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Development and Evaluation of the Assessment of Opioid Taking Behaviors and Adherence Scale (AOTBA) in Patients with Sickle Cell Disease

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Development and Preliminary Evaluation of the Assessment of Opioid Taking Behaviors and Adherence Scale (AOTBA) in Patients with Sickle Cell Disease

A Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of in of Pharmaceutical Sciences at Virginia Commonwealth University.

by

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Abbreviations

BPI	Brief Pain Inventory
BPI-SF	Short form of Brief Pain Inventory
ED	Emergency Department
EMR	Electronic Medical Record
HIPPA	Health Insurance Portability and Accountability Act
HgB	Hemoglobin
SS	Hemoglobin SS (two similar abnormal alleles, both for hemoglobin S)
SC	Hemoglobin SC (two different abnormal alleles, one for hemoglobin S and one for hemoglobin C)
SB+thal	Hemoglobin S Beta Zero Thalassemia
MMSE	Mini-Mental Status Exam
PHI	Protected Health Information
PMAQ	Pain Medication Attitude Questionnaire
SF-MPQ	Short-Form McGill Pain Questionnaire
SCD	Sickle Cell Disease
VCU	Virginia Commonwealth University
VCUHS	Virginia Commonwealth University Health Care System

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Abstract

DEVELOPMENT AND PRELIMINARY EVALUATION OF THE ASSESSMENT OF OPIOID TAKING BEHAVIORS AND ADHERENCE (AOTBA) SCALE IN PATIENTS WITH SICKLE CELL DISEASE

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A Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in of Pharmaceutical Sciences at Virginia Commonwealth University.

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The rapid growth in opioid therapy for non-cancer pain has occurred without an adequate appreciation of the consequences of this growth. Few studies provide patient-centered evidence that can be used to inform the current proposed standards for efficacious (safe and effective) opioid prescribing in non-cancer pain. Furthermore, different terms may be used interchangeably in the literature to refer to opioid-taking behaviors, resulting in imprecise or vague interpretation of existing evidence. We therefore sought to explore patterns of opioid-taking behavior and their biopsychosocial-spiritual determinants in African-American adults with sickle cell disease (SCD). Many questions surround opioid use for non-cancer pain, but little has been published about behavioral patterns of taking opioids in these conditions. The main objective of this study was to develop a disease-

specific scale for describing prescribed opioid taking in patients with sickle cell disease (SCD). As part of a multiphase, mixed-methods study, we used an adaptation of several published methods to construct 9 sequential, chronological steps for developing a new scale. We report here wide-ranging quantitative and semi-structured, qualitative interviews of 13 male and 11 female African-American adults with SCD, average age 36 years, from various socioeconomic and educational levels. We used grounded theory, priori and posteriori procedures to analyze the qualitative data, and to conduct an appraisal of translational validity. Scale development results have led to inclusion in the draft scale of new concepts namely momentary medication-taking behavior. The scale also captures concrete patterns of adherence for as-needed and scheduled medication and allows for several discovered conceptual domains that explain observed opioid-taking behaviors. These concepts challenge the current theories and models of medication-taking behavior and adherence. In summary, we found that contextual factors may drastically affect opioid-taking behaviors. Together, These uncovered phenomena raise new hypotheses that may challenge current theories and models of medication-taking behaviors and methods of assessing adherence. These hypotheses call for a new round of research on opioid-taking behavior, and need to be rigorously tested in future research

CHAPTER 1 INTRODUCTION

I. Background and Significance

Opioid use in sickle cell disease (SCD) is controversial. It has been discovered that patients may have acute, chronic, or perhaps acute-on-chronic pain, unlike what was previously hypothesized. Thus, the principle of treating patients mainly with acute short-acting opioids, and mainly during pain "crises", has now been updated to the principle of using long-acting opioids chronically as needed for chronic pain, along with short-acting opioids for break-through and acute pain. In either case, physicians may underprescribe opioids for SCD, may not trust patients to use opioids responsibly, and may inappropriately single out SCD patients to screen for abuse. Patients may not trust physicians to prescribe opioids liberally or appropriately, and may exhibit pseudoaddiction behaviors, including hoarding and taking medicines from different physicians to get pain relief.

Like any patients using prescribed opioids, SCD patients may become addicted, or may divert and/or manifest criminal behavior in their use of opioids, although this has been estimated to be rare. While a few studies of long-term opioid use for SCD have been published, no one has performed in-depth analysis of just how and exactly why sickle cell

patients use prescribed opioids in general. Specifically, no one has performed studies of time-specific and context-specific use which give the ability to identify and evaluate the temporal pattern of medication use and enable a closer assessment of the contexts (environmental, emotional, situational) underlying opioid use that are present in most biopsychosocial-spiritual phenomena (definitions of these categories of adherence are introduced in the method section under *definitions*). Current models of adherence do not capture time-specific or context-specific patterns of adherence, often important when patients are using as-needed opioids for pain. Because sickle cell pain is unpredictable, and may be managed with both as-needed and scheduled opioids, it represents an ideal disease in which to study such patterns of opioid usage or adherence. Previous work has found patterns of adherence for drugs in general, which may apply to opioids. But we found no studies that have tested whether these patterns apply to opioid use, particularly in SCD.

The current study uses a multiphase mixed-methods design to address the following objectives: a) Explore adherence and opioid taking behaviors, both over time and at particular times; b) Identify and explore attitudes, beliefs, and contextual factors related to adherence and these opioid taking behaviors; c) Capture, describe, and interpret key themes from these opioid taking behaviors and contextual factors that may generate new concepts of adherence; d) Generate key themes, concepts, and results from the qualitative interviews and the literature to construct and begin testing a quantitative survey of opioid taking behavior, and contextual factors related to these behaviors, in adults with SCD; e)

use results from the above to construct a taxonomy of opioid use in adults with SCD. The immediate goal of this dissertation is exploratory qualitative and quantitative multiphase, mixed-methods research to develop a disease-specific research instrument designed to describe prescribed opioid adherence and opioid taking behavior in patients with SCD. The results of this mixed-methods study will be used to design future quantitative studies intended to test hypotheses generated here.

A. Epidemiology of Sickle Cell Disease

SCD is an inherited blood disorder of hemoglobin structure. It is a progressive disabling illness that leads to chronic hemolytic anemia, with severe clinical consequences. It occurs primarily in people of African ancestry. [1, 2] SCD affects approximately 100,000 Americans. In the United States, approximately one in 300 African-Americans have SCD (>70,000 people) and 8% have sickle cell trait. [3]

B. Pain in SCD

Symptoms of sickle cell anemia vary, but its main symptom is sudden pain throughout the body. Pains crises constitute the most characteristic clinical feature of sickle cell disease and are considered the most common reason for emergency department visits and hospitalizations of the affected patients. [4] The pain from sickle cell anemia can be acute episodic, chronic, or a combination of both, but acute episodic pain is more common.

This acute episodic pain is caused by vasoocclusion of the microcirculation -to the organ supplied- that is obstructed by sickled RBCs. There is high significant variableness in the rate of recurrence and severity of pain SCD patient's experience.[5-7] Acute or chronic pain can be hard to tolerate and mentally exhausting and may limit the quality of life of patients daily activities. There is relationship between the frequency of painful crisis and early death.[8] Pain has a major impact on health resource utilization and quality of life.[9-11] It is significantly associated with depression,[12,13] anxiety, cognitive impairment,[14-17] decreased appetite, weight loss, as well as disturbance to sleep, gait, dysfunction general activity, mood and distorted communication, possible unnecessary loss of employment and productivity[15] by patients and caregivers, and mistrust even from family members and friends of patients relationships with other people. In the PiSCES study, results showed that daily pain in SCD patients who completed daily pain diaries for up to 6 months is far more prevalent and severe than previously described, with more significant effects on all aspects of life. PiSCES investigators found that >50% of adults with SCD experienced pain, crises, or healthcare utilization on >50% of the days. Almost 33% experienced pain nearly every day, with the mean intensity in the middle range. Only approximately 15% rarely experienced pain. Crises and healthcare utilization were far less common than reported pain days; pain days that were not associated with a crisis occurred 10 times more often as pain days associated with healthcare utilization.[18-25] Many studies have documented that depression and anxiety disorders are common in SCD and may be correlated with SCD.[17] New research reconfirms that individuals with SCD have poor baseline health-related quality of life, and painful episodes have a further

negative impact. Worse health-related quality of life in SCD patients is associated with disease severity and pain intensity. [26] Anecdotal reports from patients and new research suggests that there are sleep disturbances related primarily to SCD pain, and vice versa, in SCD patients. [27] In fact, the frequency of painful crises in Sickle cell disease is a measure of clinical severity and correlates well with early death. Because of the recurrent and chronic nature of crises, and due to severe form of pain on daily basis pain, and its complex nature and complex interaction between physical, social, and psychological factors and because pain relieve is priority for patient in sickle cell anemia, prescribing of aggressive analgesics pain-relieving medication is needed and it is an most important of multidisciplinary treatment of these patients.

C. Pain Management in SCD

Opioid analgesics are the most often used and accepted in the management of sickle cell pain. Several studies, theories and anecdotes showed that many patients with sickle cell anemia can achieve clinically significant relief from stable doses of opioid medication. In the light of research that demonstrates better patient outcomes, reduced length of stay, and reduced resource use as a result of effective pain management and mobility. [28]

Many patients need to take opioid analgesics at home in an attempt to relieve the pain. In prescribing analgesics for home use, some patients' pain is managed with" as needed" (PRN) analgesic prescription only. Since the pain in some patients will persist for a long

duration, writing analgesic orders on an "as needed" basis (PRN) results in a recurrence of pain, increase anxiety, discomfort, and ultimately, a need to prescribe a larger dose of narcotic in order to achieve the same effect which may create concerns about abuse and addiction with short acting opioid. Subsequently, a long-acting (administered "around the clock" at a frequency consistent with their duration of action) rather than a short- acting narcotic is much more effective and could provide more consistent pain relief, generate less euphoria with administration, result in slower development of tolerance, and offer a more favorable side-effect profile than immediate-release preparations. [29] However, when these methods do not control the pain, PRN analgesia should be used promptly rather than letting the intensity of the pain increase until it can be managed only by hospital admission.

As physicians have generally increased their use of opioids to treat chronic non-malignant pain, [30] patients with severe and/or chronic SCD pain have increasingly been treated with opioids, including long-acting opioids. Numerous writers have advocate that prescription of opioids for pain in SCD is both complex and challenging. [31-35]Despite this, only a little data has been published about the short-term or long-term use of short-acting and long-acting opioids in SCD pain.

Opioid use in sickle cell disease (SCD) is controversial. As controversial points of view and evidence about the unnecessary treatment and inadequate treatment of pain has increased [36, 37], there have been vast increases in the prescription of opioid medications in the US. [38] Epidemiologic studies indicate that use of opioids for chronic noncancer pain has increased substantially over the last two decades. [39] Use of more potent opioids (such as morphine, hydromorphone, oxycodone, and fentanyl) has also increased. Over the same two decades, the proportion of office visits in which prescriptions for potent opioids were given increased from 2% to 9%. A recent study found that 2% of a random sample of adults in the United States reported regular use of opioid pain medications in the last year. [40] Although the rate of prescribing and use is increasing, there is still significant data of inadequate pain management [37, 41].

Simultaneously, there has been a large increase in prescription opioid related problems, such as misuse, abuse, overdose, and litigation against physicians. [42, 43] Research on enhancing patients' proper use of prescribed pain medications has focused on identifying risk factors for criminal over-using opioids. Consequently, many screening instruments for identifying patients at risk for criminal over-using opioids have been developed (evaluated and assessed in one study [44], but with conflicting success in another one [45].

Although evidence shows that overuse and underuse is widespread with high rate of associated problems, less attention has been paid to non-criminal overuse or under-use of prescribed opioids. [46] Opioid nonadherence (as under use or overuse) is a challenging

problem because to date few have studied contextual factors involved. Underuse or overuse could spring from biological factors such as lack of efficacy, or from, emotional, social or other contextual factors. Understanding why and when patients over-use or under-use their prescribed opioid is crucial for establishing approaches to enhance the effectiveness and efficiency of pain management.

Previous studies attempted to provide insight into why and when patients' under-use or over-use medications. [47] General risk factors for medication under-use include low socioeconomic status, patient- provider relationship, severity of illness, comorbidity, complexity of medical regimen, duration of treatment, side effects, knowledge and beliefs, motivation to manage their illness, and lifestyle. [48] However, the biopsychosocial reasons patients legally (non-criminally) overuse or underuse prescribed opioids have rarely been described in non-cancer pain patients especially in sickle cell anemia patients.

Fishman et al. [49] compiled several factors such as why patients might under-use opioid medications such as fear of addiction, forgetfulness, carelessness, complexity of the medication regimen, self-treatment of early withdrawal, use of medication for other symptoms (e.g., sleep, anxiety) lack of education regarding illness/treatment, and social stigma. In this paper the authors discussed plans to address criminal over-use such as monitoring and employing opioid medications tagged with chemical markers or electronic/mechanical monitoring of drug containers. Gunnarsdottir et al. [50] identified

factors that act as barriers to cancer patients' use of analgesics: fear of side effects, fatalism about their disease, beliefs about the doctor-patient relationship, and fear of harmful effects.

Because SCD patients have perhaps acute-on-chronic pain [5] which is defined as acute pain flares superimposed on underlying chronic pain, many patients may use not only short-acting opioids, but also long-acting opioids, and may use opioids chronically. Physicians may underprescribe opioids for SCD [51-53], may not trust patients to use opioids responsibly [53-56], and may inappropriately single out patients to screen for abuse. [57] Patients may not trust physicians to prescribe opioids liberally or appropriately, and may exhibit pseudoaddiction behaviors [58, 59] including hoarding and taking medicines from different physicians to get pain relief. Like any patients using prescribed opioids, SCD patients may divert and/or manifest criminal behavior in their use of opioids, although this has been estimated to be rare [60,61].

While a few reports of long-term opioid use for SCD have been published [62-64], no one has performed in-depth analysis of just how and exactly why sickle cell patients use prescribed opioids in general. Especially, no one has performed studies of time-specific and context-specific opioid use which give the ability to identify and evaluate the temporal pattern of changes in medication use and enable a closer assessment of the ways of using pain medicine that are present in most biopsychosocial phenomena (definitions are introduced in the method section under *definitions*). Current models of adherence do

not capture the time-specific behaviors of adherence, often important when patients are using as-needed opioids for pain. Sickle cell pain is unpredictable, and may be managed with both as-needed and scheduled opioids. It represents an ideal disease in which to study time-specific and overall opioid adherence.

Previous work has found patterns of adherence for drugs in general, which may apply to opioids. Few have tested whether these patterns exist for opioid use. None have tested or even explore whether they exist for opioid use in SCD. We have preliminary data that prescribed opioid consumption is strongly correlated with pain intensity in SCD, and that opioid use is common in SCD and may be correlated with SCD outcomes. [5] Besides this preliminary data, the relationship between pain and patterns of analgesic use is unclear and studies that looked at non-adherence in sickle cell anemia populations were limited. No known studies to date have attempted to explore the links between time-specific adherence behavior and triggers in the lives of SCD patients.

To address this gap in the pain management literature for SCD, and perhaps relevant for opioid use in the world of non-cancer pain disorders, there is a need to explore how patients use prescribed opioids in SCD, as well as reasons patients under-use or over-use prescribed opioids.

The under-treatment of pain is often due to the reluctance of physicians to give SCD patients adequate dosages of opioid analgesia due to concerns about addiction, tolerance

and side effects. [65] Physicians tend to overestimate the prevalence of opioid dependence in patients with sickle cell crises. Yet the incidence of opioid analgesic addiction in patients with sickle cell disease has been reported as being no higher than three percent. [65] It has been found that under-treatment of pain can lead to 'pseudoaddiction' [66] where reports of pain by the patient are not recognized which often support the healthcare professionals' perceptions of substance dependence. [67] The evidence suggests that a high percentage of sickle cell patients are perceived to be opioid dependent when in fact the percentage of sickle cell patients who are opioid dependent is no higher than the general population. [68]

II. Purpose of the Study Protocol

The immediate goal of this dissertation was exploratory qualitative and quantitative multiphase, mixed-methods research to develop a disease-specific research instrument designed to describe prescribed opioid adherence and opioid taking behavior in patients with SCD. The research proceeds in 2 phases. Phase I explored and elicited themes. Phase II generated items to develop a draft survey, and complete the early steps of translational validity testing (face and content validity).

We acknowledge the premise of this study was exploratory. In reaching the immediate goal of the dissertation, the dissertation research generated some descriptive information about opioid taking behavior in SCD patients.

We recognized opioid taking behavior may be classified as aberrant or non-aberrant. In turn, aberrant opioid taking behavior may be classified as intentional or non-intentional. However, the target audience of this research was not those trying to distinguish between the two, or addictionologists, per se, although they may find the research helpful. Rather, the research was directly targeted toward those interested in measuring and understanding adherence and medication taking behavior, including pharmacoepidemiologists, sociologists, psychometricians, psychologists, and health behavior researchers.

III. Primary Hypotheses

There are no a priori hypotheses for Phase I of this project, the mixed-methods study, which is intended to be hypothesis-generating study.

However, with regard to opioid use, we expected that SCD patients would:

1. Report all the patterns of overall adherence; including overuse over time, underuse over time, dropout use, and erratic use, previously described in general studies of medication adherence.
2. Report previously unexplored time-specific or context-specific patterns of use and adherence.
3. Cite many of the previously hypothesized or proven attitudes, beliefs, and contextual factors related to these patterns of use and adherence.

4. Cite previously unreported attitudes, beliefs, and contextual factors related to these patterns of use and adherence.

For Phase II, we hypothesized that the intended instrument would have high face and content validity.

CHAPTER 2 LITERATURE REVIEW

I. Brief Introduction

Sickle cell disease (SCD) is an inherited blood disorder of hemoglobin structure. It is a progressive disabling illness that leads to chronic hemolytic anemia, with severe clinical consequences. It occurs primarily in people of African ancestry. [1, 2] Symptoms of sickle cell anemia vary, but its main symptom is sudden pain throughout the body. Pains crises constitute the most characteristic clinical feature of sickle cell disease and are considered the most common reason for emergency department visits and hospitalizations of the affected patients. [3] The pain from sickle cell anemia can be acute (episodic), chronic, or a combination of both. Acute episodic pain was previously hypothesized as the major portion of pain in SCD. It is caused by vaso-occlusion of the microcirculation to the organ supplied- that is obstructed by sickled RBCs. But SCD Patients also have chronic pain, [4] unlike what was previously hypothesized. The causes of this pain may be neuropathic as well as nociceptive, and little has been described other than the epidemiology of this pain. Pain in SCD is most commonly treated with opioids. Opioids are drugs that exert their activity on opioid receptors. They are considered the most potent analgesics.

II. Review Methods and Search Strategy

A. **Databases**

We searched the topics of opioids, chronic pain and adherence measure studies in the primary medical literature through PubMed®, PsycINFO®, EMBASE, CINAHL, Cochrane Database, Ovid HealthStar and The World Wide Web was searched using the Google and Google Scholar search engines, covering the time period from January 1980 to December 2012.

B. **Search Terms**

We used broad terms for indexed searching which are opioids, opiate, analgesics, narcotics combined with sickle cell. We then used the following search terms: 'patient compliance', 'medication adherence', 'medication persistence', 'treatment compliance', 'drug monitoring', 'drug therapy', 'monitor', 'monitoring', 'drug', 'drugs', 'compliance', 'persistence' 'medications', 'predictors' 'facilitators' or 'determinants' 'relationship' 'and 'barrier' combined with the terms 'questionnaire', 'survey', 'scale', 'tool', and 'self-report'.

C. **Inclusion and Exclusion criteria**

The following inclusion and exclusion criteria were used.

We included studies that met all of the following criteria:

1) Human subjects
2) Evaluated adults (≥18 years old) with SCD.
3) Were relevant to one of the Key Questions (adherence and adherence scale in sickle cell anemia, an article-measuring adherence using any adherence method and specifically self-reported questionnaires in the same patients, or their caregivers or both concurrently.
4) Either evaluated or reported adherence assessment (for opioid adherence assessment instruments, monitoring instruments, and studies of survey assessment of opioid taking behavior) or clinical outcomes
5) English language publications

D. **Exclusion criteria**

Studies only published, as conference abstracts were not included in my systematic searches. I omit the publication types of "letters," "editorials," and "comments." I limited my analysis to studies of adults over age 18, since medication adherence for children may be very different from those for the majority of adults with chronic non-cancer diseases. Studies of non-human subjects and those without original data were excluded. We

excluded studies of patients with cancer pain or end-of-life conditions because of the unique circumstances that surround medication adherence for each of these populations.

III. Results of Literature Review

A. **Review of Adherence to Opioid in Sickle Cell Disease**

My literature search identified no single study regarding scales measuring adherence to opioids in sickle cell anemia. Further, my literature search identified no single study regarding adherence to opioid in sickle cell anemia. We then searched adherence scaled medication adherence literature an in a population other than the sickle cell anemia

We began by searching the literature for systematic reviews of adherence to medications to identify topics recently reviewed, and found a large body of literature on the medication adherence. Most studies evaluated adherence in general for those patients who were chronically on medications. A majority of the articles focused on three diseases: hypertension, diabetes, and hyperlipidemia, which are asymptomatic, for which long-term medical therapy is often necessary. Below we provide a summary of my literature review in medication adherence.

B. **Self-Reported Adherence Scales**

I reviewed the literature to identify drawback and characteristics of available self-reported medication adherence scales. A large number of self-reported medication adherence studies were identified. Recent systemic review of Lavsa et al showed that self-reported measures of adherence (including interviews, diaries, and questionnaires) were the most common way in which adherence was assessed. Positive elements of the scale were summarized in this review. [123] In another review of Shi et al., the authors identified that a majority self-reported measures of adherence were moderately to highly correlated with the monitoring devices. [124] In two other reviews, the authors concluded that that self-reports measures are the most useful method in the research and clinical setting for assessing medication adherence practical interventions against non-adherence. [125, 126]

The most commonly used medication adherence scales were: The Medication Adherence Questionnaire (MAQ; also known as Morisky), The Self-efficacy for Appropriate Medication Use Scale (SEAMS), Brief Medication Questionnaire (BMQ), The Hill- Bone Compliance Scale and Medication Adherence Rating Scale (MARS). However, no consensus exists regarding adherence scale selection or criteria. Overall, MAQ is the quickest scale to administer and the simplest for clinicians to score. Further, MAQ has been validated in the broadest range of diseases. [123, 125, 126] However, the current scales

have several problems and weaknesses. Below is an overall summary of the drawback of the existing scales (See Table 2).

