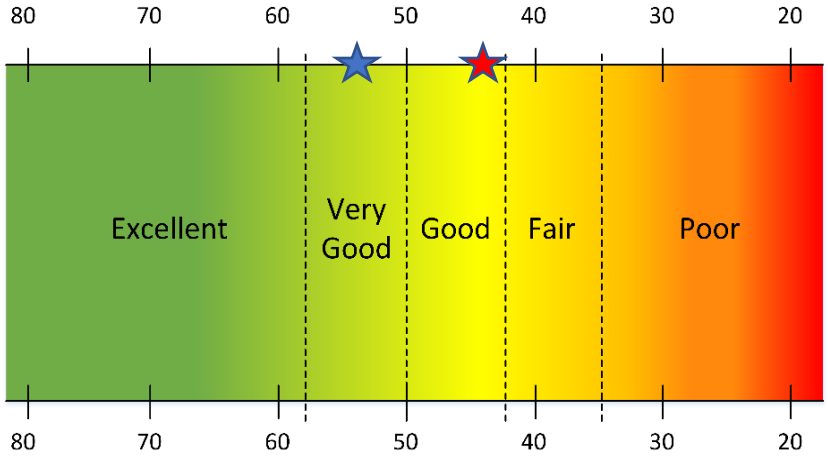
Figure 7: PROMIS Global Mental & Physical Health T-Scores

Interpreting PROMIS® Global Mental Health T-Scores



Based on Hays RD, Spritzer KL, Thompson WW & Cella D (2015). US general population estimate for "excellent" to "poor" self-rated health item. *Journal of General Internal Medicine*, *30*(10), 1511-1516.

Interpreting PROMIS® Global Physical Health T-Scores



Based on Hays RD, Spritzer KL, Thompson WW & Cella D (2015). US general population estimate for "excellent" to "poor" self-rated health item. *Journal of General Internal Medicine*, *30*(10), 1511-1516.

Healthy Non-Cancer Adults

CLL & MM Patients

NOTES

PROMIS measures use Item Response Theory (IRT), which is “a family of statistical models that link individual questions to a presumed underlying trait or concept of global health represented by all items in the scale”. Responses were scored using the HealthMeasures Scoring Service. This method uses responses to each item for each participant and is more accurate than the use of raw score/scale score look up tables. The scoring service reports T-score values on independent respondents. The T-score rescales the raw sums core into a standardized score with a mean of 50 and standard deviation (SD) of 10. Therefore, a person with a T-score of 60 is one SD above the mean. A higher PROMIS T-score on the Global Health scales is one standard deviation (more health) than the general population. The PROMIS Global scale produces two scores, a physical health score and a mental health score from 4 items each. PROMIS Global scores are interpreted based on the Hays et al. validated scale

Table 1. Demographic and Clinical Characteristics of Survey Respondents

Demographics	*Total*	*CLL*	*MM*	*Take Oral Anticancer Drugs*	*Do Not Take Oral Anticancer Drugs*
Cancer Type (count/percentage)	239	61.9%	38.1%	43.9%	72.5%
Gender (%Female)	53.6%	48.7%	61.5%	51.9%	55.6%
Race/Ethnicity					
Latino/Hispanic	4.6%	4.1%	5.6%	2.3%	7.5%
Black	2.5%	0.0%	6.6%	3.1%	1.9%
White	95%	98.7%	89.0%	93.9%	96.3%
Other	2.1%	1.7%	3.4%	2.3%	0.9%
Not Reported	0.8%	0.7%	1.1%	0.8%	0.9%
Age					
26-44	1.3%	0.7%	2.2%	1.5%	0.9%
45-54	7.1%	4.8%	11.0%	9.2%	4.7%
55-64	36.6%	35.4%	38.5%	28.2%	46.7%
65-74	44.5%	45.6%	42.9%	47.3%	41.1%
75-84	9.7%	12.2%	5.5%	12.9%	5.6%
85+	0.8%	1.4%	0.0%	0.8%	0.9%
Income					
<$20,000 - $39,999	25.0%	21.9%	30.0%	22.1%	28.6%
$40,000 - $79,999	23.7%	23.3%	24.4%	21.4%	26.7%
$80,000 - $100,000+	49.2%	53.4%	42.2%	52.7%	44.8%
Unreported/Don't Know	2.1%	1.4%	3.3%	3.8%	0%
Disease Duration					
<6 months	3.5%	2.8%	4.6%	3.1%	4.0%
7 months to <2 years	17.4%	11.3%	27.3%	18.3%	16.1%
2 years to <5 years	31.7%	29.6%	35.2%	26.7%	38.4%
6 years to <10 years	24.8%	26.1%	22.7%	27.5%	21.2%
More than 10 years	22.6%	30.3%	10.2%	24.4%	20.2%
Health Insurance					
Medicare	54.4%	55.0%	54.9%	61.1%	46.3%
Private Insurance	40.6%	40.5%	40.7%	36.6%	45.4%
Other	5.0%	5.4%	4.4%	2.3%	8.3%