Table 2: Overall of limitations of the existing adherence scale

1. No gold standard medication adherence scale exists, and no single scale is appropriate for every scenario. Several scales have many items worded specifically in regard to specific medications in specific diseases.
2. Some were not specifically addressed or assess specifically medication adherence as a discrete construct but they were a generic health status measurement.
3. They are not sensitive, and able to detect different types of nonadherence (momentary adherence, overuse, erratic use, others)
4. Most for them were developed to be simple to administer and to be used initially and primarily in clinical setting. Few items scale may have low predictive ability of subsequent future adherence.
5. Few items do not assess various biopyschosocial-spritual reasons. E.g. in MAR and Hills Bone Scales, Most reasons assessed focused on barriers to non-adherence such as forgetfulness and adverse effects.
6. Some of them developed to be based on a dichotomous yes/no response and not a graded response system. Such type of responses does not give idea about the frequency of the doing the asked actions/situations. (i.e. It will not give the fine distinction between frequent adherer and rare- adherer).
7. The constructs upon which the tools were developed also vary. More recent tools focus on intentional and unintentional nonadherence, purposeful action, self-efficacy and the influence of patient's beliefs about his/her conditions on adherence.
8. Some of the published scales have low validity and reliability score.
9. Some of the reported scales were not built based patient-reported care, which hugely influence design of items.

IV. Rationale for the Study

While a few reports of long-term opioid use for SCD have been published, [31-33] No one has performed in-depth analysis of just how and exactly why sickle cell patients use prescribed opioids in general.Specifically, no one has performed studies of time-specific and context-specific opioid use which give the ability to identify and evaluate the temporal pattern of changes in medication use and enable a closer assessment of the ways of using pain medicine that are present in most biopsychosocial-spiritual phenomena (definitions are introduced in the method section under *definitions*). Current models of adherence do not capture the time-specific behaviors of adherence, often important when patients are using as-needed opioids for pain. Sickle cell pain is unpredictable, and may be managed with both as-needed and scheduled opioids. It represents an ideal disease in which to study time-specific and overall opioid adherence.

Previous work has found patterns of adherence for drugs in general, which may apply to opioids. Few have tested whether these patterns exist for opioid use. None have tested or even explore whether they exist for opioid use in SCD. We have preliminary data that prescribed opioid consumption is strongly correlated with pain intensity in SCD, and that opioid use is common in SCD and may be correlated with SCD outcomes. [4] Besides my data, the relationship between pain and patterns of analgesic use is unclear and studies that looked at non-adherence in sickle cell anemia populations were limited. No known

studies to date have attempted to explore the links between time-specific adherence behavior and triggers in the lives of SCD patients.

To address this gap in the pain management literature for SCD, and perhaps relevant for opioid use in the world of non-cancer pain disorders, this study attempted to explore how patients use prescribed opioids in SCD, as well as reasons patients under-use or over-use prescribed opioids. We interviewed SCD patients to investigate different medication adherence behaviors and to generate new hypotheses about adherence behaviors to prescribed opioids and corresponding contextual factors that may explain those behaviors. The purpose of this part of my study was to address gaps in the existing literature on how and why SCD patients use their prescribed opioid and to explore different adherence patterns of prescribed opioids in SCD patients through semi-structured interviews.

Following the qualitative study, we used its findings and themes as well as the existing literature to develop a survey tool that quantifies opioid utilization patterns and contextual factors in SCD. We will pilot and administer the tool at least once, but realize full validation is beyond the scope of the current project. The purpose of this phase of my study was to gauge the prevalence of various kinds of opioid adherence behaviors and their contextual factors, and to begin testing a tool for future use in quantifying these behaviors in ours and other patients.

Together, the three phases of my mixed methods study will add in-depth information to the limited literature on opioid use in SCD and as formative research for further quantitative study.

V. Study Objective

A. **Primary Aim (Phase I)**

1. Use qualitative and quantitative interviews of adults with SCD to:

    a. Explore adherence and opioid taking behaviors, both over time and at particular times.

    b. Identify and explore attitudes, beliefs, and contextual factors related to adherence and these opioid taking behaviors.

    c. Capture, describe, and interpret key themes from these opioid taking behaviors and contextual factors that may generate new concepts of adherence.

B. **Secondary Aims (Phase II and III)**

2. Use the key themes, concepts, and results from the qualitative interviews and the literature to construct a quantitative instrument survey of opioid taking behaviors, and contextual factors related to these behaviors, in adults with SCD.
3. Use results from Phases 1 and 2 to construct taxonomy of opioid use in adults with SCD.

CHAPTER 3 METHODS

I. Study Design

A. **Overview or Design Summary**

Using a cross-sectional design and a mixed method approach, I conducted two phases of mixed methods (quantitative and qualitative components) study in order to generate and add in-depth information to the limited literature on opioid taking-behavior in SCD. The three phases were formative research for further quantitative study.

I conducted direct semi-structured interview observations (n=20-30) and a subsequent cross-sectional structured survey (n = 50) of patterns of opioid use among adults with SCD. Between these two phases, I generated a pool of items and evaluated their face and content validity. Data was collected between Nov 2011 and May 2013.

II. Stages of New Instrument Development

The process of developing my new instrument went through the various stages of research to ensure adequate and accurate information related to instrument content or structure. There are three main phases in generating a new instrument developing

that instrument and validating the instrument. These three phases may in turn be further divided into 20 sequential, chronological steps of instrument development and validation of a new instrument in a previously unexplored field.

Table 1 lists these three phases and links them to the 20 sequential steps. I constructed these sequential, chronological steps by adapting methodologies from 5 highly cited sources. [DeVellis, 2003, Sage Publications; DeVon HA et al. 2007, Journal of Nursing scholarship; Patrick DL et al. 2011; Passmore C, et al. Fam Med. 2002; Prior ME et al. 2011, BMC Med Res Methodol] [135-139] I followed these steps. The first five steps included reviewing relevant literature, framing the concepts, specifying domains, and conducting qualitative research. Specifically, one elicited key concepts using qualitative interviews to inform content and structure of the new instrument, and establish preliminary content validity of the new instrument.

The second five steps were based on completion of the first five, and involved item generation and pre-validation development methodology. Specifically, the pre-validation stages of the new instrument included initial item generation, initial item reduction and question formatting, assessment of patient understanding of the draft instrument, and planning steps for instrument revision. The final10 steps involved validation of the draft instrument, including assessing coherence across items, discrimination, and all types of validity and reliability, (content validity, descriptive statistics, construct validity, criterion validity (concurrent and predictive validity), convergent validity, discriminant validity,

and reliability (internal consistency and test-retest reliability) with removal of poorly discriminating, unreliable or invalid items.

For this research, Table 3 shows details of each step, the purpose of each step, and the status of this dissertation research relative to each step. This dissertation research included completion of the first 10 of the 20 required steps of development and validation.

A. **Project Status**

I completed nine of the 9 steps of development and validation planned as part of this dissertation. Several steps were completed to create a pool of items. I conducted a thorough literature review, examined existing scales, and applied my own clinical and research expertise. I consulted with expert, intelligent patients to obtain a rigorous review and revision. I adapted grounded theory to construct and analyze my interview.

Table 3: 20-step new instrument development and validation methodology

Phase #	Step #		Purpose
Phase I	Step 1	Determining the context of use • Understand the disease or condition in the target population • Consider the target population – cultural/language groups • Consider preliminary issues related to instrument content and structure (the possible range of instrument content and structure) • Consider the theoretical and qualitative methodological	a. To considered the targets concept throughout the instrument development process. b. To ensure that the context of use in medical product labeling is clearly defined, and the approach for concept measurement is appropriate for the intended context. c. A hypothesized disease model can help can inform the evaluation of the suitability of existing instruments for the development program and/or the development of a research protocol

		approach • Develop an hypothesized conceptual framework	for eliciting concepts to be included in a new instrument.
Phase I	Step 2	Developing the research protocol for qualitative concept elicitation and analysis • Define the target sample characteristics • Select the data collection method - individual interviews. • Determine the setting and location for data collection • Develop the interview guide—draft, pilot, revise	a. To understand patients' perspectives and experiences—including rare perspectives or uncommon experiences— be- cause understanding the entire range of patient experience and perspective is crucial for developing sensitive and comprehensive new instruments. b. To generate a pool of potentially relevant items for SCD pain-specific instruments, most studies focus on an inductive 'bottom up' approach using qualitative methods (e.g. one-to-one interviews with the target population), which ensures items reflect the perspective of the majority of individuals in the population of interest [3,4]. Helps ensure that the final instrument measures the key concepts that come from the target population.
Phase I	Step 3	Conducting the concept elicitation interviews • Obtain institutional review board approval • Recruit participants; monitor sample characteristics to assure diversity of participation from the target population • Select and train interviewers • Conduct interviews—implement quality control measures • Record interviews • Transcribe and clean transcripts	a. To obtain patient quotes that provides a picture of patients' experiences with the target concept and to show the relationship between the concepts, the words and phrases, and the final instrument. b. To translate meaning of the data into a set of items that can be scored to represent the targeted concept(s) quantitatively. c. To document evidence that will inform the content and structure of the new instrument.
Phase I	Step 4	Analyzing the qualitative data • Analyze qualitative data according to the theoretical grounded theory approach • Establish preliminary coding framework; update as data are coded • Establish coding procedures and train coders • Organize data using a qualitative research software program • Assess saturation • Interpret results	a. To organize and catalog a patient's descriptions of their experiences within the context of use. b. To develop concept codes ensures that the ideas generated from patients during the interview process have appropriate influence on the variety and labeling of the codes assigned and the overall organization of the qualitative results.
Phase I	Step 5	Documenting concept development and elicitation methodology and results • Provide objectives and context for use • Describe target population • Provide hypothesized and revised disease model and any input from content experts • Provide conceptual framework and revisions made from preliminary to revised • Provide study methods via protocols and guides	a. To provide to document the content validity of a new instrument.

		• Provide summary of results, including evidence of saturation • Provide transcripts of interviews • Track origin and derivation of concepts captured in the instrument • Summarize qualitative data • Provide key references	
Phase II	Step 6	Item generation: a. Systematic identification of existing related instruments meeting explicit eligibility criteria. b. Selection of additional instruments (e.g. generic instruments) to be administered alongside the new instrument. c. All items from the identified instruments form the initial 'item pool' (to which Steps 2-5 are applied).	Steps 6 to 8 involve the synthesis of the products of research (i.e. validated instruments). The items that result from the systematic application of these steps form the basis of a new SCD pain-specific instrument.
Phase II	Step 7	Item de-duplication. Items are discarded if: a. They are literal duplications (identically worded items, or duplication of item content) b. Their content differs only by timeframe or attribution to a condition of interest (e.g. do you have difficulty... because of your condition) c. Their content overlaps with generic measures to be administered alongside new instrument (e.g. adherence self report measure)	Identify redundant or poor questions and provide an early indication of the reproducibility of the responses.
Phase II	Step 8	Item reduction: d. Macro level: items discarded if associated with content themes (dimensions of health) that are not appropriate for inclusion in the new instrument (e.g. treatment satisfaction) e. Micro level: application of explicit, study-relevant criteria to select items for inclusion in draft instrument (actual content area)	Further refinement to Identify redundant or poor questions and provide an early indication of the reproducibility of the responses.
Phase II	Step 9	Assessment of content coverage against a relevant pre-existing theoretical framework	To provides clarity on the dimensions of health covered in the new instrument (i.e. how well the construct under measurement is represented by an instrument).
Phase III	Step 10	Exploratory pilot work with target population to assess comprehensibility, acceptability, relevance and answerability in order to inform instrument refinement (item removal &/or re-wording)	To explore of the target populations' views of the new instrument and the items it contains.
Phase III	Steps 11-20	Other validation steps: construct validity, criterion validity (predictive and concurrent validity), convergent validity, discriminant validity reliability.	To ensure having valid and reliable instrument for the intended goal in the target population.

III. Design Rationale

A. **Why Mixed Method**

Because I was also interested in developing a tool that gauge and quantify the prevalence of various kinds of opioid adherence behaviors and their contextual factors in SCD, and to begin testing this instrument for future use in my and other patients, it was necessary to choose a mixed-method (qualitative and quantitative) design.

A mixed methods research design defined as "a procedure for collecting, analyzing, and mixing quantitative and qualitative data in a single study to understand a research problem". [(140)]There are six major types of mixed methods designs, which are the triangulation design, the embedded design, the explanatory design, the exploratory design, the transformative design and the multiphase design. [(140)]

The descriptions of six designs are as the following: 1) the convergent parallel design, which seeks to obtain corresponding yet different data on the same subject matter; 2) the explanatory sequential design, a two-phase design that often begins with the collection and analysis of quantitative data and follows up with a qualitative design; 3) the exploratory sequential design, a two-phase design that often begins by using qualitative data to explore an event and then moves to a quantitative stage; 4) the embedded design, which mixes quantitative and qualitative data styles at the design level by embedding one

data style within a methodology framed by the other data style; 5) the transformative design, a design based on a transformative theoretical framework; and 6) the multiphase design, a design that combines both sequential and concurrent strands in a study.

Of the six designs, only the multiphase mixed method design allows both concurrent (simultaneous) qualitative and quantitative components of data collection in a single phase, as well as multiple, sequential phases of data collection, each step informed by the prior phase(s). Thus, I chose to have a multiphase mixed method design because my project called for multiple phases (three) each using mixed methods:

1- First Phase was an exploratory phase that began by collecting qualitative interview data along with some quantitative data from SCD patients. This phase set the foundation for the second and the third phases where the findings from Phase I were evaluated and used to generate items and form the development of the survey instrument for Phase II and III. [140-147]The role of the qualitative component of this phase was dominant.
2- Second phase was evaluating face and content validity through collecting quantitative and qualitative data from a panel of clinical and research experts, colleagues and few patients.
3- Third phase is piloting and pretest the new instrument where I will collect quantitative and qualitative about this opioid taking behaviors in SCD and preliminary data about validity and reliability of my new instrument. The role of

quantitative component of this phase is dominant. I planned to execute this phase but however, the plan was amended.

B. **Why Grounded Theory Methodology**

There are three major theoretical approaches to qualitative research: 1) phenomenology 2) ethnography 3) grounded theory. [145-147] Grounded theory approach differs from phenomenology design where with the later focuses on studying existing concepts or theories of which I am aware but do not fully understand or not validated yet. [141-144] In addition, the grounded theory approach allow for the following features: a) development of new knowledge about a phenomenon through collection and analysis of data about that phenomenon without getting biased by existing phenomena; and b) simultaneous collection and analysis of data using a process known as constant comparative analysis. [141-144] Since, my goal from the qualitative phases was to support the development of new model or theory about medication taking behavior and not validating existing theories, grounded theory methodology was particularly useful to answer my inquiries. Thus, I chose to follow grounded theory approach for my study.

C. **Why Individual Face-to-Face Interviews**

Various qualitative data collection techniques are used to develop grounded theory, particularly interviews, focus group and observation. [141-143] Observation of patients' environment (ethnographic study) or direct observing patients for medication taking behaviors is more reliable than the other two qualitative techniques. However, it was not feasible and practical with my limited resources. Focus group has the advantage of collecting information from group interaction among participants, which has the potential for developing greater insights. [143-147] However, the sensitivity of discussing the potential for addiction and diversion of opioids made us avoid using focus group and I decided to choose individual face-to-face interview.

D. **Why Semi-Structured Interviews**

I chose to do semi-structured interviews. The semi-structured interviews involved a series of open-ended questions chosen beforehand by the interviewer. They provided opportunities for both interviewer and interviewee to discuss some topics in more detail and give the interviewer the freedom to probe the interviewee in order to elaborate on the original response within a specific time and specific key issues to be covered. [141-145] In addition, semi-structured interviewing [141] describes the "emic" or the insider's view. This was considered an excellent method to examine patient perspectives of their illnesses. [148]

In contrast, I did not choose to do unstructured interviews. These interviews have very little structure. The interviewer (and probably the interviewee) must have free space and lengthy time to discuss openly every response in detail. Further, there is no "script"-- the questions asked of each interviewee will not be the same. Similarly, I chose not to use a structured interview. Structured interviews allow only close-ended questions (e.g., answers must be "yes", "no", etc.). This method was not appropriate for an exploratory inquiry.

IV. Phase I (Steps 1-5, Qualitative, Semi-Structured- Interview-Dominant)

In phase I, I collected both qualitative and quantitative data, however; the qualitative component of data collection was dominant.

A. **Setting**

This study was conducted on patients using the Ambulatory Care-Sickle Cell Anemia Clinic in Virginia Commonwealth University Health System. The Virginia Commonwealth University Health System is an urban, comprehensive academic medical center in central Virginia.

B. **Sample Size**

The sample size for phase I was 21 patients, where saturation was achieved.
As recommended for grounded theory research with a naturalist inquiry, at least 20 individuals were defined in my disseration, they were recruited and interviewed, in-depth, in Phase 1. [141-143] Individuals were interviewed until redundancy of occurring themes was achieved. As I expected before executing the project, the saturation and redundancy of recurring themes were achieved by 21 interviews. [141-143]

C. **Duration of interview**

Study participation consisted of a one-time, approximately 1.5 hour in-person interview for Phase I.

D. **Sampling**

During the study, a purposive, heterogeneous sample design was employed to recruit SCD patients in the three phases of this study.
Because the purpose of this phase in this project was to acquire new and detailed knowledge on a topic, and because random sampling does not necessarily decrease respondent bias in the interpretative paradigm of qualitative research, I decided that using

purposive methods for participant selection was the most suited sampling for the purpose of this study. [146, 147]

E. **Data Collection**

A single semi-structured qualitative interview and quantitative interview was used for the first phase of this study. Literature review and expert opinion was gathered informally to provide supportive and background information for my interview guide. Three patients were interviewed as a pilot for Phase One interviews. Interview questions and procedures were assessed and modified. Pilot participants' interview data was not used in the analysis.

This study focused on a narrow subject area (opioid medication adherence and pain). Subjects were first asked open-ended questions, which allow free response by patients (see attached Interview Guide) (See Figure 1). Interview questions were centered on pain descriptions, and on instances of use of prescribed opioids, as well as reasons, situations, or circumstances that challenged or facilitated their utilization of prescribed opioids. Interviewees were asked probing questions based on responses to the open-ended questions. I used these open-ended and close-ended questions to generate hypotheses, by seeking to elicit the interviewee's experiences and obtain related information from those experiences. Overall, the interview questions created an open-ended context for participants to talk about his/her experiences.

In addition, after the semi-structured interview that included a series of open-ended questions and probing questions (according to their responses), subjects were asked

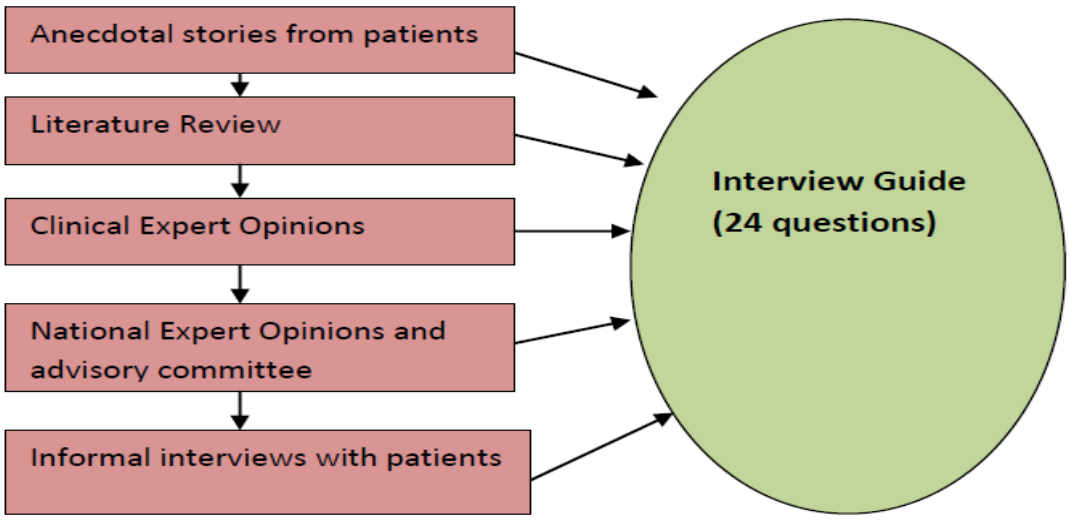
close-ended questions. I used these close-ended items adapted from the literature to identify and classify adherence behavior categories based on 6 previously described categories in the literature. [149]In addition, I used close-ended survey questions to pilot some survey questions for the subsequent quantitative survey.

The interview was audio-recorded. Throughout the interview, researchers took detailed notes on subject responses, and the audio recording as well as the detailed notes, were subsequently transcribed for further qualitative analysis.

In order to make sure that the interview fit the proposed time (90 minutes), I tested the interview guide and the preliminary survey on two co-workers for time and found it time-appropriate.

After completing approximately three of the planned interviews, I reviewed and discussed the data collected to determine whether the interview questions were sufficient and appropriate to capture the emerging themes and findings. A key question driving the reviewers was whether there were emerging patterns of adherence or non-adherence, including overuse or underuse, and emerging reasons for use, and/or whether these could better be captured by adjusting questioning.

Figure 1: Developing My Interview Guide



F. **Quantitative Component of Phase I**

The quantitative components of this phase was: 1- Brief Pain Inventory (BPI-SF); 2- Short-Form McGill Pain Questionnaire (SF-MPQ); 3- Adapted closed ended items from previous adherence; and 4- Information extracted from the electronic medical record.

I administered the short form of BPI-SF to measure pain intensity and resulting interference with life activities. BPI-SF was a brief and easy to use tool for the assessment of pain in research settings (See the attachment). The BPI-SF uses simple numeric rating scales from 0 to10 that are easy to understand. On the BPI-SF, mild pain is defined as a worst pain score of 1 - 4, moderate pain is defined as a worst pain score of 5 - 6, and severe pain is defined as a worst pain score of 7 – 10. The BPI-SF has been

used effectively to measure the severity and interference of pain in patients with sickle cell disease. The BPI-SF takes only 2-5 minutes to administer. [150] In addition, I assessed pain characteristics by using the SF-MPQ. The SF-MPQ is structured to assess qualitative and quantitative aspects of pain, including location, intensity, quality, and temporal dimensions. Subjects were asked to rate the current intensity of each pain-related adjective by circling "none, mild, moderate, or severe." Participants rated these items on a 100-mm Visual Analog Scale. The Visual Analog Scale consists of a 100-mm line with "no pain" written at one end and "worst imaginable pain" written at the opposite end, and will be used to assess spontaneous pain. The distance in millimeters from the no pain end to the location of the mark gives a measurement of pain intensity. The SF-MPQ took only 2-3 minutes to administer. [151]

In addition to the open and close-ended questions, subject descriptive information was extracted from the electronic medical record, including demographics, type and timing of prescriptions and refills, prescriber history, clinic visits, emergency department visits, hospitalization and substance use diagnoses.

G. **Interviewer**

Interviewers for the phase 1 of this study included me as a graduate student, and included a research assistant that assisted with language interpretation when require, since I uses English as a second language.

H. **Data Analysis Process for Qualitative Interviews**

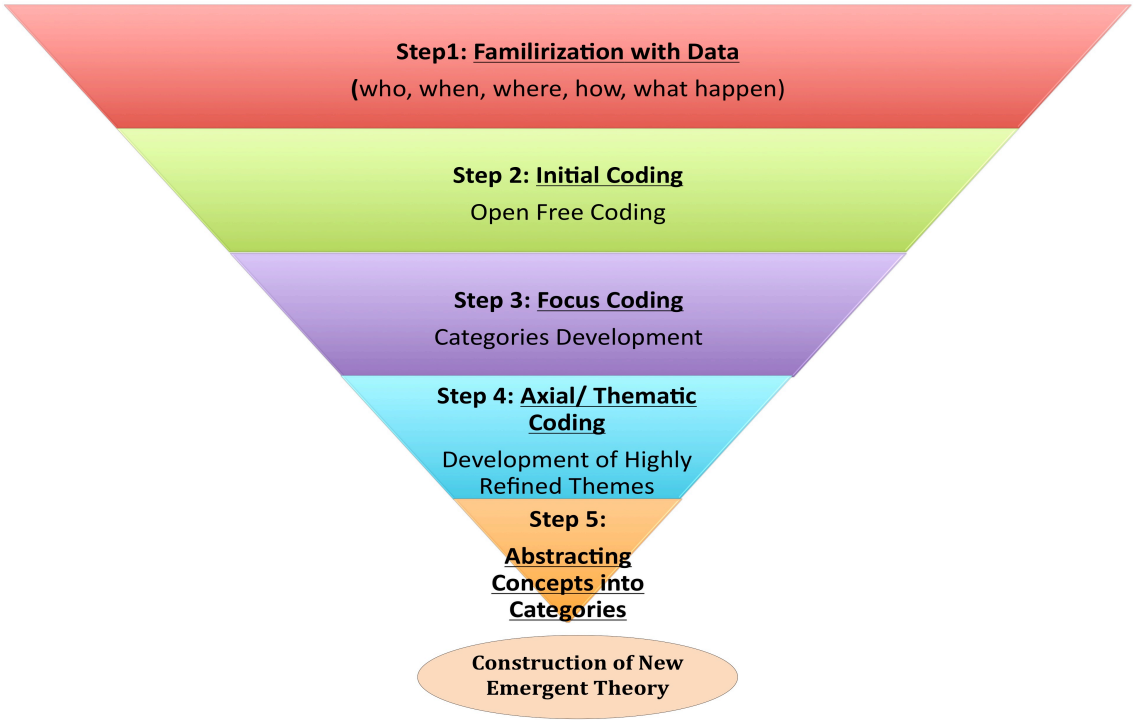
In accordance with a naturalistic approach and in light of the exploratory nature of the study, I used the grounded theory approach to guide the data analysis. I did not have any specific expectations for the data before the analysis start. Rather, I expect that concepts and themes related to opioid taking-behaviors would emerge from the texts through inductive content analysis and the constant comparative method. [144-147]

The interviews were audio recorded and transcribed. The transcriptions of the interviews were summarized and used for analysis. The qualitative interview data was not quantified but was used to explore the range and variety of perceptions and phenomena. I started the process of qualitative analysis during the early stages of data collection. This early involvement in the analysis phase helped us move back and forth between concept development and data collection, and helped change the interview guide. [144-147]

Using the approach of the grounded theory, (See Figure 2) inductive reasoning was applied to the emergent themes in the data, within the participants' voices, to help build a new theory and a new theoretical framework. [144-146]The theory development process took place throughout the research process to inform the study's data collection, coding, and analysis to build emergent themes into theory. [144-147] (See Figure 3) Again, here I was not deriving variables/categories from existing theories or previous related studies, and I had no intention of verifying existing theories; rather, I immersed myself in the interview transcripts and let the categories emerge on their own.

I defined a coding unit as "a segment of text that can give a concept and can be coded under one criterion category". [148] Responses to each interview were unitized before they are coded. Concepts were grouped and related to form abstract categories. Relationships between categories were identified to develop "formal theory". Based on data from the first few respondents, the scheme was significantly revised three times and was tested by 3 coders until inter-coder agreement reached acceptable levels". [147]

Figure 2: Analysis for Qualitative Components



To systematically build theory, I followed three phases of coding: an initial open coding phase, followed by subsequent axial and selective coding phases. [147, 148] Through each phase of the analysis, I followed a structured pattern to assist with thorough, accurate,

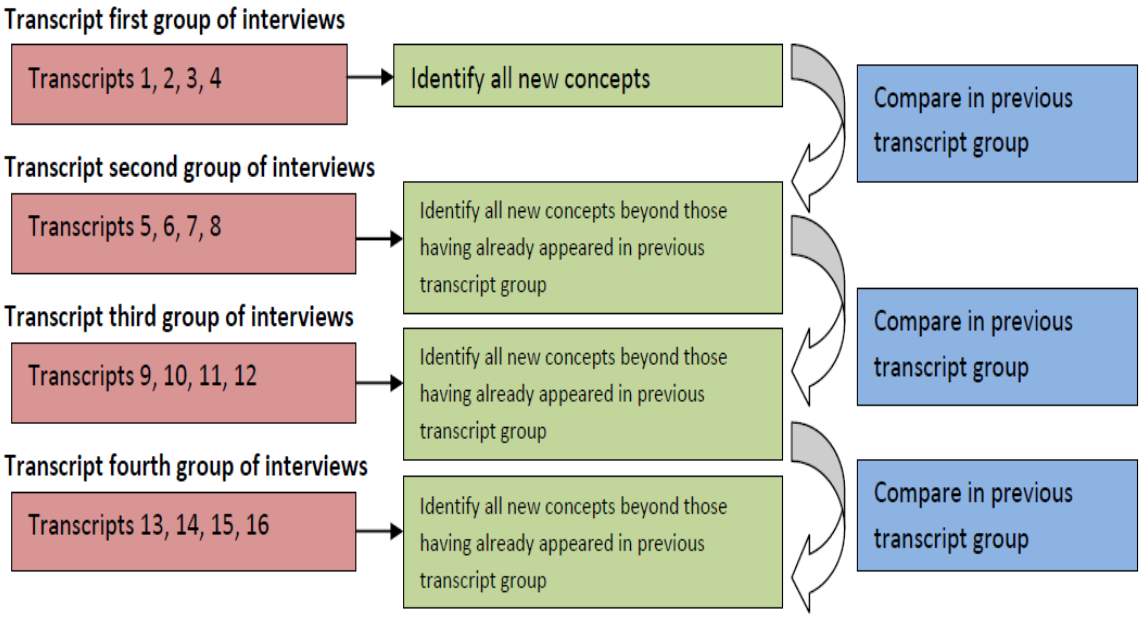
organized, and efficient coding. First, I coded the data using the margins of the interview transcripts to assign tags or labels to segments of text. After coding, I developed a codebook. The codebook was organized and contained definitions of the identified codes. Following the reviews, the research team met to discuss the findings, to analyze the data collectively, and continue the process of theory development. A conditional matrix was created connecting context, conditions, properties, dimensions and consequences of the discovered phenomena.

For the issue of trustworthiness (internal validity, external validity, reliability, and generalizability) of the qualitative results of my project, were reported and discussed in terms of the four criteria suggested by Lincoln and Guba: [144] credibility, dependability, transferability, and conformability, and were used to evaluate the trustworthiness of research work conducted within an interpretive paradigm.

During this study, I carefully designed and controlled the data collection and data analysis procedures to ensure the credibility of the research results. Furthermore, credibility was established mainly through member checking and peer debriefing. The peer debriefing process involved in the coding development steps ensured the credibility of the research by reducing the bias of a single researcher.

The transferability of the qualitative part of my project was made and ensured by "rich description and reporting of the research process" [144] and detailed documentation of the data processing in a Codebook.

Figure 3: Constant comparison technique using grounded theory



As suggested by Lincoln and Guba, [144] conformability was primarily addressed and established through a conformability audit. I gave a detailed documentation of data handling and my research notes (recording decisions, queries, working out, and the development results). By referring to these materials, I audited my own inferences and interpretations, and other interested researchers reviewed the research findings, which provided means for conformability checking.

The dependability of the research findings in this study was established by the transparent coding process and inter-coder verification. Coding consistency in this study was addressed by including three iterations of coding conducted over a period of one semester.

V. Phase II (Steps 6-9, Item Generation and Translational Validity)

Between the two phases of patient data collection, I generated a pool of items and evaluated their face and content validity. In this phase, I collected both qualitative and quantitative data from a panel of clinical and research experts, colleagues and few patients.

To complete steps 6-10 planned for the completion of this dissertation research, overall translation validity (content and face validity) for my draft instrument was measured through: a) use of panel of clinical and research expert (in the field of pain management); b) examination of the instrument by few intelligent and expert patients' and colleagues' feedback prior piloting the instrument; and c) further of evaluation of face validity and content during the pilot study phase of data collection.

A. **Transforming Qualitative Interview Results to Instrument Items**

Transforming qualitative findings to instrument items was a critical and important step therefore systemic in-depth approaches to the assessment of content validity were followed including priori and posteriori procedures. The priori approach was conducted by specifying my instruments' content domain. The posteriori procedures were conducted by having a panel of judges assess the content validity (will be discussed further below). For priori procedures for domain specification, I followed linguistic-transformation approach [152, 153] that helped in delineate the instrument content domain of items. In this

approach, a passage from written material is transformed by the use of certain rules for generating items. The content domain was specified. Certain categories within the content domain were identified and linked by my conceptual framework. Items were easily grouped by changing the items in one or more of the created categories. Items are very specific in the way in which the content domain was defined and how items are generated.

Key themes and concepts from thematic analyses of these interviews were used to guide the development (item writing) of a draft quantitative survey. I started with multiple quotes, group them into themes, and generated items for each theme. Using common recurring emergent themes yielded that I identified as important dimensions of understanding opioid-taking behavior, I based the individual item wording on actual statements made by participant during the qualitative interviews. I included any key important themes directly addressed participants' values and perceptions of prescribed opioid. Because I wanted my work to reflect accurate language of participants' worldview, I included the same words of any relevant experience the participant used to express their current understandings of the issues I addressed.

Further, to ensure that my items address patient's reported experience within the reported context, I documented the early steps of coding which allowed us to trace initial origins of items or language, as well as later iterations of emergent or evolving concepts. In addition, an inductive approach to developing concept codes (based on grounded theory)

help ensure that: a) ideas generated from patients during the interview process have appropriate influence on the variety and labeling of the codes assigned and the overall organization of the qualitative results; b) ideas generated before the patient interviews are not superimposed on or adversely bias the data. Please see Table 4 for an example of my transformation of qualitative themes to instrument items.

Table 4: Development of Selected AOTBA items from themes emerged during the qualitative interviews

Theme from qualitative interview	Domains/Dimensions	Generated Item in the draft instrument
A. Underuse of Prescribed Opioid Due to:	1. Fear of addiction	During the last week, I took LESS prescribed opioids because: 1. I thought I might become addicted or hooked on the medication 2. I wanted to avoid addiction to my medicine.
	2. Side effects	1. I know I will experience bad side effects. 2. I do not always know what side effects will happen to me. 3. I know I will experience unpleasant side effects. 4. I can't seem to bear side effects if I don't take some less of pain medicines. 5. The pain medication made me feel bad.
	3. Forgetfulness	1. I do forget to take my medicine. 2. I forgot when I last took my medication and was scared to take another.
	4. Carelessness	1. I do not worry about taking my medicine, so I just take less. 2. I am careless at times about taking my medicine
	5. Social stigma	1. I was embarrassed or ashamed of taking pain medicine in front of others. 2. I was afraid that others would judge me,

		even when having severe pain. 3. I was afraid that people would treat me differently if they knew I took pain medicine.
	6. Cost of medication	1. I couldn't afford to pay for taking pain medicine. 2. I did not have money to purchase the medication (or its refills). 3. 1. I had no insurance to pay for my medicine.
Overuse of Prescribed Opioid Due to:	1. Forgetfulness	<u>During the last week, I took LESS prescribed opioids because:</u> 1. I sometimes have trouble remembering if I already took my medication(s). 2. I forgot when I last took my medication and felt that I should take more just in case.
	2. Uncontrolled and Unbearable (excruciating) pain	1. I have a need for medication because I constantly have unbearable pain. 2. I have a need for medication because my crisis pain is very severe. 3. I have a need to take medication because I cannot handle the pain without them.
	3. Maintaining Functionality at work/ school	1. I thought I would lose my job because of my pain. 2. My prescribed dose does not help my ability to do well at school or work. 3. I was afraid I would fail doing tasks for my work. 4. My prescribed dose made my school life difficult. 5. My prescribed dose made my work life difficult. 6. I cannot function very well with my prescribed dose of pain medicine. 7. Using any less, I still could not function at work with less side effects. 8. I need to function at school.
	4. Meeting Obligation and Responsibilities	1. I had to deal with social obligations or responsibilities. 2. My pain makes it hard for me to take care of kids. 3. I find it difficult to find others who can take care of my kids. 4. I would not be able to maintain my family social life. 5. There seemed to be more good than bad about using pain medicine for me to meet my responsibilities.

B. **Content Validity**

Content validity is "the extent to which an instrument measures the important aspects of concepts that developers or users purport it to assess". [135] A preliminary appraisal of content validity was performed to assess the draft of AOTBA scale for clarity, relevancy to the domain of interest. Content validity was established by a) a priori descriptions of the psychometric development of the instruments and b) Evaluation by a panel of three researchers and by the calculation of a content validity index (CVI). [154] An expert was asked to rank the items on an index of content validity (CVI), showing the proportion of agreement by the panel, was calculated for each item and the total instrument. The scale-content validity index (S-CVI) was determined by assessing the proportion of expert reviewers who score items as a three or four on the relevancy scale, where 1 = not at all relevant and 4 = highly relevant, to the total number of items on the scale. The item-content validity index (I-CVI) is determined by assessing the proportion of relevance of each item to the number of expert reviewers. This index should be as close to 1.0 as possible to be acceptable. [154] Many agreed that for a scale to have exceptional content validity it should have an I-CVI of .78 or higher and an S-CVI of .90 or higher. [155] See Table 5 and 6 for an example of how I used CVI methods.

For the content Validity indices from expert reviewer, all reviewers rated items in term of wording clarity and relevance. For clarity, items were rated on a four-point scale: 1= item

is not clear, 2= item needs major revisions to be clear, 3= item needs minor revisions to be clear, 4= item is clear. For relevancy, items were rated on a four-point scale 1= item is not clear/representative of content domain. 2= item needs major revisions to be relevant, 3= moderately relevant or 4= highly relevant

C. **Face Validity**

Face validity defined as an instrument having the appearance of measuring the content of interest. [135] In my project, face validity was determined by:

A) Having three colleagues review the instrument. [135,136] They were asked to read the instrument and evaluate the content and look at the measure and decide whether or not it appears to reflect the concept the researcher intends to measure‖ to look at the measure and decide whether or not the test measures the desired domain of interest. See Table 5.

B) Interviewing few expert intelligent patients (before piloting the instrument) about their perceptions of the instruments. [135, 136] Participant feedback served as a measure of face and content validity too. See Table 7 for an example of questions that were asked to get patient feedback.

In addition, participant feedback during field-testing provided additional data to increase instrument face and content validity.

After receiving comments from colleagues, expert faculty and expert patients, I considered and addressed appropriate comments received and presented the revised final draft instrument for final review to the advisory committee. Once all authors reached consensus, the final instrument was submitted to IRB.

Table 5: Drafts of the CVI for expert reviewer ratings of the wording clarity and relevancy

	Wording Clarity Rated items on a four-point scale: 1= item is not clear, 2= item needs major revisions to be clear, 3= item needs minor revisions to be clear, 4= item is clear Yes=Items will be rated as 3= moderately clear or 4= highly clear					Relevancy 1= item is not clear/representative of content domain. 2= item needs major revisions to be relevant, 3= moderately relevant or 4= highly relevant Yes=Items will be rated as 3= moderately relevant or 4= highly relevant					Comment
Item	Expert #1	Expert #2	Expert #3	Expert in Agreement	I-CVA	Expert #1	Expert #2	Expert #3	Expert in Agreement	I-CVA	
1	No	Yes	Yes	2	0.67						
2	Yes	Yes	Yes	3	1						
3	No	No	No	0	0						
4	No	No	Yes	1	0.33						
5											
6											
7											
8											
9											
10											

Note: Yes=Items will be rated as 3= moderately relevant/clear or 4= highly relevant/clear are considered in the table No= item rated as 2 and lower will not be considered in the table.

Table 6: Drafts checklist for expert opinion overall feedback on AOTBA instrument

	1=Not Appropriate	2= Slightly Appropriate	Moderately (Quite) Appropriate	Highly Appropriate	Comment
Appropriate ness of instrument Format					
Appropriate ness of instrument Order					
Appropriate ness of instrument Length					
Appropriate ness of instrument Complexity level					
Appropriate ness of instrument Readability					

Table 7: Drafts checklist for participants' feedback

	Yes	No	Suggestions/comments?
Did you feel that all the questions on this page were readable? By readable, I mean could you understand all of the terms or words in the question. If no, which items did you feel were not readable?			
Did you feel that all the items on this page were clear? By clear, I mean could you understand what all of the questions were asking? That is, did they make sense to you? If no, which items did you feel were not clear?			
Did you feel that any of the items on this page were ambiguous or double-barreled? By ambiguous or double-barreled, I mean were any of the questions confusing or seemed to be asking more than one thing? If so, which items did you feel were ambiguous or double-barreled?			
Did you feel that any of the items on this page were sensitive either for you or you would think for participants taking this survey? By sensitive, I mean were any of the questions likely to make either you or a participant feel uncomfortable to answer? If so, which			

items did you feel were sensitive?			
Did you feel that all of the items on this page had complete choice categories? By complete choice categories, I mean that each question had all the choices that should be available for that question. If not, which items did you feel were incomplete in their choice categories?			
Did you feel that any of the items on this page were not with the correct scale? By not with the correct scale, I mean were any of the questions with a group of questions that asked something different? Did any questions seem out of place? If so, which items did you feel were not with the correct scale?			
Now, thinking about the survey as a whole ...			
Did the format seem appropriate? If not, what should be different?			
Did the order of the scales (categories), questions, and choices for each question all make sense? If not, what seemed out of order?			
Did the length of the survey seem appropriate? If not, why not?			
Did the survey seem too complex?			
Did the survey seem to be too repetitive throughout?			
How easy was this for you to complete? How likely do you think it would be for others to complete?			
Do you think that there should be any additional questions added or taken out of the survey?			
Did the survey seem to have merit? That is, did it seem to go along with my overall purpose (The purpose of this study is to assess opioid taking behaviors and their reasons)?			
Additional comments……..			

D. **Instrument Items and Content**

The exact content of the draft items that comprised my survey of opioid adherence and reasons for adherence was finalized, I used analogous patterns, themes, and templates used by McCracken, et al, [156] who studied how patients view their pain medications. McCracken conducted qualitative research to construct a set of 78 items regarding beliefs and concerns about pain medication. Item and scale analyses resulted in a 47-item measure, the Pain Medication Attitude Questionnaire (PMAQ) [156] that assesses 7 areas of patient concern: addiction, perceived need, unfavorable scrutiny by others, adverse side effects, tolerance, mistrust in the prescribing doctor, and withdrawal. As discussed below, the survey aimed to assess adherence for a particular time as well as over a period of time, and worded items and responses differently to reflect these two types of assessments.

My draft instrument was designed based on preliminary qualitative research, designed to produce three categories of measurement: two of the "what" of opioid taking behavior, and one of the "why" of opioid taking behavior.

The two "what" measures, one of behavior over a prolonged time, and one of momentary behavior, each seek to classify opioid taking behavior into mutually exclusive categories based on (temporal and momentary) patterns of use. This categorical approach used a battery of questions to first characterize all opioid taking behavior, and then other

questions to richly quantify the frequency of behaviors. The goal was a set of adherence scores that represent the type, level, and direction of (non) adherence.

Further, the "why" measure, again conceived based on qualitative research, uses the draft survey instrument to capture concepts related to or predictive of opioid taking behavior in the target population (SCD) —to capture the other health behaviors/attitudes of SCD individuals, comprehensive with respect to patient concerns. Concepts include how patients behave in relationship to their prescribed opioid medication and their disease. The goal was to measure the concepts most significant and relevant to SCD and prescribed opioid medications in SCD. The survey then included items to quantify the frequency of occurrence of each of these behaviors/attitudes. The goal was to create quantitative scores in each of these behavioral/attitudinal items/domains.

VI. Structure of AOTBA Instrument and Format of Responses

My instrument was divided into three brief sets of survey questions, each with a different purpose and response format. Formats included dichotomous questions (two possible answers yes/no), multiple-choice closed ended questions, partially closed multiple-choice questions and scaled questions.

A. **Part 1**

The first part of the questionnaire included some questions that have a dichotomous

response format, which means only two mutually exclusive responses are provided. Others are multiple-choice closed ended questions. The purpose of the questions was to obtain classification and demographic information and respondent characteristics.