Have Prescription Drug Coverage (%Yes)	96.6%	94.4%	95.8%	93.8%	92.5%
Take oral drugs as part of Cancer treatment	54.8%	43.9%	72.5%		

Total sample size was 239 for demographic analysis

Table 2: Subjective Financial Burden by Anticancer Drug Use

Financial Burden	*Total*	*Take Oral Anticancer Drugs*	*Do Not Take Oral Anticancer Drugs*
Caused family financial hardship? (%Yes)	39.5%	44%	32.9%
Level of difficulty			
Very difficult	19.8%	18.2%	23.1%
Difficult	34.6%	32.7%	38.5%
Less difficult	45.7%	49.1%	38.5%
Level of financial burden			
Catastrophic	4.29%	4.8%	3.5%
Significant	14.8%	16.0%	12.9%
Moderate	24.3%	28.8%	17.6%
Minor	29.1%	32.8%	23.5%
Not at all	27.6%	17.6%	42.4%

Total sample size for financial burden was 210 (29 respondents did not complete all required responses)

Table 3: Predicted Factors Associated with Subjective Financial Burden

	Predictors of Financial Burden			
	Unadjusted	**P-value**	**Adjusted**	**P-value**
Use Oral Rx	1.195 (.90 - 1.58)	0.21	1.18 (.89 - 1.56)	***0.04**
Don't use Oral Rx				
Under 65	1.34 (1.0 - 1.76)	***0.03**	1.29 (.95 - 1.75)	0.1
65 and Older				
Female	1.15 (1.02 - 1.78)	***0.04**	1.13 (0.85 - 1.52)	0.38
Male				
Medicare	1.04 (0.78 - 1.37)	0.8	1.13 (0.81 - 1.57)	0.48
Private & Other				
CLL	0.65 (0.50 - 0.85)	***0.00**	0.77 (0.588 - 1.03)	0.08
MM				
6 years - <10 years	1.67 (1.08 - 2.58)	***0.02**	1.64 (1.06 - 2.55)	***0.03**
More than 10 years				
$80,000 - $100,000+	0.71 (0.31 - 1.63)	0.42	0.72 (0.3 - 1.72)	0.46
<$20,000 - $39,999				
$40,000 - $79,999				
Unreported				

Table 4: Cost-Related Non-Adherent Behavior by Cancer Versus Non-Cancer Drugs

Cost-related Non-adherence	*Total*	*Cancer Med*	*Other Med*	*Both*
Skipped medication doses	6.1%	12.5%	25.0%	62.5%
Took less medicine	9.9%	23.1%	38.5%	61.5%
Delayed filling a prescription to save money	13.0%	5.9%	64.7%	29.4%
Asked doctor for a lower cost medication	18.2%	29.2%	33.3%	37.5%
Bought prescription drugs from another country	2.3%	0.0%	100.0%	0.0%
Used alternative therapies	6.8%	33.3%	11.1%	55.6%
	Total		*CLL*	*MM*
CRN Indicator (Cancer Meds Only)	(23) 17.6%		(11) 16.9%	(12) 18.2%