Example:

1. *Are you:*
   - ○ *Female*
   - ○ *Male*
2. *Do you smoke cigarettes? ___Yes ___No*
3. *What is the highest level of education that you have completed?*

   - ○ *Grade school*
   - ○ *Some high school*
   - ○ *High School Graduate*
   - ○ *Some College*
   - ○ *College Graduate (Bachelor's degree)*
   - ○ *Professional degree*

B. **Part 2**

The second part of the questionnaire included some partially close-ended questions. I asked the respondent to choose, among several possible categories, the response that most closely represents their behaviors and the frequency of repeating that behavior. Although the survey items were comprehensive and highlights of the themes emerge from the interviews, other themes or data potentially emerge from piloting the survey and since the purpose here was to pilot test the first version of the instrument (with the aim of later formulating a multiple choice or closed version of questions. Accordingly, I left a space for other reasons and behaviors.

Example:

1. *Which of the following statements best describes the way that you take your as-needed (short-acting) pain medicine over the last week month?*
    a. *I usually took my medication as prescribed*
    b. *I usually took LESS medicine than prescribed*
    c. *Over the last month, I usually took MORE medicine than prescribed*
    d. *Over the last month, I sometimes took MORE medicine than prescribed and sometimes LESS medicine than prescribed.*
    e. *Over the last month, I usually took my medicine more than prescribed when I had little pain and less than prescribed when I had (great) pain.*
    f. *Over the last month, I stopped taking my medicine.*
    g. *Other….*

C. **Part 3**

The purpose of the third part of the questionnaire was to quantify behaviors and reasons for these behaviors. Thus, several scales, which are presented (worded) as a set of statements, not questions. The wording of items in the instrument reflected the exact themes or wording in the qualitative thematic analysis. This part of instrument was divided into several brief sets of subscales. Each subscale had different dimensions and each dimension had different items. These series of items were developed to express a wide range of behaviors and their reasons. All the statements were phrased in terms of how often particular events occurred. The nature of response options ran between "never" and "always" on a 5-point scale as descriptors of amount or frequency. Each of these response categories have a score ranging from 1 to 5 (1=Never, 2= Rarely 3= Sometimes 4= Often 5=Always) along an underlying frequency continuum (See Table 8). In this part of the scale, I will ask the respondent to select (locate) one answer to rank their (level) amount of frequency. The advantage of having more than two choices in the scale was to

allow for more choices that would permit a finer distinction in the intensity of the frequency. Some statements going from negative to positive, then a number of items in the questionnaire were designed to have 1 as the most positive alternative and 5 as the most negative.

Example:

Which of the following statements best describes the way that you took your pain medicine during the past week? Please mark the one statement below that best describes how you took your pain medicine in the last seven days. Please mark tables, one for short-acting (as needed) and one for long-acting (scheduled) pain medication. Please note that "as prescribed" means according to the directions on the bottle

Table 8: Example of drafted items in AOTBA

	Short-Acting Opioid					**Long-Acting Opioid**				
	Never ▼	**Rarely ▼**	**Sometimes ▼**	**Often ▼**	**Always ▼**	**Never ▼**	**Rarely ▼**	**Sometimes ▼**	**Often ▼**	**Always ▼**
1. I consult my health care providers before making some changes	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
2. I may change the way I take my pain medication when I am dealing with difficult situations	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
3. I may take less pain medicine than usual to finish	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

school/work assignment.										
4. I may take more pain medicine than usual to finish Household chores /duties.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
5. I take more pain medicine than usual because my crisis pain is very severe.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

D. **Mode of Instrument Administration**

The instrument is planned to be a self-administered survey, with guidance by writing specific instructions on how to answer the question.

VII. Definitions: General Definitions of Patterns of Adherence

Definitions of problematic use of prescribed opioids are not standardized across studies, [66, 67] but problematic use is typically defined as overuse. Problematic use seems to encompass both criminal use of opioids and non-criminal, but still "problematic" use. Criminal use may occur in patients prescribed opioids, but is not my interest in this study. Rather, I was interested in opioid *nonadherence,* i.e., non-criminal opioid overuse *and* non-criminal opioid underuse. Overuse was defined as taking more opioid than prescribed. Underuse is qualitatively different from overuse, and may have different causes and associated behaviors. Many opioids are prescribed to be taken PRN (as needed) up to a maximum dose. Patients may choose, for many reasons, not to take their opioid medication, or to take as little as possible of it, even though they report that their level of pain negatively impacts their life. I was therefore define underuse of opioids as taking less than the dosage allowed by prescription and still reporting either inadequate pain relief, or reporting (in the interview) that pain impairs ability to engage in normal

daily activities. [68] The definition of underuse or over-use is not based on how frequently a patient fills a prescription. [68]

A. **Patterns of Overall Adherence for Long-Acting Opioids**

Long-acting opioids are generally prescribed to be taken regularly, not as needed. For the purpose of this study I have defined the following terms:

Adherence to long-acting opioids: use as prescribed [prescribed dose, frequency and duration] for 80%-100% of doses.

Underuse non-adherence: taking less long-acting opioid than prescribed [in terms of dose, frequency, or duration] and still reporting inadequate pain relief or that pain impaired their ability to engage in normal daily activity.

Overuse non-adherence: taking more long-acting opioid than prescribed over a given time interval.

Erratic adherence: mixture of underuse and overuse over a given time interval.

Dropout adherence: discontinuation of use after beginning.

B. **Patterns of Overall Adherence for Short-Acting Opioids**

Use of short-acting opioids is usually as needed, not prescribed as timed doses.

Adherence to short-acting opioids: is defined as use as prescribed [prescribed dose, frequency] when needed. "Needed" may be defined as pain of a given intensity or duration, or pain that impairs ability to engage in normal daily activity, but must be self-defined by patients.

Overuse non-adherence: taking more [dose, frequency] short-acting opioid than prescribed.

Arbitrary adherence: mixture of underuse and overuse over a given time interval.

Dropout adherence: discontinuation of use after beginning.

C. **Patterns of Time-Specific Adherence for All Opioids**

Time-specific adherence: is related to ways of opioid use [in term of prescribed dose, frequency and duration] at a specific time of the day; it is not related to situation or location, however, it is related to time unit, specific hour, specific part of the day along the 24-hour day, for example: [night/day time], [breakfast, lunch time or dinner time] or [sunrise, sunset, dusk, twilight, or dawn times]. Patterns include:

Time-specific Adherent: opioid use as prescribed [prescribed dose, frequency and duration] for 80%-100% of prescribed/expected doses at a specific time of the day.

Time-specific Underuse: opioid use [dose, frequency, or duration] at 0-79% of allowable/prescribed at a specific time of day and still reporting inadequate pain relief or that pain impaired their ability to engage in normal daily activity.

Time-specific Overuse: opioid use [dose, frequency, or duration] at >100% of allowable/prescribed at a specific time of day.

Time-specific Erratic adherence: mixture of underuse and overuse at a specific time of day.

Time-specific Dropout adherence: discontinuation of use after beginning using at a specific time of day.

D. **Patterns of Context-Specific Adherence for All Opioids**

Context-Specific Adherence: is related to ways of opioid use [in terms of prescribed dose], in specific locations, conditions, and/or situations [that are not related to unit of time or part of the day]; it is related to what happened before or during the process [steps] of deciding to take one specific dose of opioid. This type of adherence could be related to emotional conditions, sudden circumstances, anticipated conditions, unexpected incidents, social events, public or community occasions, or responsibilities (such as work, finishing assignments, or sitting for an exam). Patterns include:

Context-specific Adherent: at a specific instance, specific location and specific situation, use of the appropriate prescribed dose for long-acting or allowable dose for short-acting opioid when needed.

Context-specific Overuse: at a specific point of time, specific location and specific situation, temporal (episodic) use of more than the appropriate prescribed dose for long-acting, or more than the allowable dose for short-acting opioid when needed.

Context-specific Underuse: at a specific point of time, specific location and specific situation, temporal (episodic) use of less than the appropriate prescribed dose for long-acting, or less than the allowable dose for short-acting opioid when needed.

XIII. Subject Selection

In the proposed study, a successive and purposive, heterogeneous sample design was employed to recruit SCD patients for the phase 1 and is planned to be used in phase 3 of this study.

A. **Inclusion Criteria**

The inclusion criteria for phase I of this study were:

1- SCD diagnosis (four Hgb types: SS, SBothal, SC or SB+thal)

2- African-American patients (self-identified)

3- Pain for > 30% of days in the last month

4- Received three outpatient prescriptions for at least one Schedule II or Schedule III opioid medications from Virginia Commonwealth University Health Care System (VCUHS) within the previous 12 months (by chart review and medical record [EMR] system).

5- Between the ages 18 and 65 years.

6- No known hearing or visual impairment (by chart review).

7- Fluent in English.

8- No serious psychiatric diagnosis (by chart review and electronic medical record [EMR] system).

9- No history or current drug use problem (by chart review and electronic medical record [EMR] system).

B. **Exclusion Criteria**

Patients were excluded when they are not capable of being interviewed for the semi-structure interview or for taking the survey (e.g., dementia, mental retardation, illiteracy). Subjects were excluded if the chart shows evidence of dependence on any psychoactive substance or of Emergency Department (ED) or hospital use on the day of the interview. Subjects were excluded also if they contact the investigators or study personnel after enrolment is complete. Pediatric patients were excluded, because they are suspected to differ substantially from adults in both their clinical course and healthcare utilization patterns. Patients on chronic exchange transfusion were excluded because of effects on hematologic factors and pain. Patients who are not oriented to person, place and time (Mini-Mental Status Exam <24), [165] and unable to answer questions were excluded, because of inability to comply with interview completion. At any time, included subjects were able to withdraw.

XIV. Ethical Considerations

The VCU IRB reviewed the study. The usual ethical standards were followed including written informed consent. An incentive of $45 was provided to clients in appreciation or

their time for phase 1 and a $25 patient incentive is planned to be used phase 3 of this study. A light snack was offered to clients before, during, or after interviews. Travel vouchers were offered to patients needing transportation. Prior to being screened and interviewed, patients were asked to sign a formal written informed consent form, which describes the nature and purpose of the study, and indicated that participation in the study was voluntary. Patients were told that if they are interested, they could sign a written informed consent before screening. All of the participants volunteered to answer all of the questions that were posed. As a condition of treatment at VCU, patients sign authorization forms allowing pre-screening of their medical records for research purposes.

A. **Subject Recruitment Plans and Consent Process**

1. Recruitment Plan

The same recruitment plan was used for phase 1 and 2 in this study. The source of recruitment was direct recruiting via Adult Sickle Cell Clinic Sickle of Virginia Commonwealth University (VCU) Medical Center in Richmond, Virginia. The sample was recruited using a method that was designed to reduce the likelihood of systematic selection bias. All patients that came to the outpatient clinics during selected time periods were given written information about the study. A sample of patients was selected for screening.

Recruitment times were coordinated with clinic schedules to obtain a representative sample of outpatients with regard to sickle cell Hgb phenotype, age, gender, and treatment/follow-up regimens. One day before the outpatient clinic day (Thursday or Friday), the provider reviewed the list of patients who are scheduled to have medical appointment with Dr. Smith to determine who is qualified as a potential subject for this study. I was trained to pre-screen all available charts for eligible patients and placed study information on their chart. The next day (in the outpatient clinic day), when patients come to the clinic, those who meet the initial screening criteria were invited to participate in this study. Patients were approached and invited by the principal investigator or the recruiter in a private setting, during their routine scheduled visit to the clinic, and were asked verbally if they are interested in hearing about a new study called the "Understanding Adherence to Prescribed Opioids in Sickle Cell Disease." Patients were given a study information sheet. After reading the information sheet, full details about the study was presented and all questions answered. Participants signed the informed consent form before starting the screening and the interview. Patients completed the study interview in private room at VCU health system. Contact information was obtained from patients who were willing to hear about the study or wanted to participate but did not have time on that clinic day. These patients were then contacted at a more convenient time.

Following signing formal written informed consent form, patients were screened for eligibility using a short structured questionnaire (screening interview). The information

for those that were not recruited or not eligible was destroyed immediately. The enrollment visit was conducted in a private room at VCU Health System. Eligible participants were given more details about the project and then formal written informed consent was obtained (see attached consent form). Participants were recruited from November 2011-May 2013.

2. Participants

The majority of study patients were from the Richmond, Virginia and areas around it, as these areas have high population of African Americans who are visiting the Adult Sickle Cell Clinic Sickle from Virginia Commonwealth University (VCU) for treatment. The only source of recruitment was direct recruiting via Adult Sickle Cell Clinic Sickle from Virginia Commonwealth University (VCU) Medical Center in Richmond, Virginia.

3. Sample Enrichment Features:

As much as possible, patients were chosen to represent a wide range of the SCD population in terms of gender and frequency of pain. Patients were identified using data extracted from the VCUHS electronic medical record (EMR) system. Data from the EMR revealed more than 350 SCD patients. Painful conditions for which opioids were prescribed were ≥ 30% of the days (identified by self report). I attempted to enrich the invited sample for patients who are more likely to be at risk for problematic use of

prescription opioid medications by sampling those with specific characteristics as in table 9 and 10.

Table 9: Sample enrichment features for Phase 1

Gender / Pain frequency	Female	Male
> 50% of the days	N=10	N=10
> 30-50% of the days	N=10	N=10

4. Risks and Benefits

The risks to subjects involved in this study were minimal. Subjects participated in semi-structured interview about a sensitive topic, use of potentially addictive and abusable substances, although the intent was to ask about non-criminal use. No subjects experienced discomfort when sharing personal information. All patient data was de-identified. No subject interview reported confidential information, identified by the subject including demographic data. Subject identifying information was stored separately from their results information once transcribed and analyzed. There was no way to match subjects with their identifier characteristics. Only the interview analytic team had access to the identity of individuals, and identifiers were kept separate from the remainder of the data. This data was filed separately and remains under lock and key in offices where only the team works. These procedures were required by VCU IRB.

I worked to ensure that interviews are conducted in a fashion that minimized the stress or discomfort a subject may experience while reporting information. The subject was able to withdraw from the interview at any time and could refuse to answer any particular question asked in the interview. No names were used during interview as they were being recorded (subjects were given a study number instead). I was experienced with handling interview data.

B. **Baseline Data Collection**

I collected baseline information as part of the interview. Baseline information included past medical history and demographic characteristics, pain-related variables, treatment-related variables.

C. **Resources**

I spent a large proportion of my time collecting information. I was responsible for coordinating the advisory committee meetings, developing dataset to collect data, and collecting the data by reviewing medical files and by conducting semi-structure interview. In addition, I was responsible for conducting data analysis, interpreting the results, and writing the first draft of the manuscript. The investigator was responsible for protecting the privacy of the subjects by de-identifying all data collected, so that no investigator or outside party could match data with a particular research subject. Occasionally, research assistants helped in interviewing subjects or collecting information.

XV. Study Procedures

A. **Screening for Eligibility (for Phase I and planned for Phase III)**

The only source of recruitment was direct recruiting via Adult Sickle Cell Clinic Sickle of Virginia Commonwealth University (VCU) Medical Center in Richmond, Virginia. A random sample of patients was selected for screening. Patients were approached and I invited them into a private setting, during their routine scheduled visit to the clinic, and asked verbally if they were interested in hearing about a new study called the "Understanding Adherence to Prescribed Opioids in Sickle Cell Disease." If they agree, a

brief description of the study was read to them. Subjects received a letter signed by the principal investigator inviting them to this study and describing study details. Patients were told that if they are interested, they should speak to me following their visit. I introduced the study using the following script. "This study was designed to find out about patterns of prescribed opioid use at home in patients with sickle cell disease and to find out about the reasons of using prescribed opioid in different pattern. You are being asked to participate in this study because you have been diagnosed with sickle cell disease, and may meet the study entry requirements. If you are interested and eligible to participate you will be interviewed today, or at any another convenient date/time. If you are interested, I will need to ask you some questions to determine your eligibility." Following oral and informed written consent, patients were screened for eligibility using a short structured questionnaire (screening interview). The enrollment visit was conducted at the Adult Sickle Cell Clinic at VCU Medical Center. Eligible participants were given more details about the project and then a formal written informed consent was obtained (see attached consent form). Participants were recruited over nine months' period from November 2011to May 2013.

B. **Research Material**

Medical Records: For Phase 1 and 3, data were extracted from VCUHS electronic medical records (EMR) system. A minimal amount of data was obtained from the medical records to limit attempts to enroll non-eligible patients. After consent, medical records data regarding medications, health status, ER visit, and concurrent illness was obtained.

Digital audio recorder was used for recording the interview for Phase 1.
Interview guide: semi-structure interview guide and preliminary survey. Please see the attached interview guide. Transcripts: include transcription of audio file into written form documents. I conducted the Semi-structure Interview and coordinated for Phase 2 and plan to coordinate Phase 3. Pre-screen form, recruitment form, screening form and data collection form was used for screening purposes and for collecting the other related research data in the Phase 1 and is planned to be used for Phase 3. (Please see the attachment):
Subjects received a recruitment letter signed by principal investigator inviting them officially to the study and describing briefly about study details during their routine scheduled visit to the clinic for both phases.

C. **Privacy of Participants**

After getting permission from patients' health providers, I approached individuals during their clinic visit and provided them with study details. I moved to a private area to discuss sensitive information. The interview was held in private rooms. Subjects enrolled in the study received a study identification number. No attempt was made to match subjects by name with any data collection material after data collection. Recruitment materials include a letter signed by principal investigator inviting them to this study and describing briefly about study details. Only de-identified data was used. All de-identified information was maintained in a HIPAA-compliant manner. Patient data was entered into a computer database (including audio digital electronic files); these data files are password-protected.

D. **Compensation Plan**

One hour and a half minimally was allotted for a given interview visit. Subjects received financial compensation of $45.00 for Phase 1 and $25 for Phase 3 and cab/bus vouchers (for those in need).

E. **Consent Process**

The study required that subjects complete an interview and an informed consent was collected using the attached consent form.

F. **Safety and Adverse Events**

There was no risk to subjects involved in this study. Subjects participated in semi-structured interview about a sensitive topic, use of potentially addictive and abusable substances, although the intent was to ask about non-criminal use. Subjects did not experience discomfort when sharing personal information. All patient data was de-identified. Subject interview was necessity report confidential information, identified by the subject an including demographic data. Subject identifying information was stored separately from their results information, once transcripts have been made and themes coded of the transcripts and matched with identifier characteristics. Only the interview analytic team had access to the identity of individuals, and identifiers were kept separate from the remainder of the data (this data was filed separately and remains under lock and key in offices where only the team works).

G. **Safety and Compliance Monitoring**

1. Data and Safety Monitoring

Phase 1 of this study was a qualitative and quantitative interview study. Phase 3 will be a quantitative survey interview. The research involved no more than minimal risk to the subjects. All patient data was de-identified in Phase I and will continue to be de-identified in Phase 3.

This study included subject participation in interviews and surveys. Patient medical records were used partly to pre-screen patients for eligibility. As part of conditions for treatment, patients signed a medical authorization for this reason. Retrospective medical history, interview and survey de-identified data were used. All de-identified information was maintained in a HIPAA-compliant manner. All patient data was entered into a computer database (including audio digital electronic files); these data files are password-protected. The same data and safety monitoring procedures were used for the second phase (quantitative) of the study.

2. Medical Monitoring

I worked to ensure that interviews were conducted in a fashion that minimized the stress or discomfort a subject could have experience while reporting information. The subject was able to withdraw from the interview at any time and could refuse to answer any particular question asked in the interview. No names were used during interview as they

are being recorded (subjects was given a study number instead). I was experienced with handling interview data. All patient data was de-identified.

3. Definitions of Adverse Events

Subjects participated in semi-structured interview about a sensitive topic, use of potentially addictive and abusable substances, although the intent was to ask about non-criminal use. Subjects experienced no discomfort or emotional disturbance when sharing personal information.

XVI. Statistical Analysis

A. Sample Size Determination and Power

Phase 1: The planned sample size was 20-30 patients, or until saturation is achieved. However themes saturation was achieved after conducting 21 interviews.

B. Interim Monitoring and Early Stopping

See above. Early stopping in Phase 1 of this study was related to early achievement of saturation with 21 patients. I did not expect to have to stop the study on the basis of unanticipated harm to subjects.

XVII. Data Analysis

A. **Analysis for Phase I and Phase II**

Qualitative data analysis was done by coding and categorizing for common themes in interview transcripts using organizing features in Microsoft Office (Word and Excel). I identified all of the statements the subjects offered about how they used their opioid medication and their reasons for using prescribed opioid. Statements and words within each explanation were grouped into sub-themes, and statements that did not fit into one of these explanations were grouped and given an appropriate label. Then I sorted the statements into types of explanations. For example, statements about opioid use may be coded as overuse, underuse, appropriate use, arbitrary use, or dropout use. Similarly, statements about reasons for certain types of use were sorted as biological, psychological, environmental, or social factors. Statements were coded as "psychosocial" when they combine the two categories social and psychological factors. Theme names were assigned by mutual consent of at least two analysts. Categorization and coding of statements was confirmed/validated by a third analyst who was blind to the first two analysts' assigned themes, codes, and sub-themes.

In addition to empiric thematic analysis, analysis were made to classify adherence behavior over time based on previously described 5 overall adherence categories:

adherent, underuse, overuse, arbitrary adherence (mixture of underuse and overuse), and dropout adherence (discontinuation of use after beginning). Although no prior idea about medication taking behavior, I classified adherence behavior that were time-specific or context-specific, into several categories in order to categorize behavior at specific times or in specific contexts as a) inappropriately under-using b) inappropriately over-using, or c) using appropriately. These theoretical classifications have not been previously used. I determined that adherence behaviors can be classified this way based on the context of the answers given, leading to quantification via a survey.

B. **Statistical Methods**

Descriptive statistics (frequencies and proportions; means ± standard deviation) were used in Phase 1 and Phase 2 as appropriate to describe characteristics of the sample.

XVIII. Data Handling and Record Keeping

A. **Confidentiality and Security**

This research was conducted with the participants' Protected Health Information (PHI). The retrospective collection of baseline data for this study involved no more than minimal risk to the subjects. All patient data was de-identified immediately after linking charts data with interview data. The PHI was not disclosed for purposes other than approved. The PHI was not reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

Information obtained was recorded in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects; and no disclosure of the human subjects' responses occurred outside the research study. The information for those that were not recruited was destroyed immediately. Subjects enrolled in the study received a study identification number. There was an adequate plan to protect identifiers. Identifiers were destroyed (immediately after linking charts data with interview data for each patient). Subject identifying information was stored separately from their results information. Once transcripts were made and themes coded of the transcripts responses were matched with identifier characteristics only when necessary. No attempt was made

to match subjects by name with any data collection material after data collection. Only the interview analytic team has access to the identity of individuals, and identifiers were kept separate from the remainder of the data (this data was filed separately and remained under lock and key in offices where only the team works). No names were used during interview as they are being recorded. All information were maintained in a HIPAA-compliant manner. All patient data was entered into a computer database (including the audio digital electronic files); these data files are password-protected. Some patient data was obtained from existing medical records. The data collection sheet (see attached appendix for collection form) for each patient was assigned a study number and no identifying information (such as medical record number, name, initials, or exact date of birth) was recorded on the data collection sheet. All data was stored in a locked and secure cabinet. Also, no identifiers were collected, published or presented. The interviews were held in a private room.

B. **Training**

I am a PhD student at the VCU School of Pharmacy; I have completed my B.S. and M.S. in pharmaceutical sciences. I have participated (as a trainee researcher and trainee data analyst) on several research projects located within the American medical system. I have finished all the required and research-related courses, IRB training, HIPPA training, interviewing training which prepare me to carry out this research. I am experienced with handling interview and survey data.

C. **Subject Stipends or Payments**

Subject incentives include refreshments, transportation expense coverage (if needed), and stipends of $45 for Phase1.

XIX. Attachments (Appendices)

A. Pre-Screening Form

B. Recruitment Form

C. Screening Form (MMSE)

D. Copy of the VCU- IRB Approval, Recruitment Invitation Letter/brochures consent, and HIPPA Authorization and Informed consent Form

E. Special procedures protocols

F. BPI Form

G. McGill Pain

H. Interview Guide

I. The preliminary Surveys

J. First Draft of AOTAB Scale

K. Revised Draft of AOTBA scale

L. Summary of Themes Related to Domain 3

CHAPTER 4 RESULTS

I. Phase I Findings

A. **Demographics and Clinical Characteristics**

The total number of patients recruited into the study was 22. One patients experienced excruciating pain just before starting the interview and withdrew from the study. The total number of patients analyzed was 21.

In addition to the interview, key clinical and demographic information on each patient was gathered at the time of the visit. A summary of demographics and participants' characteristics is Table 11. All descriptive statistics were used to summarize and describe the data. All analyses were done using JMP 10.

As shown in Table 11, approximately 57% (n=12) of the participants were women. Patients ranged in age from 18 to 58 years. Of the 21 patients, 5 (24%) participants were married. More than half (57%) of my participants have the SS genotype of SCD. While approximately one-third (33%) of my participants have the SC genotype of SCD. When asked about rating their pain intensity on the average in last 30 days, the

mean reported pain intensity was 5.5 (SD=1.7). A higher proportion (62%) of my sample reported more than >50% of pain days in the last 30 days. More than half (52% (n=11)) of the participants were on both long-acting and short-acting prescribed. Notably a higher proportion (62%) of my participants has either college or some college education. Approximately 57% of my sample reported their income to be in the range of $0 to $25,000. Approximately 24% of my samples are smokers. Similarly, around 24% of sample reported drinking alcohol.

Table 11: Demographics and Characteristic of Participants

Variables	Frequency % (n = 21)
Age Mean (SD)	35.4 (11.4) years
Gender	
Female	57% (12)
Marital Status	
Married	24% (5)
Education	
High school or less	38% (8)
College or some college	62% (13)
Household income	
$ 0 to $25,000	57% (12)
$25,001 to $50,000	19% (4)
$50,001 and Over	24% (5)
Genotype	
SS	57% (12)
SC	33% (7)
SB+thal	5% (1)
SBothal	5% (1)
% Pain Days	
≥ 30-50 %	38% (8)
>50 days %	62% (13)
Average Pain intensity (1-10) Mean (SD)	5.5 (1.7)
Prescribed Opioid Regimen	
Short-acting (PRN) Only	52% (11)
Both short- and long-acting	48% (10)
Drink Alcohol	
Yes	24% (5)
Smoke Cigarette	
Yes	24% (5)

B. **Qualitative Findings, Phase I**

For phase I, the final sample consisted of 11 men and 10 women, average age 36 years, ranging from a diverse background of socioeconomic and educational levels. Qualitative thematic analysis uncovered several patterns of opioid-taking behavior and several related biopsychosocial-spiritual phenomena, some hypothesized and some not. These patterns and phenomena portrayed a new six-domain conceptual framework for prescribed opioid taking-behavior in SCD: 1) Pain and its consequences; 2) Impact of Prescribed opioid on biopsychosocial-spiritual function. 3) Prescribed Opioid-Taking Behavior and their biopsychosocial-spiritual determinants on opioid-taking behaviors; 4) Aberrant behavior; 5) Physician prescribing behaviors and attitudes; 6) Hypothetical targets for interventions to improve prescribing and opioid taking-behaviors. Further, the data portrayed explanatory factors that could be classified into various levels or domains based on models proposed in prior research. Factors included intra-patient (biological, spiritual, psychological) and extra-patient (social support, provider relationships, institutional norms, culture, legal and governmental policy) domains.

1. Findings Related to Domain 1: Impact of Pain and Its Consequences on Biopsychosocial-Spiritual Function in Patients with Sickle Cell Disease

Patients reported their perceived feeling of being a burden on family members; that pain negatively impacts maintenance of family relationships, obligations, friendships; and that pain inhibits social interactions, reduced participation in social or community obligates, interfered with activities of daily living, interfered with work and school productivity, cognitive abilities, and emotional well-being. Patients described their pain as causing mistrust by physicians caring for them (especially emergency). Patients also described their pain as differing when they lived in cities with special sickle cell care. Specific negative emotional states included stress, feelings of guilt, and severe mental and physical exertion.

2. Findings Related to Domain 2: Impact of Prescribed Opioids on Biopsychosocial-Spiritual Function in Patients with Sickle Cell Disease

Based on my qualitative study, participants reported positive, negative, or variable effects of prescribed opioids. Prescribed opioids had some negative effects on patients such as isolation, dependency on others and stigma. However, positive effects countered included feelings of independence from a pain-centric lifestyle and avoidance of pity or sympathy. Furthermore, personal pain management experiences created divergent effects on relationships, moods, activities of daily living, functioning, productivity in the school/workplace, fulfillment of social and spiritual obligations, and overall world-view. See Table for the emerged themes related to these domains.

Table 12: Summary of Impact of Opioid on Biopychosocial-Spritiual

• Planning for increased vigilance for activities based on prior experience with medicationSp • Stress relief • can manage pain at home (prevent trips to ER, bring fast relief, convenience & normality all achievable) • Backup plan for any other health aches as self-treatment • Anticipation of pain due to diligence for taking oral prescribed opioids • Make one stay at home • Personal responsibilities are easier to meet. • Stigma that goes with using opioid and having to deal with those that abuse opioid. • Long acting drugs decrease need for short acting drugs. • Mental fatigue • Having to worry about dependency/overdose impact of opioid vs. impact of taking a medication overall - heightened paranoid/OCD over times.

3. Findings Related to Domain 3: Prescribed Opioid-Taking Behaviors and their Biopsychosocial-Spiritual Determinants in Sickle Cell Disease

Qualitative thematic analysis revealed three phenomena First SCD patients exhibited various opioid-taking behavior patterns including adherence, overuse, underuse, and

erratic use Second, a wide variety of biopsychosocial-spiritual factors hindered or motivated opioid use: pain intensity; side effects; fear of addiction; perceived stigma or judgment by others; senses of responsibility, productivity, hopelessness, or obligation; stress; social role pressure; social desirability; bullying; and anticipatory fear of adverse outcomes; and Third, behaviors varied based on the time of day, week, month, or year, and based on context at times of doses.

4. Findings Related to Domain 5 and 6: *Advices for other providers*

i. Advice for health care providers

The interviewees gave several pieces of advice for the healthcare providers responsible for patients with sickle cell disease(see Tables 13 and 14). They also gave advice for fellow patients and suggested interventions to improve prescribing and opioid-taking behaviors. See Table13.

Table 13: Summary of Participants Advice for their Health Care Providers

1. ER doctors should be more informed about disease (Environmental, leading to psycho, AKA bad relationships) ---in emergency situations, inadequate care is provided, patients may not have listened to patients because they know what kind of medications works for them (bio-psycho-social, environmental stigma, patients believe they know what is biologically beneficial for them)
2. Patients should be trusted (psycho-environmental, there must not be a lot of trust displayed by physicians towards patient)
3. Patient-centered prescribing is effective: Listening to patients will improve medication prescribing according to their preferences, health status and functioning (again, high level of patient awareness, they don't think they're helpless or stupid. Psycho-Environmental---they believe their condition would be mollified under their own jurisdiction).
4. Utilize patients' experiences and perspectives about SCD disease and medications to guide in prescribing which opioid agent/dose/frequency is most effective for them (psycho-environmental…potentially bio, but not verifiable, perhaps a placebo effect through psychological well-being?)
5. Emphasize on taking long-acting prescription as directed (bio-environmental…suggesting that not enough information is provided?)
6. Trust patients in order to maintain optimum and favorable patient-physician relationships (enviro-psycho, apparently there is mistrust of physicians too, mistrust on both sides? Patient dissatisfaction/lack of explanation/lack of trust could lead to misuse)
7. Stories about selling prescribed opioid pr (selling medication, misuse, taking advantage of healthcare providers, trying to defend themselves, warning physicians of misuse)..? (← What is

this?)

8. their questions answered or needs met.)
9. ER doctors should understand patients (environmental, perception throughout all advice given is that patients truly think they know best, and that there is mistrust on both sides resulting in ineffective treatment. Maybe if physicians listened to patients they wouldn't be compelled to misuse if they had more drugs. Dosage is not "one size fits all").
10. Place emphasis on securing prescriptions to prevent drug abuse (by whom? The patient?)

Advices for physicians and health care providers

1. Focus on optimizing the patient-physician relationship; ensure that your patient trusts you.
2. Work hard to ensure that your patient understands how his/her medication works. Emphasize the need to take medication as directed, particularly to potentially reduce substance abuse. Listen to their concerns regarding medication, make adjustments to their medication if it is to their benefit, and trust your patient.
3. Treat your patient with respect and do not assume that they lack intelligence based on their socioeconomic background. Provide both medical and emotional counsel for your patient.
4. Work to educate nurses and emergency room staff on SCD.
5. Be aware that there is drug misuse in the hospital, and that sometimes patients are under pressure from friends or family members to share or sell medication. Work with patients to secure medication.

Advices for society/government/other environmental influences

1. The government should invest in additional SCD research.

Table 14: **Summary of Advices for fellow patients**

Advices for fellow patients
1. Manage pain more effectively by taking medication on time and as directed, particularly long-acting opioids. Do not abuse medication.
2. Promote self-wellness to reduce/avoid pain: limit activity, get rest, eat healthily and drink plenty of fluids, particularly water (consider getting an IV to ensure hydration).
3. Understand the mechanism of sickle cell disease, and how what happens at a cellular level translates to pain on a macro level. Realize and accept that severe and even unexplained pain is typical of SCD.
4. Trust physicians, they would never hurt a patient intentionally. Do not be afraid to communicate your concerns and ask for better explanations. Work with your physicians if you think there is something wrong with your prescription.

5. Overview of Global Themes That Emerged During Phase I for Domain 3

This dissertation and instrument development part was only be focused with the results of domain 3, Prescribed Opioid-Taking Behaviors and their biopsychosocial-spiritual Determinants of Opioid-Taking Behavior in Sickle Cell Disease. See Appendix I for a summary of all theme emerged from qualitative data.

i.Reasons for Taking Less of Prescribed Opioid of Taking

For those participants who took less or no prescribed opioids continuously or episodically, reasons from refraining from opioid use are listed in Table 15.

Table 15: Reasons for Taking Less Opioid than Prescribed

1) Feeling no pain or low pain intensity
2) Forgot to take the pill(s) (inattentive)
3) Conscious decision to endure pain based on feeling capable of handling pain without need for opioids
4) Attempt to handle/endure/deal with/carry pain without need for opioids based on insecurity about level of incoming pain
    A) Episodic
    B) Continuous
5) Nonchalance regarding prescribed opioids
6) Hesitation & indecision with regards to taking medication (i.e., choosing between responsibilities or lessening pain)
7) Forget the time intervals/frequency (inattentive)
8) Leaving medicine at home (unintentionally)
9) Social commitments
10) External influences
    A) Family and/or close friends' discouragement (inner circle)
    B) Society's discouragement
    C) Physical environment (e.g., weather, physical location)
11) Worries of impact of associating family with negative stigma

12) Reduced perceived pain through use of opioids

13) Reduced perceived pain through pleasant outlook & demeanor

14) Fear of feeling worse due to effects of taking opioids (side effects, personal bias towards taking medication)

    A) Uncertainty

    B) Concern (i.e., "what if")

15) Sense of hopelessness regarding effects/effectiveness of opioid use

16) Using other remedies for managing pain and using opioids as a "last resort" with low priority

17) Use of opioids hindering activities of daily living, family and social responsibilities

18) Safety of self and others upon taking opioids (e.g., driving under influence, accidentally starting a fire after cooking)

19) Becoming a burden to families or burden transfer of responsibilities to family members

20) Need to be productive throughout day

21) Fear of addiction

22) Negative attitude towards taking opioids

23) Financial burden of buying medication or its refill

24) Availability

    A) In market or local phrmacy

    B) With patient's stock

i. Lack of transportation

ii. Running out before next appointment

25) Worries about running out of medication early

26) Completely separate self from negative stigma of being a "drug seeker" [avoiding stigma before it is attached]

27) Attenuate stigma to perpetuate better image as an opioid user

28) Danger of carrying opioids (fear of opioids being stolen)

29) Personal preferences/judgment, perceptions, beliefs towards opioids (benefits of opioids not worth the risk for self)

30) Fear, worries, and concerns of being judged in any fashion (e.g., as looking weak, foolish, crazy, cold, unproductive, slow) by others when under the effects of opioids

31) Bullying related to SCD and opioid use

32) Self-mistrust about self-management with opioids and strong inclination to be cared for by healthcare professionals

33) Perception of experiencing SCD to a lesser degree relative to other SCD patients

34) Confusion/uncertainty regarding severity of pain and stress

ii. Reasons for Taking More of Prescribed Opioid of Taking

For those participants who took more prescribed opioids continuously or episodically, reasons for taking more of prescribed opioid use are listed in Table 16.

Table 16: Reasons for Taking More Opioids than Prescribed

1) As an excuse to take a break from responsibilities (e.g., work)
2) As a routine to function "normally"
    A) Housework
    B) Attending school and related responsibilities (e.g., assignments, exams, Greek life)
    C) Work and related duties
    D) Family and social obligations and etiquette (e.g., family gatherings, church, parties, maintain relationships etc.)
3) Perform activities of daily living (Ex: going to the bathroom, getting up and going back to bed)
4) To avoid pain and anticipated pain associated with movement, preceding signal and/or environment
5) Not experiencing/perceiving/believing negative effects and outcomes
6) Concealing pain (avoiding pity, sympathy, ridicule etc.)
7) For safety of self and others
8) Perception that benefits outweigh the disadvantages
9) Influenced by family and community
10) Indirect influence of family and community
11) Avoidance of hospitalization

A) Long wait-times (vs. immediacy of higher dose)

B) Financial burden

C) Avoidance of being seen as “drug-seeker”

D) Preference for self-management

E) Perception of being healthier than “other” patients with SCD

F) Perception of taking time away from other patients that require hospitalization

12) Belief of self-sufficiency with respect to taking more opioids instead of requiring other means of management

13) Perception of ineffectiveness of prescribed dose

14) Avoid stress - psychological

15) Increased frequency or level of pain than usual

iii. Notable Quotes Related to Domain 3

Please see Table 17 for notable selected participants' quotes related to opioid taking behavior.

Table 17: Notable themes and participants quotes from qualitative interview data

Emergent Theme	Participants
Taking less opioid in order to meet family obligation	**Participant# 2:** "I don't like it, because, when I take it, it takes me two days to get back into everything; into doing the things for the kids and taking care of the household…I wouldn't take it if I had to do a lot with my children, but it does make you sleepy"
Taking less opioid due to vulnerability (opioid makes others take advantage of users)	**Participant# 20:** "I do not take my meds cause the kids take advantage. They always want [to] take advantage of it. Cause they know it makes me drowsy, and it puts me to sleep, so they kind of take advantage of that"
Taking opioid in anticipation of pain	**Participant #21: "**there was a time when I was less experienced, I might anticipate that it would come back. And I might take it, you know, as a precaution. Um, but nowadays, I've gone through it enough times to know that each crisis is different and there's no way of anticipating when you're gonna hurt, not gonna hurt. So, I mean, I just take it when I need it."
Taking more tablets	**Participant #21:** "I take more of the long-acting,..and

of long-acting and short-acting opioid per one dose and more frequently.	more of the immediate-release, probably take it more frequently and probably take more tablets in one dose."
Taking opioid as precaution or taking more before going to social gathering, outdoor activities or church	**Participant # 12:** "Medicine during church, I make sure I take it before I leave home . . . so I don't have to take while I'm in church. Or worry about like if I'm in . . . gathering outside, it going to be a while. So normally I'm going to take the medicine before I leave. But if it's time for me to take it, we still got to . . . (pause) gathering with the people . . . I go and get me something to drink, open my uh my container take my medicine . . . Go about my business" **Participant #11:** "Mm, depends on the activity or the situation . . . Oh, outdoor, I'll take more . . . Outdoor, I'll take more. Family gathering, same amount. If I'm at church, I'll take more, cause I-I do get a little excited . . . before . . . yeah, as a preventative. And then, after, if I, depending on how I feel. But, usually, for both my answers that I mentioned, usually I take more beforehand, and then I just try- I try to gauge just how I feel during and after, see how much of–cause you know, church, that's before-before, and during. I-I don't have to worry about during, it's usually before and after, because it's just a block of time between dosages, usually . . . I usually try do it beforehand . . . "
Taking more of opioid	**Participant # 10:** "I'll probably take more during the day . . .

during the day to finish responsibilities	Um, usually I'm trying to get more done during the day . . . And, moving around, you know, I don't want to be in pain . . . Or, I don't want to think about it, so I'll take more during the day so, maybe I'll get more relief, and . . . Not worry about it."
Taking more of the short-acting when having excruciating pain	**Participant #21:** "What do I do differently?...Uh, yeah, always take the medicine when I'm in pain. I don't, I mean – sometimes if I'm in an unusual amount of pain, I might take a bit more of the immediate- release. Not the extended-release, but the immediate-release." **Participant # 33**: "Cause I'm having severe pain . . . And I'll take it a little sooner than it says on the bottle . . . Well, it says every 3 hours on the bottle, I might take it every 2 hours… Mm-hmm, when I have severe pain."
Taking long-acting earlier when having excruciating pain	**Participant # 6:** "Um. With the long-acting, I wait at least 8 hours . . . If the pain is really bad, then, uh, I might take it, uh, a little bit sooner, I might take it um, you know, 7 ½ hours. You know, 7 [hours] . . . Sometimes if it's like real bad. Normally, uh, just at the 8-hour mark . . . Um, okay, well that was the long-acting . . . OK, the short-acting, um, I take it, pretty much like I said, twice a day. Normally it's like 8-10 hours in between when I take it. Like I said, unless I have breakthrough pain, or have, uh, a major crisis or something going on, I take it a lot sooner, but, um . . . The 3-hours. Uh, it's always the 3-hour mark…At least, yeah, I don't take it, uh, sooner… But, uh, normally at least the 3-hour mark."

Refrain from using opioid at the first feeling of pain and prefer to wait longer till having more pain.	**Participant # 7:** "I'll wait, I think I'll wait kinda late because it seem[s] like if you go ahead and take it when you first feel the pain, it can work faster, but with me, I'll wait 'til I'm really in pain to take the medicine."
Forgetfulness of taking long-acting opioid	**Participant # 3:** "Difficulty taking my scheduled medication. Like, when I'm-I'm out and about, shopping and doing some things that I don't [do at home] and I might forget it at home, or, um, just forgot. "
Side effects as a Factor that make it difficult to take medication	**Participant # 6:** "Right, uh. I have to think about that. Um, well. Definitely there's a time where I was working. I was a courier, and, um, normally on Saturdays, my, um, my schedule would be earlier . . . And, um, I would start, uh, around 12 o'clock, my route. And, uh, normally I wouldn't take, uh, the medicine, uh, in the mornings like I normally do. So, uh, but the time I normally finish my route and all that, it would be, kind of, mid-evening. And, um, and so that kind of made it difficult for me to take it as prescribed. Um . . . As far as the time, and you know. When I need to take it, um, because I was working. And, um, for the wait until I was hope, I could let, you know my body rest and things like that. Plus, sometimes it can make you drowsy, and doing this job on the road, so sometimes on Saturdays when I was working as the courier . . . Um, that would make it difficult, but . . . Um, just the time. It would be considerable later than I normally do . . . Yeah, uh, like I said, it was night. It'd be 5, 6, 7 [o'clock] even, before I take my first dose of medicine, you know. You know, so that's way off when I normally take

	it. It's way off. It would normally be my time to take it again, but it would just be my first time, so." **Participant # 2:** "Hmm, the only think I know is it makes it difficult for me, is I have nausea . . . Nausea, or vomiting– it's-it's miserable to take. And you know this is what's going to happen, and you're already not feeling good, and you gotta strain. No, I don't wanna take it then . . . It's just the nausea. That's the only thing that I could seethat I could remember thatthat refused me from not taking it. And then, sometimes, when I think, and this was a while back, when I think the dosage is just too-too much, that it makes me more, like, out of it, drugged up, than I would, I would, if I know that's what it's gonna do to me, then I won't take it. I don't like to be sleep and f– I don't like that . . . I don't like the feeling . . . And it's more so I don't like to have nothing that's in control of me, I like to be in control all the time . . . So, that would make me refuse, from taking it. That and nausea, those are the only two things." **Participant # 7:** "You know, you don't wait til the pain gets severe to take the medicine,–… But I wait til I'm hurting –if I'm hurting, and then I take my medicine, instead of taking it as soon as I feel the pain…Mm-mm. I just. [sigh] It's just gonna have me doing funny things…I might run through the house and say, um, ...[strange things]. One time I was in a crisis, and I was saying, 'Yessir! Yessir!' [both laugh]…No, because, um, when I'm like that, whatever my son is doing, he's gotta stop; like, say he's on the internet or on the phone, he'll say, 'Now lemme call you back because my mother, she

	done took her medicine and she sick and I gotta keep an eye on her cause she's gonna get into stuff.'…And then sometimes it makes me active; I get in the kitchen and I get [to] cooking stuff and everything, and, I don't need to be going through that, because, just imagine if my son wasn't at home, and just imagine if he's at work or something, and I get into some kind of activity, and something happens. Just imagine, I'm cooking on the stove and suddenly I [have] got a fire…You know. And that-that's not a good situation. "
Fear of ineffectiveness, providers mistrust and lack of knowledge about opioid as factors of non-adherence behaviors	**Participant #21:** "in days when I was younger, um, I could see how fear that the medication wouldn't work [would be a reason]…Um. Not understanding how the medicine works. Not understanding how the extended-release and the, um, immediate-release, how one works with the other…Uh, not trusting the doctor. Uh, and he knew what he was talking about… Um. I could see how those factors in my younger days, I would have taking my medication willy-nilly. Um, but me personally, I mean, if I'm not in pain, I won't take it."