*131 patients are used for this sample who responded "Yes" to taking oral meds

Cost-Defraying Strategies	***Total***
Obtain samples from a doctor	10.7%
Cut back on leisure activities	32.1%
Reduced spending on basics	26.7%
Used savings set aside for other purposes	34.4%
Borrowed money or used credit to pay for medications	19.9%
Sought pharmaceutical company assistance	38.2%
Shopped around at pharmacies to get med at lowest price	18.3%
Cost Defray Indicator	(83) 63.4%

Table 5: Health-Related Quality of Life by Anticancer Drug Use

Self-Reported Health	*Total*	*Take Oral Anticancer Drug*	*Do Not Take Oral Anticancer Drugs*
General Health			
Excellent	4.7%	5.6%	3.5%
Very Good	36.3%	36%	36.8%
Good	35.4%	38.4%	31.0%
Fair	20.3%	17.6%	24.1%
Poor	3.3%	2.4%	4.6%
Quality of life			
Excellent	10.9%	10.4%	11.5%
Very Good	37.7%	38.4%	36.8%
Good	28.3%	32.8%	21.8%
Fair	19.8%	16.8%	24.1%
Poor	3.3%	1.6%	5.8%
Physical Health			
Excellent	3.3%	2.4%	4.6%
Very Good	34.9%	37.6%	31.0%
Good	32.6%	36.8%	26.4%
Fair	25.0%	20.0%	32.2%
Poor	4.3%	3.2%	5.8%
Mental Health			
Excellent	16.1%	16.1%	16.1%
Very Good	36.0%	39.5%	31.0%
Good	26.1%	26.6%	25.3%
Fair	19.9%	16.9%	24.1%
Poor	1.9%	0.8%	3.45%
Satisfaction with Social Activities			
Excellent	12.9%	12.8%	12.9%
Very Good	35.7%	39.2%	30.6%
Good	30.0%	31.2%	28.2%
Fair	13.8%	11.2%	17.7%
Poor	7.6%	5.6%	10.6%
Carry out social activities and roles			
Excellent	14.6%	14.4%	14.9%
Very Good	33.5%	36.0%	29.9%
Good	25.0%	24.8%	25.3%

Fair	19.3%	20.0%	18.4%
Poor	7.6%	4.8%	11.5%
Carry out physical activities			
Completely	46.7%	47.2%	45.9%
Mostly	27.1%	26.8%	27.6%
Moderately	13.8%	14.6%	12.6%
A little	12.4%	11.4%	13.8%
Bothered by emotional problems (anxious, depressed, irritable)			
Never	24.3%	26.6%	20.9%
Rarely	23.8%	25.8%	20.9%
Sometimes	35.7%	30.6%	43.0%
Often	13.8%	14.5%	12.8%
Always	2.4%	2.4%	2.3%
Fatigue			
None	9.6%	9.8%	9.3%
Mild	34.6%	36.9%	31.4%
Moderate	41.4%	40.2%	43.0%
Severe	10.1%	10.7%	9.3%
Very Severe	4.3%	2.5%	6.9%
PROMIS Scores			
PROMIS Physical Health	47.6 (+/- 9.59)	48.4 (+/- 8.87)	46.4 (+/- 10.47)
PROMIS Mental Health	46.5 (+/- 9.26)	47.0 (+/- 8.9)	45.8 (+/- 9.72)

Total sample size for PROMIS Score Analysis was 212 (27 respondents did not complete all required responses)

Table 6: Estimates of Financial Burdens Associated with Mental and Physical Health-Related Quality of Life, Unadjusted

Parameter	*Estimate*	*Standard Error*	*95% Confidence Limits*	*Z*	*P-value*
Mental Health					
Financial Burden	-6.6181	1.1881	[-8.9467, -4.2894]	-5.57	<.0001
Physical Health					
Financial Burden	-6.0126	1.2725	[-8.5066, -3.5186]	-4.73	<.0001

Table 7: Estimates of Financial Burdens Associated with Mental and Physical Health-Related Quality of Life Controlling for Covariates

Parameter	*Estimate*	*Standard Error*	*95% Confidence Limits*	*Z*	*P-value*
Mental Health					
Financial Burden	-4.8637	1.3403	-7.4908	-2.2367	-3.63
Physical Health					
Financial Burden	-4.1591	1.2578	-6.6243	-1.6940	-3.31