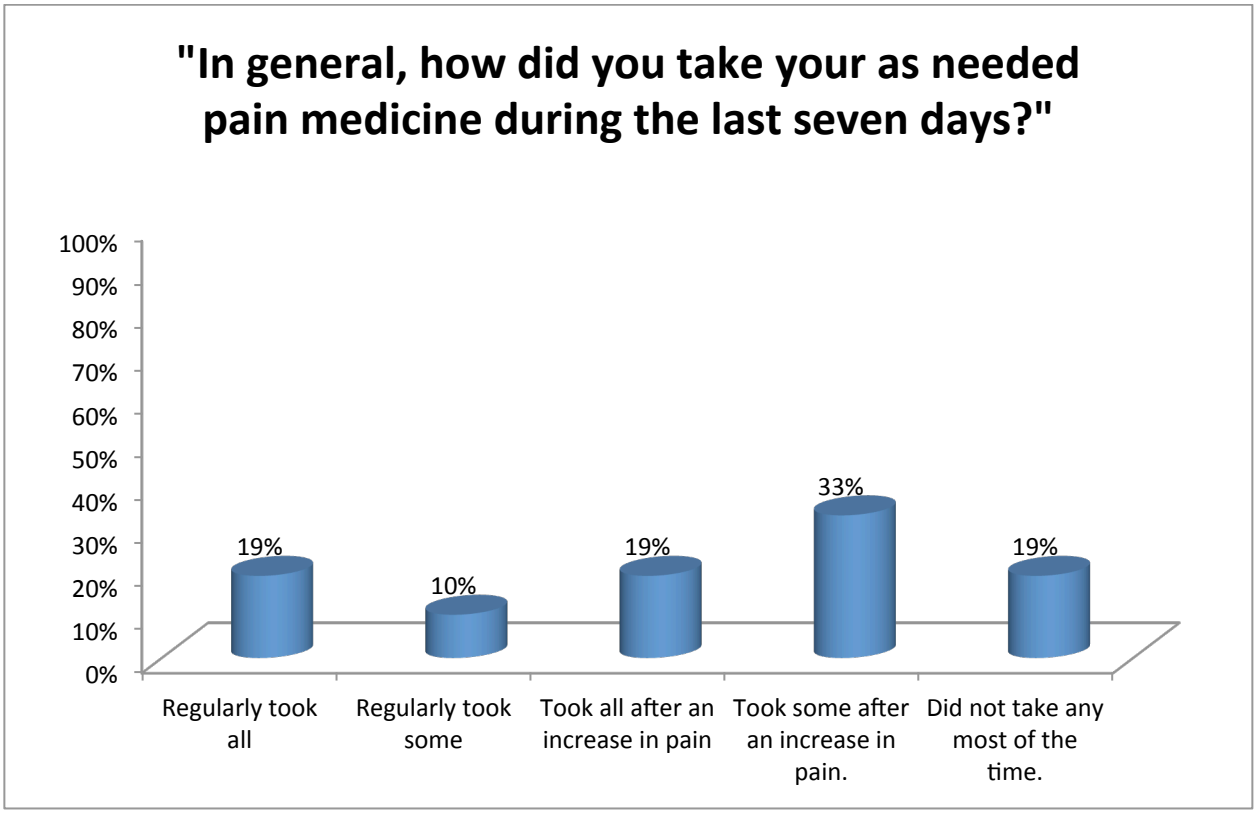
C. **Results of Preliminary Survey**

After I finished each interview, I administered a preliminary survey of 11 questions about opioid taking behaviors and their factors.

In the current study, one of the measures for opioid adherence was measured by patient self-report of prescribed pain medications taken during the previous seven days. A one-item self-report questionnaire with five options was adapted from previous research.

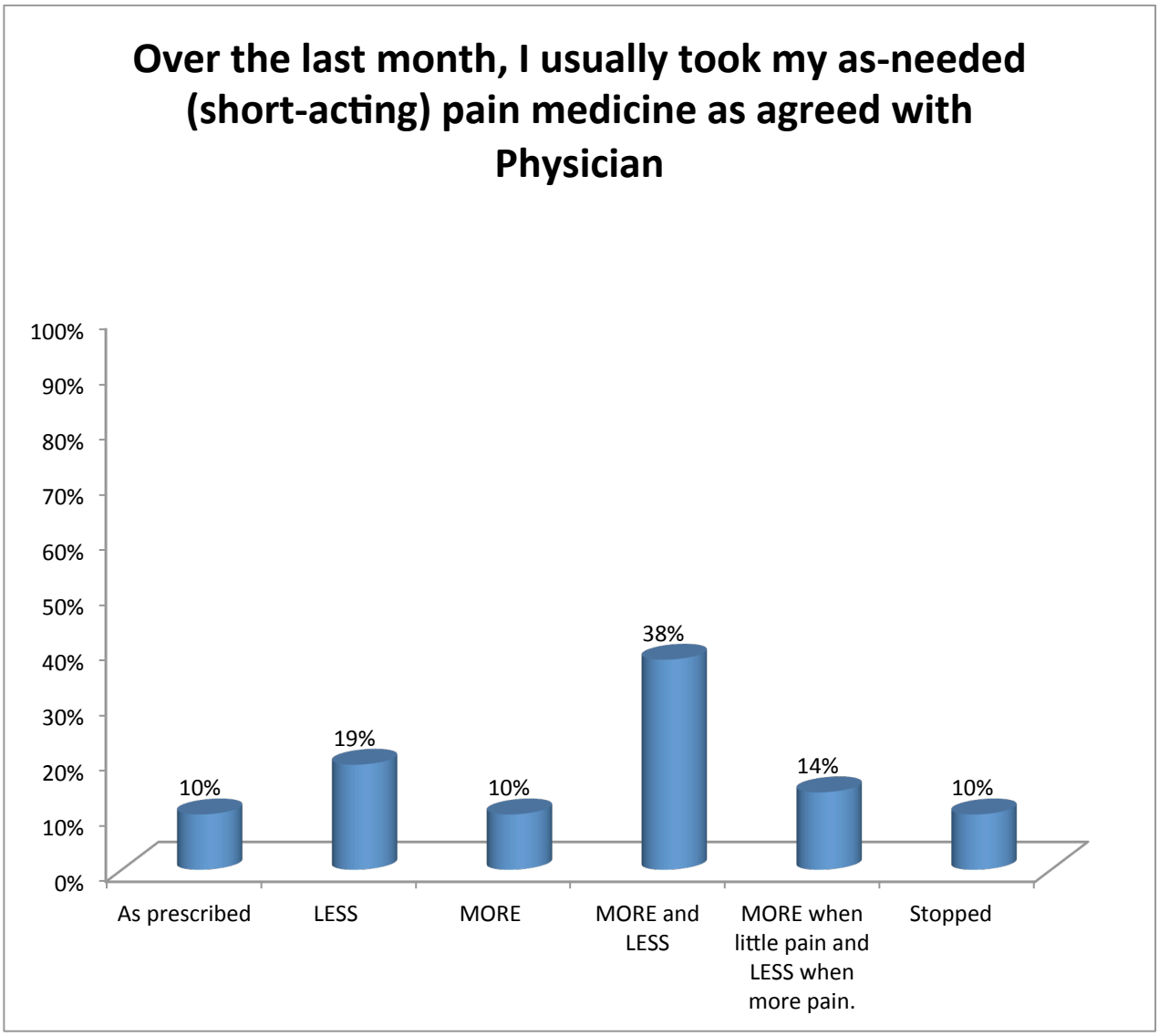
The five analgesic-taking options included: 1) regularly took all pain medications, 2) regularly took some prescribed pain medications, 3) took all prescribed pain medications after an increase in pain, 4) took some medications after an increase in pain, and 5) did not take prescribed pain medication most of the time. Adherence was defined in this item as "regularly taking all pain medications as prescribed by the physician." If a patient took all prescribed pain medication regularly, he/she would be further categorized as adherent. All others were categorized as non-adherent. Only one-fifth of participants (19%, n=4) fully adhered to prescribed analgesics. Among the four non-adherent patterns Figure 4, the largest subgroup was "took some medications after an increase in pain" (81%, *n* = 17).

Figure 4: Distribution of participants' answers to a survey questions related to taking as-needed pain medicine during the last seven days



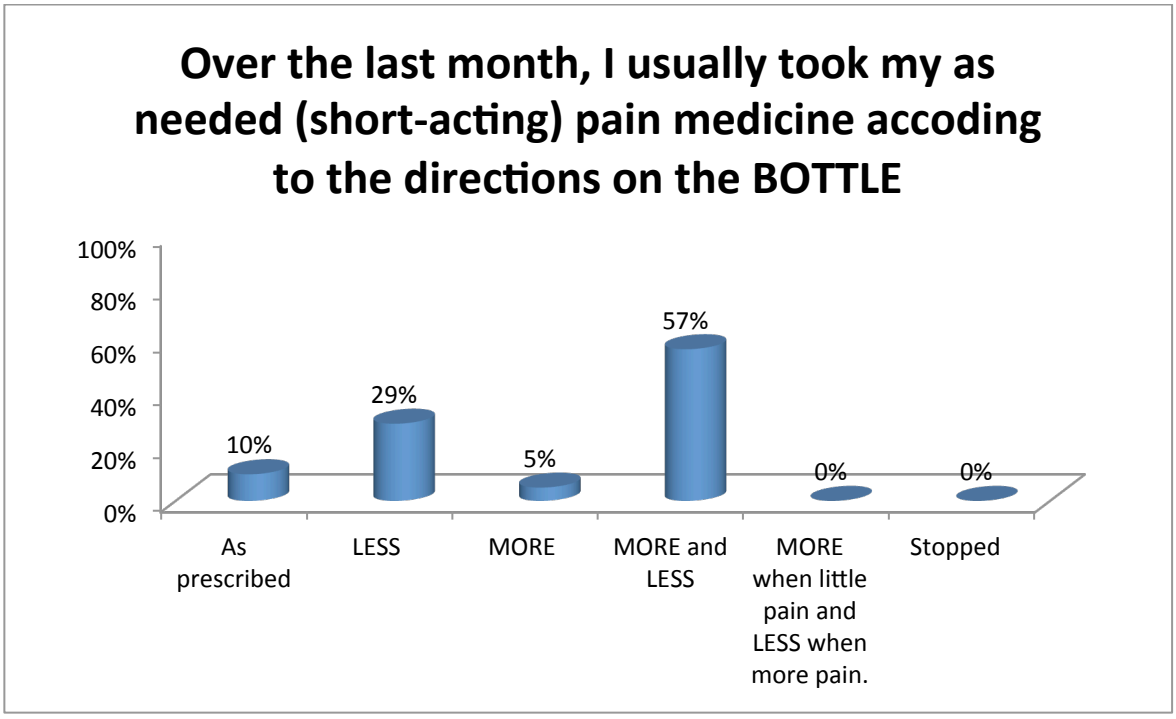
For the remaining 10 questions, I received a wide range of responses and frequencies to each question. For question 2 which asked about taking short-acting opioid based on provider verbal agreement, most respondents (62%) indicated that they do not take it as prescribed and exhibited various non-adherence behaviors. The most frequently reported non-adherence behavior was taking more and less than prescribed followed by (19%) "Take less". See Figure 5.

Figure 5: Distribution of participants' answers to a survey questions related to Overall Short-acting Opioid Taking Behavior based on provider verbal agreement



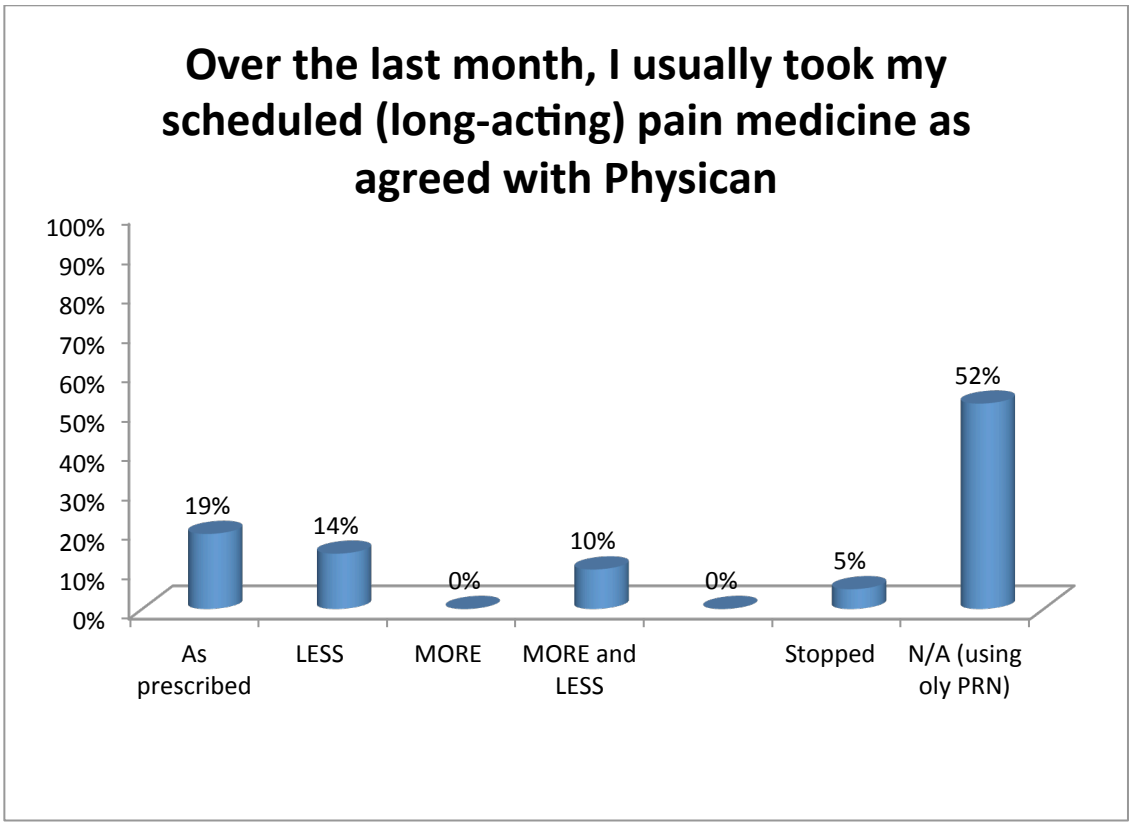
For question 3 which asked about taking short-acting opioid based on the direction on the bottle, most respondents (90%) indicated that they do not take it as prescribed and exhibited various non-adherence behaviors. The most frequent (57%) reported non-adherence behavior was taking more and less than prescribed followed by (29%) "Take less". See Figure 6.

Figure 6: Distribution of participants' answers to a survey questions related to Overall Short-acting Opioid Taking Behavior based on the direction on the bottle



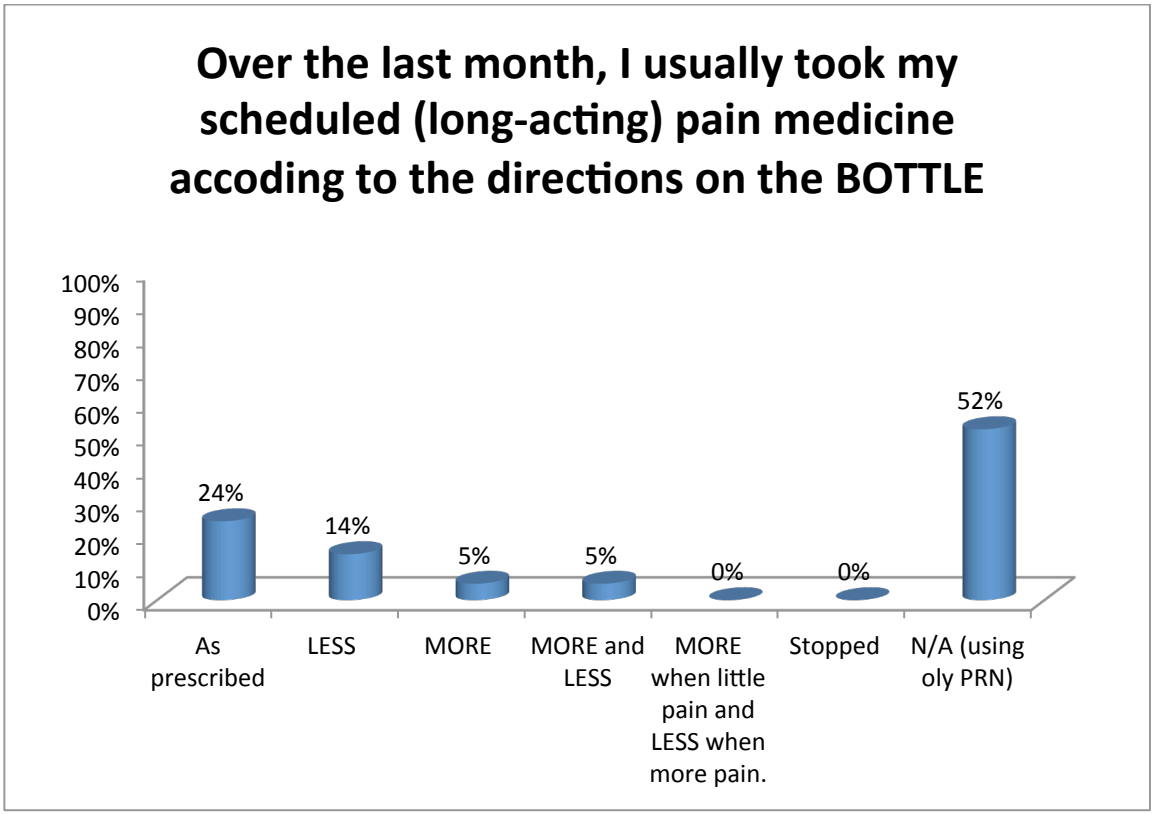
For question 4 which asked about taking long-acting opioid based on provider verbal agreement, most user respondents (24%) indicated that they do not take it as prescribed and exhibited few non-adherence behaviors. The most frequent reported non-adherence behavior was taking less than prescribed. See Figure 7.

Figure 7: Distribution of participants' answers to a survey questions related to Overall Long-acting Opioid Taking Behavior based on provider verbal agreement



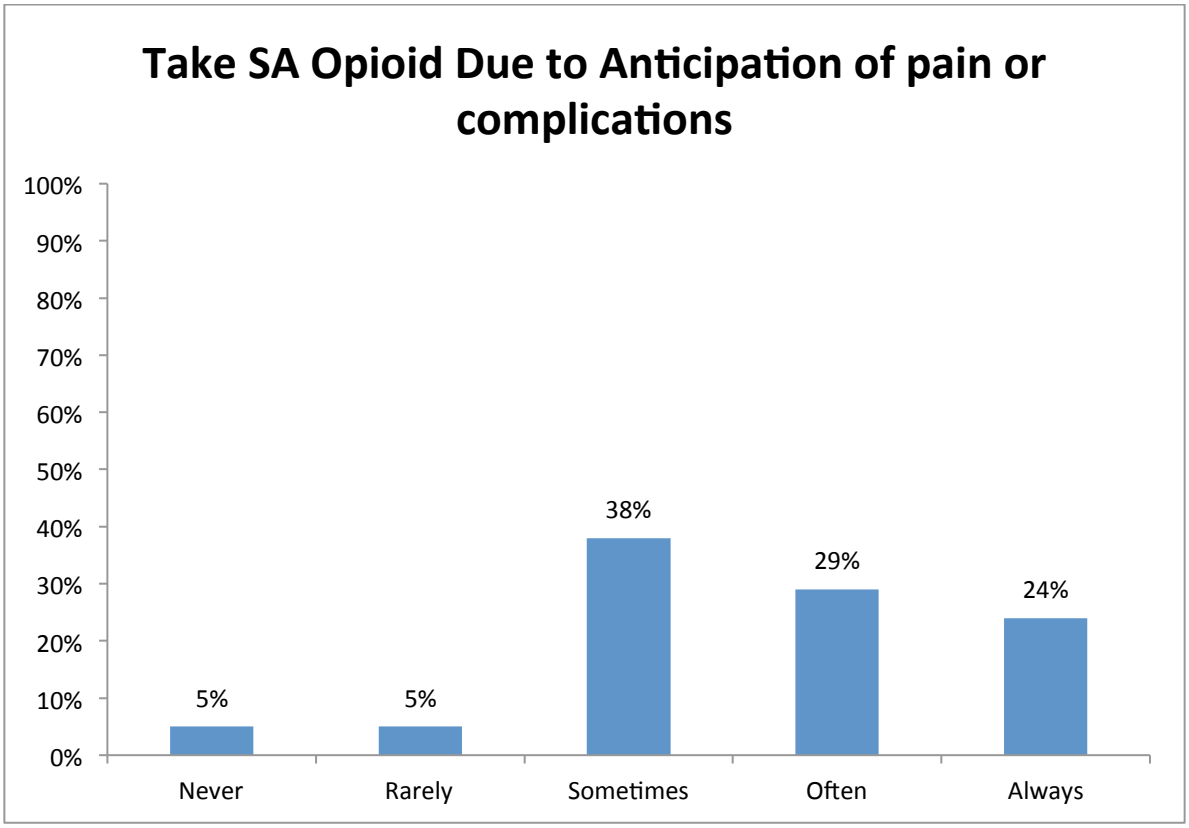
For question 5 which asked about taking long-acting opioid based on the direction on the bottle, there was an approximate 50% split between user respondents. However, the most frequent (14%) reported non-adherence behavior was taking less than prescribed. See Figure 8.

Figure 8: Distribution of participants' answers to a survey questions related to Overall Long-acting Opioid Taking Behavior based on the direction on the bottle



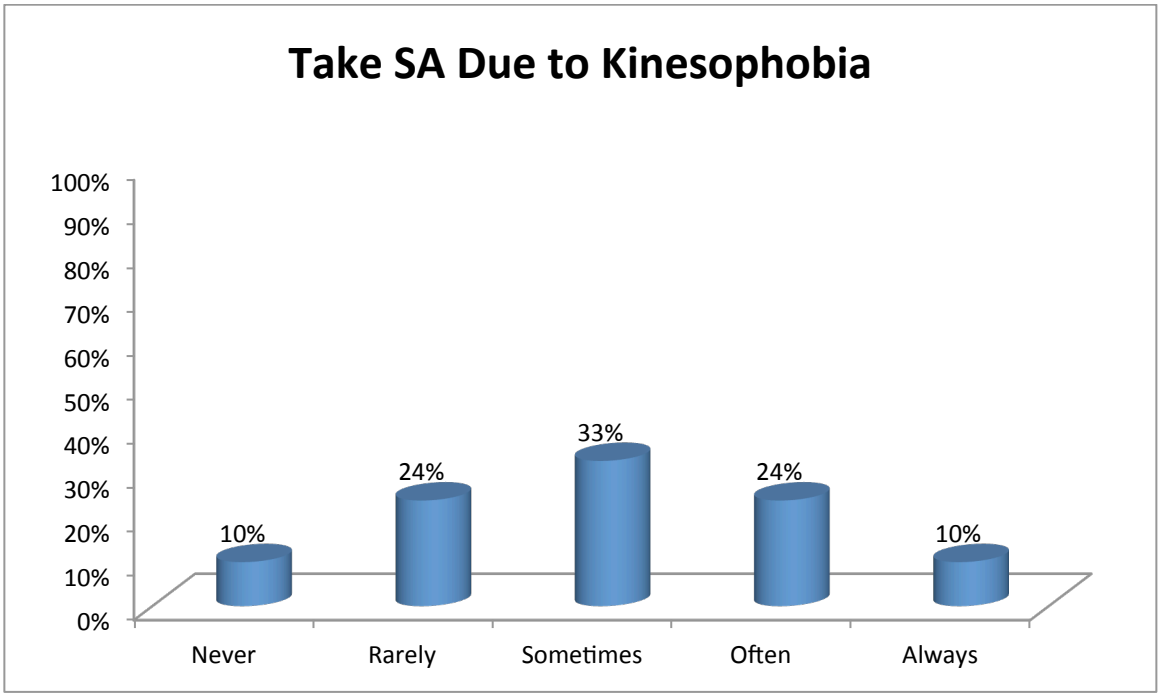
For question 6 which asked about the frequency of taking of short-acting (SA) opioid in anticipation of pain or complication, most participants (90%) indicated any of "sometimes", "often" or "always" as how frequent they did take their SA opioid for this reason. While 10% of the participants indicated either "never" or "rarely" did take their SA opioid for this reason. See Figure 9.

Figure 9: Frequency of taking short-acting (SA) opioid in anticipation of pain or complication



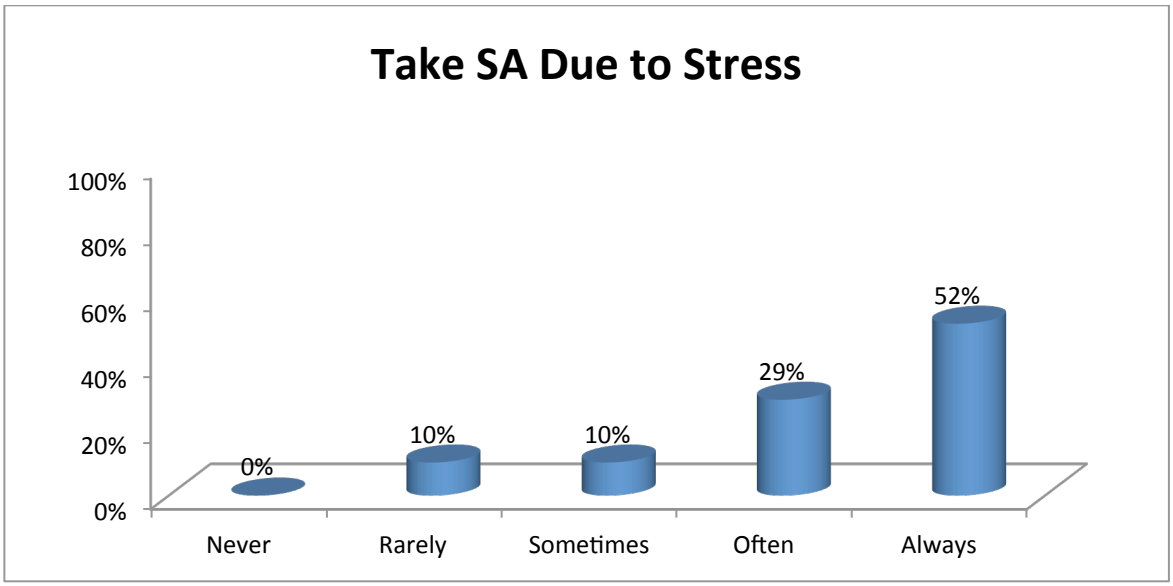
For question 7 which asked about the frequency of taking of short-acting (SA) opioid due to kinesophobia, most participants (66%) indicated any of "sometimes", "often" or "always" as how frequent they did take their SA opioid for this reason. While 34% of the participants indicated either "never" or "rarely" did take their SA opioid for this reason. See Figure 10.

Figure 10: Frequency of taking short-acting (SA) opioid due to Kinesophobia



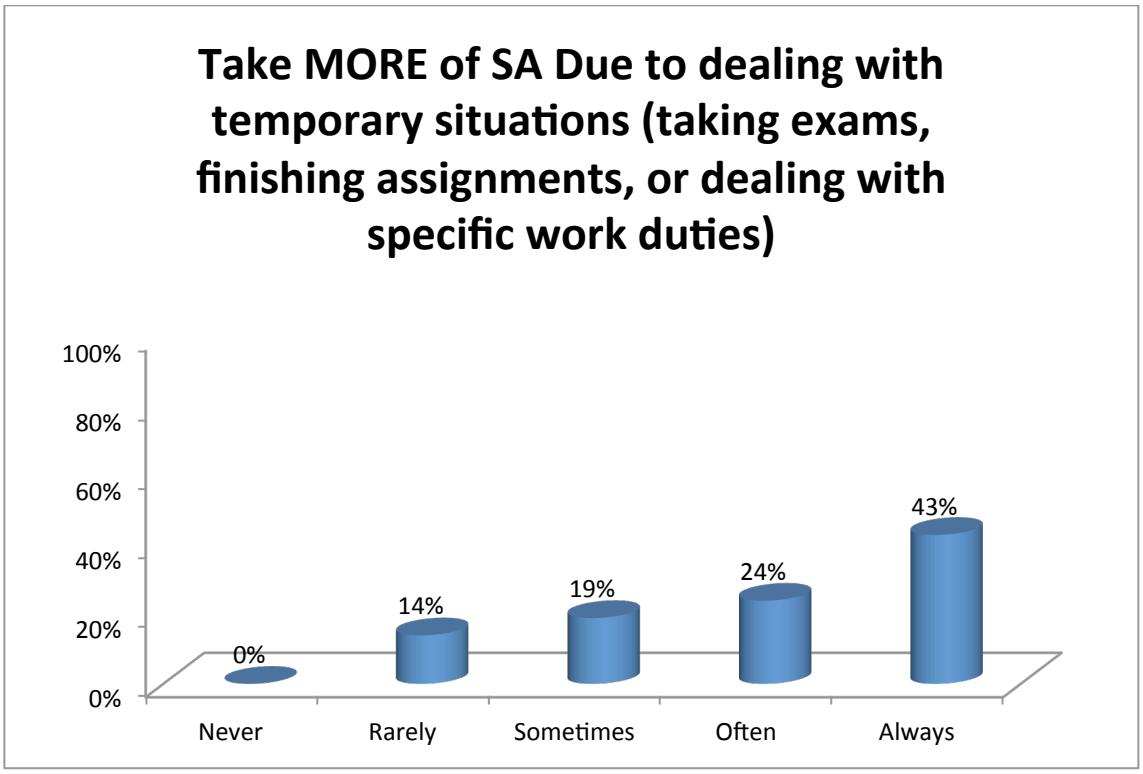
For question 8 which asked about the frequency of taking of short-acting (SA) opioid due to stress, most participants (90%) indicated any of "sometimes", "often" or "always" as how frequent they did take their SA opioid for this reason. While 10% of the participants indicated that they "rarely" did take their SA opioid for this reason. See Figure 11.

Figure 11: Frequency of taking short-acting (SA) opioid due to stress



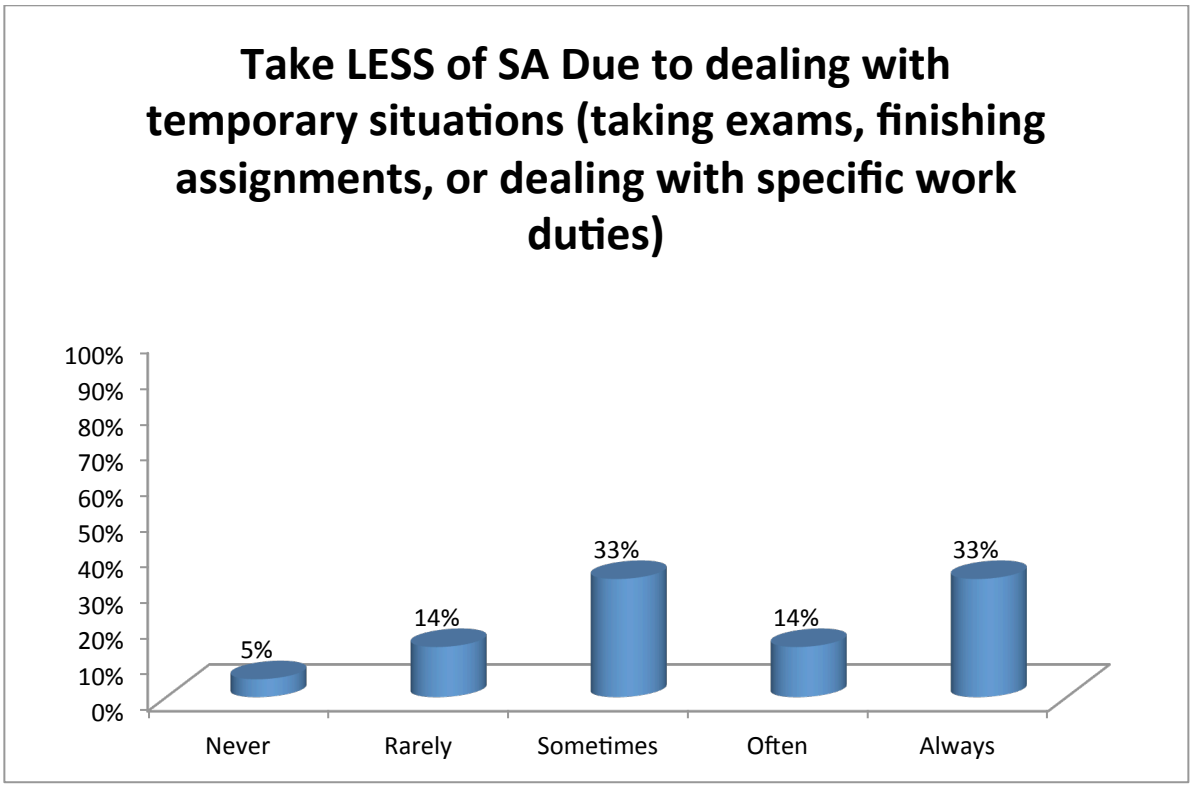
For question 9 which asked about the frequency of taking more of short-acting (SA) opioid when dealing with temporary situations, most participants (90%) indicated any of "sometimes", "often" or "always" as how frequent they did take more of their SA opioid for this reason. While 14% of the participants indicated that they "rarely" did take more of their SA opioid for this reason. See Figure 12.

Figure 12: Frequency of Taking MORE of SA Due to dealing with temporary situations (taking exams, finishing assignments, or dealing with specific work duties)



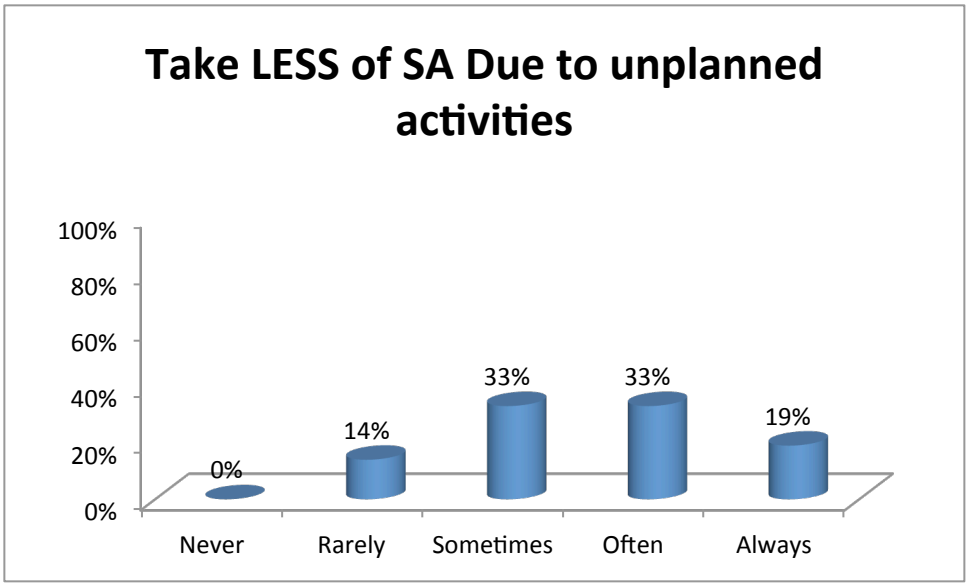
For question 10 which asked about the frequency of taking less of short-acting (SA) opioid when dealing with temporary situations, most participants (81%) indicated any of "sometimes", "often" or "always" as how frequent they did take less of their SA opioid for this reason. While 19% of the participants indicated either "never" or "rarely" did take less of their SA opioid for this reason. See Figure 13.

Figure 13: Frequency of Taking LESS of SA Due to dealing with temporary situations (taking exams, finishing assignments, or dealing with specific work duties)



For question 11 which asked about the frequency of taking less of short-acting (SA) opioid due to unplanned activities, most participants (86%) indicated any of "sometimes", "often" or "always" as how frequent they did take less of their SA opioid for this reason. While 14% of the participants indicated that they "rarely" did take less of their SA opioid for this reason. See Figure 14.

Figure 14: Frequency of Taking LESS Due to unplanned activities



II. Phase 2 Findings

A. **Writing and Evaluation of the items**

First, I transcribed all of the interviews. I developed specific categories according to the general themes that emerged from my qualitative analysis. Each individual quotation was assigned to the appropriate division. I evaluated each quotation for both its explicit and implicit concepts. A general consensus was utilized for the following:

1. Each quotation was evaluated in order to place it in the appropriate category, based upon its general interpretation.
2. Each quotation had multiple facets. Three research colleagues' members explored each possible interpretation.
3. All final themes and their respective categories were approved by the members.

I developed a number of statements to articulate each individual aspect of every quotation, which became the themes. Each group member wrote statements on the same common themes, but expressed them in their own voice, using the linguistic transformation approach.

The statements were then analyzed for brevity, clarity, relevance, redundancy, ability to represent the original theme, simplicity of language. More than 500 survey items were initially proposed and reviewed. After deliberation by review panel, 162 items were

chosen to be included in the first draft survey. These items reflected all of the original themes. It was determined that each of the selected items was necessary in order to reflect the complete spectrum of my themes.

B. **Review Panel**

I formed a panel comprised of three clinical and research experts in pain management of non-cancer pain and three patient experts living with SCD and trained in a medical science. The purpose of this panel was to confirm that each item in the survey was unique and appropriate.

The panel reviewed each item for redundancy and relevancy, and determined whether the meaning of each item expressed adherence or non-adherence and could be characterized as continual or momentary in nature. For an item to be accepted, it was required that two of the three panel members agree that the item was not redundant, attained the same degree of relevancy, and was consistent with momentary or overall adherence/non-adherence. Each panelist's comments were evaluated to determine consistency in their responses and the reasons why they reached each conclusion (See Figure 15).

C. **Scale-Content Validity Index (S-CVI) and Item-Content Validity Index (I-CVI) or AOTBA Scale**

The scale-content validity index (S-CVI) was determined by assessing the proportion of expert reviewers who score items as a three or four on the relevancy scale, where 1 = not at all relevant and 4 = highly relevant, to the total number of items on the scale. This is determined by assessing the proportion of relevance of each item to the number of expert reviewers. Almost all the items have I-CAV equal 1.00. Also, the S-CVI index was 0.989 for relevancy and 0.971 for clarity. Both these readings (findings) are very acceptable for content validity and indicate that AOTBA scale has exceptional high content validity.

Table 15: CVI for Expert Reviewer Ratings of the Wording Clarity and Relevancy

item #	**Relevancy** 1= item is not clear/representative of content domain. 2= item needs major revisions to be relevant, 3= moderately relevant or 4= highly relevant Yes=Items was be rated as 3= moderately relevant or 4= highly relevant Note: Yes=Items was be rated as 3= moderately relevant/clear or 4= highly relevant/clear are considered in the table No= item rated as 2 and lower was not be considered in the table.					**Wording Clarity** Rated items on a four-point scale: 1= item is not clear, 2= item needs major revisions to be clear, 3= item needs minor revisions to be clear, 4= item is clear Yes=Items was be rated as 3= moderately clear or 4= highly clear Note: Yes=Items was be rated as 3= moderately relevant/clear or 4= highly relevant/clear are considered in the table No= item rated as 2 and lower was not be considered in the table.				
	EXP.1	**EXP. 2**	**EXP. 3**	**Expert in Agreement**	**I-CAV**	**EXP.1**	**EXP. 2**	**EXP. 3**	**Expert in Agreement**	**I-CAV**
1	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
2	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
3	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
4	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
5	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
6	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1

7	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
8	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
9	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
10	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
11	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
12	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
13	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
14	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
15	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
16	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
17	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
18	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
19	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
20	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
21	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
22	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
23	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
24	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
25	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1

26	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
27	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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29	Yes	Yes	Yes	3	1	Yes	No	Yes	2	0.67
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31	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
32	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
33	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
34	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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39	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
40	Yes	Yes	No	2	0.67	Yes	Yes	No	2	0.67
41	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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44	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
45	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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53	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
54	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
55	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
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67	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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69	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
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74	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
75	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
76	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
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85	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
86	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1

87	Yes	Yes	Yes	3	1	No	Yes	Yes	2	0.67
88	Yes	No	Yes	2	1	Yes	No	Yes	2	0.67
89	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
90	Yes	No	Yes	2	0.67	Yes	No	Yes	2	0.67
91	Yes	No	Yes	2	0.67	Yes	No	Yes	2	0.67
92	Yes	No	Yes	2	0.67	Yes	No	Yes	2	0.67
93	Yes	No	Yes	2	0.67	Yes	No	Yes	2	0.67
94	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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100	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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106	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1

107	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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110	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
111	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
112	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
113	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
114	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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121	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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123	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
124	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
125	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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128	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
129	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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131	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
132	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
133	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
134	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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136	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
137	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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141	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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143	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
144	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
145	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
146	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1

147	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
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150	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
151	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
152	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
153	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
154	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
155	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
156	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
157	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
158	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
159	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
160	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
161	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
162	Yes	Yes	Yes	3	1	Yes	Yes	Yes	3	1
S-CVS					0.989					0.971

D. **Acting Based on the Feedback**

Based on the expert panel review, each item was reworded or eliminated based on the aforementioned panel review. The revised AOTBA scale was returned to the panel for a final review and approval. They were asked to evaluate the overall appropriateness of the instrument format, order, length and level of complexity.

The AOTBA scale was designed to reflect the panel's evaluation of its applicability to the patients to be surveyed. The scale was formatted and printed for its initial administration. I selected three patients based upon the following criteria:

a. The use of different opioid regimens (long-acting, short-acting, or use of both)
b. Gender (the importance of the inclusion of at least 1 subject of the opposite sex)
c. Literacy level
d. Competency on the MMSE

1. Editing of the Scale:

The authors wrote each statement included in the scale. These statements were then edited by the research assistant for brevity, clarity and grammar and spelling. An expert senior colleague (a family nurse practitioner for SCD patients) reviewed each statement for correct grammar including: the agreement between subjects and verb, consistency in verb tense, simplicity and readability. She edited the statements to ensure the items met English grammar standards, with subject-verb agreement and consistent use of tense for

each item. The complexity and length of items were also changed to simplify the language used in each item.

The wording of the items was discussed among the authors, the research assistant and the senior experts. The final wording for each item was chosen so that each statement would be interpreted in the same way across all participants.

A health education specialist reviewed and simplified the items in order to ensure their readability and simplicity. Each item was edited to match the literacy level of fifth grader. The health education specialist then recommended the following tools:

1. Readability statistics through Microsoft Word
2. Plain Language Thesaurus For Health Communication

These tools were used to modify the wording of the statements and increased the validity and reliability of all items in the scale. The health education specialist read the revised statements and met with the researcher for approval of the final wording.

The scale was then presented again to the panel and the panel members individually wrote their final comments on the items to ensure that the statements met all criteria as outlined above. With the help of a panel of three Expert Patients trained in medical sciences, I further identified redundant or poor questions and provided an early indication of the reproducibility of the responses.

2. Detailed Summary of Scale Feedback and Editing

The following items were accepted without modification by Clinical and Patient Experts as being appropriate and essential to the scale and utilizing simple and clear language: 1, 2, 5, 17, 25, 37, 45, 47, 55, 65, 66, 69, 75, 82, 83, 84, 85, 86, 87, 88, 109, 112, 114, 120, 134, 135, 139, 140, 147 and 158. A number of items were removed from the scale entirely due to redundancy, confusing wording, inapplicability or other problems with the item. Items 3, 4 and 6 were removed because they were noted to be redundant with item 5 by Clinical Expert 2. Items 14 and 15 were removed because they were noted to be redundant by Clinical Expert 2 and poorly worded and inapplicable by Patient Expert 2. Clinical Expert 2 also noted that item 15 was poorly worded. Item 18 was also eliminated because Patient Expert 2 suggested that it may not be necessary and the issue was addressed in items 19 and 20. Item 21 was also removed from the scale as it had a number of issues. Clinical Experts 1 and 2 commented that it was not appropriately worded. Patient Expert 2 also noted that it was redundant with items 117, 71 and 72 and Patient Expert 1 found it to be confusing.

Items 23, 40, 74, 144 were deleted from the scale based on review by the authors, but was received no comments from the expert panelists. Item 29 was removed due to poor wording noted by Clinical Expert 2 and a vague meaning noted by Patient Expert 2. Clinical Expert 1 suggested that item 30 was not clear and the item was deleted from the

scale. Item 41 was also not included because Patient Expert 2 noted that it was not pertinent to the scale. Clinical Expert 3 suggested that item 43 was too close to item 42 and the item was deleted. Clinical Expert 3 also noted that item 48 was too similar to item 47 and Patient Expert 2 said that it was too closely related to 49; therefore item 48 was not included in the scale. Clinical Expert 3 found that item 51 was repetitive with item 50, so it was removed. Both Clinical Expert 3 and Patient Expert 2 found item 54 to be another redundant item (similar to item 57) and it was subsequently deleted. Item 71 was dismissed because it was noted by Patient Expert 1 to be poorly worded and by Patient Expert 2 to be redundant. Patient Expert 2 also suggested that item 78 was too similar to items 61-64 and it was subsequently removed from the scale. There were grammar issues in item 90 noted by Patient Expert 2 and it was also found to repeat the meaning of item 91, therefore it was deleted. Clinical Expert 3 and Patient Expert 2 both noted that item 95 was not applicable and it was removed from the scale. These two panelists also found that items 97, 98 and 99 were not strong and meaningful statements and may be answered by other items. These three items were not included in the scale. Patient Expert 2 also found that items 101, 103 and 104 was not necessary and these were removed. Both Clinical Expert 2 and Patient Expert 2 found item 108 to be redundant with item 106, therefore 108 was not included. Patient Expert 2 suggested that item 121 be removed because it was too much like items 47, 49,51,54,56, therefore it was deleted. Item 126 was deleted because Clinical Expert 1 said that it was unclear. Clinical Expert 1 also said that item 132 was unclear and Patient Expert 2 said that it was redundant; therefore it was subsequently removed from the scale. Patient Expert 2 pointed out that item 133 did not

have meaningful content and it was removed. Item 137 was found by Patient Expert 2 to need revision and was deleted. Item 141 was noted by Patient Expert 2 to be redundant with items 136-137 and therefore it was removed. Patient Expert 2 commented that items 149, 150 and 152 are all redundant and they were deleted. Clinical Expert 3 noted that item 149 was also redundant with item 144. Patient Expert 2 said that item 151 was vague and it was deleted.

The remaining items were given further consideration with respect to commentary from Clinical and Patient Experts and were modified according to their comments. The following is a summary of the comments. For item 7, Clinical Expert 2 suggested that "the medicine" should be added after "do not take". Patient Expert 2 proposed that item 7 be deleted, and suggested the rewording "I fill the prescriptions I receive from my health care provider but I do not take them." Patient Expert 2 suggested for item 8 the rewording "I do not fill the prescriptions I received from my health care provider on time." Patient Expert 2 also reworded item 9 to "I do not fill the prescriptions I receive from my health care provider " The same patient expert suggested item 10 be reworded to "I am able to follow the agreement regarding pain meds that I made with my prescriber to the letter (or faithfully)." For item 11, Patient Expert 2 suggested that the wording of the first part be changed to "I can describe accurately" or "I can state exactly". The same patient expert also proposed that the wording for item 12 be changed to "before I make any change in the way I take my pain medicine". Clinical Expert 2 suggested that for item 13, "the" should be added after "follow" and that 12 and 13 can be combined. Clinical Expert 2

also noted that in item 16 “advice” should be added after “my HCP’s” and Patient Expert 2 noted that “instructions” should be added after “providers”. Clinical expert 2 pointed out that 19 and 20 should begin with “I choose NOT to” and Patient Expert 2 suggested that these two may be redundant. Patient Expert 3 noted that the wording for item 20 should be changed to “I choose not to take a certain medication because of side effects/stigmatized/tolerance/dependence”. Patient Expert 1 said that item 22 was not applicable for short-acting medication and Patient Expert 2 noted that items 22 and 23 are too similar. Patient Expert 2 said that item 24 was not applicable for short-acting medication. For item 28, Patient Expert 3 said that “as” should be removed and “there are” should be added. Patient Expert 1 suggested that item 32 is a redundant item and that in item 33, “to manage my pain” should be moved from the end of the statement to after “myself”. Item 38 was said to be redundant by Patient Expert 2 and inappropriate by Patient Expert 1, since nothing is ever written about non-pain symptoms in scripts. Patient expert 2 recommended that items 39 and 40 be combined to "I remove some pain medication from the original bottle for convenience and/or emergencies."

In item 42, Patient Expert 2 proposed that "prescribed" be deleted because the patient cannot change the prescribed instructions. Instead, the following rewording was suggested by the patient expert: "I change the way I take my pain medications from the prescribed instructions when I am dealing with difficult situations." Clinical Expert 2 noted that items 42 and 58 should be reworded to be more generalized because they are explicitly detailed real-life situations. Clinical Expert 3 noted that item 44 was redundant

with item 47. Patient Expert 2 said that the topic in item 46 was addressed better in other items. Patient Expert 1 said that item 49 was redundant with 48 and that item 50 was redundant with item 47. Patient Expert 2 and Clinical Experts 2 and 3 agreed that items 52 and 53 were too similar. Clinical Expert 2 also included the word “opinion” after “influence”. Clinical Expert 2 recommended that “changed” be switched to the present tense for item 56, Patient Expert 2 suggested the item be deleted, and Patient Expert 3 suggested that the date range be changed to “months to a couple of months“. Clinical Expert 3 said that item 57 was redundant with item 54 and Patient Expert 2 said that it was redundant with item 58. Patient Expert 2 also said that item 59 overlapped too much with item 60. Clinical Expert 1 noted that item 61 may or may not be appropriate for the scale. Patient Expert 2 said that item 64 was redundant with both items 49 and 60.

Patient Expert 1 said that item 67 was vague and Patient Expert 3 suggested that “emotionally” or “physically” should be added after “better”. Patient Expert 2 said that item 72 was redundant with 21, 71, 117 and 118. Patient expert 1 said that in item 72 "after consulting with physician" or "without" should be added. Patient Expert 2 noted that items 73, 74 and 75 were all the same question. For item 76, Patient Expert 2 suggested the rewording "I changed the way I take my pain medications because I used other prescribed non-pain medications" and Patient Expert 3 noted that the item did not apply. For item 77, Clinical Expert 2 suggested that “do” is changed to “does” and Patient Expert 2 changed the wording to "I changed the way I take my pain meds because my doctor does not believe or understand my pain." Patient Expert 2 said that item 79

was unnecessary and that item 81 may be redundant with items 82-88. Patient Expert 1 recommended that "after consulting with physician" or "without" be added to item 89. Patient Expert 1 said that items 92 and 93 were vague and Patient Expert 2 said that items 92, 93 and 94 were all redundant. For item 94, Patient Expert 1 said that the item did not make sense and Patient Expert 2 commented that the "patient must learn responsibility." Patient Expert 2 also said that items 96, 97 and 98 were too similar and that item 96 was the best of the three. Patient Expert 2 also thought that Item 100 was redundant. For item 102, Clinical Expert 2 suggested the rewording from "instead of consultation with" to" without talking with".

Patient Expert 2 read items 109 and 110 to be essentially same question, and that item 111 was similar to items 90-95 and 113-114, and that item 113 and 114 are also too similar. For item 115, Patient Expert 2 proposed the rewording "I cut back or stop taking my pain medication when I feel better even if I still have some pain." Patient Expert 3 said that item 115 should be clarified based on whether the pain is mild or severe because "it makes a difference how many pills I would cut back". Clinical Experts 2 and 3 and Patient Experts 1, 2, and 3 all reworded item 118 to include "it" after "when" and "else" after "something". Patient Expert 2 objected to item 119 by questioning "Why take in first place if moral dilemma?" Clinical Expert 2 and Patient Expert 2 both said that item 122 should be supported with examples. Patient Expert 2 recommended that "s" be removed from "times" in item 123. Patient Expert 2 also suggested that in item 124 "or on an as-needed basis" should be removed and that it was redundant with items 47, 49,

51, 54, 56. Clinical Expert 2 said that item 124 is poorly worded. Clinical Expert 2 said that item 125 was confusing and Patient Expert 2 suggested that "type of" be deleted and "pain" be added after "prescribed", and "severity I have at the moment" be deleted. Patient Expert 1 and 3 noted that both items 127 and 128 are not applicable for short-acting medications and items 129, 130, and 131 are not applicable for long-acting medications. Clinical Expert 1 noted that items 129 and 130 might have answers that vary based on etiology of pain. For item 136, Patient Expert 2 said that it was a redundant item, Patient Expert 3 said it needed supporting examples and Clinical Expert 1 said the scoring was questionable.

Patient Expert 2 said that item 138 was not of the appropriate reading level for the scale and that “I take a different number of pills at different times of day than what is written on my prescription.” Patient Expert 2 said that item 142 was redundant with items 143 to 144. Patient Expert 3 said that item 145 does not apply to long acting medications and Clinical Expert 1 said that item 148 does not apply to long acting medications. Patient expert 1 said that questions 146 and 147 were too similar. Patient Expert 2 said that items 153 and 154 were redundant. Patient Expert 1 said for item 155 that there is no maximum and that item 156 is not applicable for short-acting medications. Patient expert commented that item 156 is unclear and that for item 157, PRN medications don’t have specific day’s supply. Patient Expert 3 noted that item 159 is not applicable for long-acting medications and that example should be given for item 160. For item 162, Patient

Expert 2 added "for pain" after "I take medicine" and Patient Expert 3 noted that other medications and treatments be apply.

1. Qualitative Comments of the Clinical expert Panel and Patient Panel

I met with the expert panel to describe the evaluation process for the scale. Each member was asked to review the item for readability and relevancy.

Upon completion of the review, the panel submitted the quantitative rating of the item along with qualitative comments. After panel review of the survey tool, I reviewed all qualitative comments and suggestions.

Documentation of comments and suggestions was placed into appropriate excel sheet. Covered items included appropriate grammar (the agreement between subject and verb [singular and plural], use of adjective, missing basic verb, missing pronoun);, redundancy; synthesis of two or more statements; separation of one item into two statements; simplification of words to fifth grade reading level, word order within the statements; additional words to clarify statements; agreement in verb tense within statement, revised the statement but keeping its intent; consideration of combination or separation of responses to similar influences on medication taking behavior , adding example for more clarifications.

Some items could be classified as either overuse or underuse, or could be classified as momentary or overall adherence. Consistent with the logical formula (tautology), if only statement A is true then the opposite of statement A (which is statement B) cannot be

assumed, however; if both statement A and B are true then a combination of statement A and B are also True. If only A or B is true and the other is not true, then a combination of A and B cannot be true. Therefore, substitution of two separate statements instead of one-combined statements is logically valid and justified.

With as-needed medications, it is difficult to assess adherence versus non-adherence, and overuse versus underuse as the same patient may respond with opposite reply to the same question at different times. The experts recognized this conundrum and this was reflected in their assessment of the items. Some thought that the statement indicated adherence while other thought it indicated non-adherence; some thought it indicated overuse and others that indicated underuse. Therefore, I decided to eliminate the items from the scale where the experts did not a gree on what the item represented (adherence or nonadherence).

The disagreement among the clinical expert because patient behavior varies due to several factors: etiology of the pain, prescriber instructions, effectiveness and side effects of the medications. Sometimes prescriber write prescriptions that allow the patients to modify the number of pills they take at one time. This is dependent upon level of pain which varies from mild to moderate to severe. At other times, prescribers allow patient to take both a milder PRN opioid (which offers less sedation, but also provides less analgesia) for mild pain and a stronger opioid (more sedative properties but also more analgesic effect) for severe pain.

CHAPTER 6 DISCUSSION

I. Review of Goals and Methods

The primary purpose of this project was to explore and describe the opioid taking behavior in adult Sickle Cell Disease (SCD) patients and to describe the comprehensive biopyschosocial-spiritual reasons for these behaviors.

For phase I, the final sample consisted of 52% (n=11) men and 48% (n=10) women with a mean age of 36 years, ranging from a diverse background of socioeconomic and educational levels. Medical history and psychological variables were assessed at baseline. Relevant medical history predictors included history of pain days and history of analgesics medications.

This multi-phase mixed method study described the opioid taking behavior and the reasons for adherence to prescribed opioid of 21 SCD patients in the Adult Sickle Cell Anemia Clinic at Virginia Commonwealth University Health System (VCUHS) in the Richmond, Virginia.

Adherence was described and assessed by the investigator following an extensive semi-structured interview and preliminary survey regarding adherence behavior. I used 24

questions in an open-ended, face-to-face interview and preliminary survey to collect data about adherence to the prescribed opioid regimens.

The discussion of my findings is organized by the major concepts described opioid taking behavior and their reasons (pain, stress, knowledge, beliefs, side effects etc.). There is currently no published literature about adherence to prescribed opioids in SCD for comparison. Therefore, I offer alternative explanations and comparisons of the current results with past research on non-cancer pain conditions. The discussion also includes commentary on the data collection method of adherence. The limitations are also discussed. Preliminary implications for clinical practice are presented and finally, directions for future research are proposed.

II. Summary of Findings

Qualitative thematic analysis uncovered several patterns of opioid-taking behavior and several related biopsychosocial-spiritual phenomena, some that I expected and others that I did not. These patterns and phenomena portrayed a new six-domain conceptual framework that addresses the complex individual, relational, environmental, cultural, and systemic issues surrounding opioid taking-behavior in SCD. From this six-domain framework, I organized the explanatory factors into a new method of classification, which included two overarching domains: intra-patient (biological, psychological, spiritual), extra-patient (social support, provider relationships, institutional norms,

culture, legal and governmental policy). This classification provides a roadmap for future research. The explored six domains offer guidance in understanding a complex explanation of the effect of pain, its pharmacotherapy, and medication taking behaviors on an individual's health that simultaneously bridges all healthcare domains.

A. **Unanticipated Findings**

My experience suggested that a) the only reason for taking opioids in SCD patients is pain, b) SCD patients would report taking more of prescribed opioid due to excruciating pain, c) the pain-free patients would not report taking prescribed opioid, d) SCD patients would exhibit few behaviors of opioid taking behavior. I found, however, that this was not the case in my SCD patient sample. One of the major findings in this study was that as a whole, my patients showed various types of opioid-taking behaviors with various forms of non-adherence, and many different reasons for non-adherence. Further, one of the most striking findings was that the patients demonstrated arbitrary behaviors of opioid use. Although this finding is consistent with previous adherence literature in other diseases condition such as asthma, I did not expect to find it sickle cell with pain medicines.

B. **Opioid taking behavior**

The sample reflected a heterogeneous group of individuals with various socioeconomic

backgrounds. All subjects in this sample had SCD and many individuals were very ill. Participation in this research was restricted to individuals with SCD pain with prescribed opioids, unique from many descriptive research studies on SCD pain.

This research was focused on the behavior of opioid taking behavior, which was explored in detail. A wide range of opioid agents and dosages were prescribed. In this sample, 9 (48%) subjects were prescribed long-acting opioids with short-acting opioids PRN (as needed), and 12 subjects (52%) were prescribed only short-acting opioids PRN. The percent of subjects prescribed short- and long-acting opioids does not represent the actual distribution of the clinic's current patients (include VCUHS clinic's numbers). It is also higher than most research samples, where only a minority is prescribed long-acting opioids, [171-173] but lower than the 88% reported by Ferrell and colleagues. [174]

Surprisingly, in the one-item self-report adherence questionnaire, only one-fifth of participants (19%, n=4) fully adhered to prescribed analgesics. Among the four non-adherent patterns Figure 4, the largest subgroup was "took some medications after an increase in pain" (81%, $n = 17$).

C. **Underuse and delay in opioid taking behavior**

Underuse and delay in taking opioid medication to treat pain was reported; 19% of subjects (n=4) reported not taking opioids even though pain was experienced, and 48% of subjects reported delaying opioid use by an hour or longer.

In this study, participants varied in their use of long-acting and short-action opioid, with fewer adherents to short-acting opioid. Half of the participants did not use their long-acting opioid every day. This is consistent with previous studies reporting high levels of non-adherence of short-acting and long-acting opioid among cancer patients. [171,174]

All patients included in the current study were prescribed short-acting PRN opioids. However, 10%-29% either discontinued their use or took less than prescribed. In their reporting, subjects varied the dosages of short-acting medication they took during the day and there was a within-subject difference in the type or dosage of short-action opioid. The low (10%-29%) reported use of PRN is also consistent with other samples in cancer literature. [171,174] One interesting finding was the participants reported using short-acting opioids because it was time to take it, implying that even though the medication was to be used for breakthrough pain, some individuals put themselves on a regular schedule of short-acting medication with a lower interval than the available schedule.

In this sample, although all patients reported having more than 29% of pain days in the last month with level 5.5 as an average of pain intensity on a scale of 1-10, overuse of prescribed opioids was ranging from 5%-10% and may be related to reported pain level. This was consistent with findings in cancer patients, where patients reported using only half of their available short-acting opioid when experiencing severe pain.

The highly varied pattern of non-adherence with short-acting PRN opioids and the less varied use of long-acting opioids proved to be a consistent finding in the literature. Conceptually, several explanations may account for this finding. Use of long-acting opioid is simpler, generally twice a day dosing at scheduled times, and no decision or evaluation of symptom experience is required. The fewer doses per day, the more likely the medication is taken, which is a consistent finding in medication adherence studies. However, it is proposed that, conceptually, the use of a short-acting PRN opioid may not an adherence issue. PRN, short for *pro re nata* in Latin, meaning "in the circumstance" in English, implies that patients make the decision of when to take the medication. In fact, a PRN opioid prescription is not meant to be used at 100%; if 100% of the PRN is used, it is an indication for dose increase or drug change. As discussed in Chapter 1and 2, individuals with pain may believe that the management of symptoms is a distinctive behavior choice and different from following recommendations for management of their disease. Whereas management with hydroxyurea or long-acting opioid may be thought of in terms of adherence, management of symptoms is uniquely tied to an interpretation of a sensation and thus is essentially under the individual's own making power.

D. **Reported Factors**

In this study, I explored biopychosocial-sipritual factors that are not commonly explored or examined in the current pain literature in relation to pain and opioids. These included pain intensity, stress, fatigue, accurate education about opioids, beliefs about reporting using opioids, side effects, and many other reasons. See appendix K.

1. Education

The sample did not demonstrate accurate knowledge about opioid use. The variance in the awareness and knowledge about opioid use may be sufficient to provide a meaningful explanation of varying behavior. Although accurate understanding of opioids is critical in appropriately taking medication, this factor may not be sufficient to drive behavior. Given the current clinical guidelines and accepted standards of care, it would be clinically ethical and logical in future research to correct any inaccurate understanding of medication use. However, there may be a role in future research on SCD pain to test interventions designed to improve knowledge of opioid side effect management.

2. Beliefs

This study explored the beliefs and attitudes held by the patients about using opioids. Various attitudes and beliefs toward taking opioid were reported. Below in the discussion, I provide a classification of the different attitude reported. The various attitude and beliefs were consistent with what was previously reported in the literature. [175,176] This finding is most likely related to the fact that all patients included in the sample were taking opioids for many years. I found that non-adherence is more likely reported if the patient also reports a low perception of the need for taking his/her opioid. This perception may arise due to the preconception about SCD is incurable diseases.

3. Side effects

Given the wide array of responses to a general question in the interview regarding side effects, it is recommended that a specific side effect questionnaire be used in future research. Various side effects reported in this sample were present in all patients. Opioid side effects are consistently cited in the literature as a factor contributing to under use. [177] However, in this study, physiological side effects were not an important factor. One explanation is that in this sample, side effects were well controlled, reflecting practice in an academic medical center. Another possibility is that individuals with severe side effects stopped using opioids completely and were not included in this study.

Side effects should be considered as creating a feedback loop both as a result of opioid use and as an influence on future use of opioids. Specifically, increased opioid doses or overuse resulting in increased side effects. Increased side effects then lead to reduced opioid use. [49,50] Although conceptually the occurrence and management of side effects remain important in research about SCD pain, the influence of side effects needs to be investigated as both an outcome of opioid use and as a potential influence on future opioid use.

4. Importance of pain relief

The importance of pain relief was a common concern for subjects taking both long-acting and short-acting opioids. Interestingly, importance of pain relief ranged from not at all to the most important motivation for taking the opioid. Although this has previously been identified as a factor influencing the experience of SCD symptoms, this is one of the first reports discussing the importance of pain relief.

One of the major research aims of the study was to explore the relationship between pain severity and opioid use. As I expected, not all subjects increased their use of opioids on the days when their pain was more severe. Fifty percent of subjects increased their use of the short-acting opioid when pain increased, 40% took the same amount regardless of pain severity, and 10% of subjects had inverse relationships between pain severity and PRN opioid use. This finding has interesting implications. About half of the subjects

with pain due to SCD used their pain level as a guide to medication use, the common clinical recommendation. Yet, at least a third of participants displayed arbitrary o counterintuitive behavior, taking more short-acting opioid with less pain or using less short-acting when pain was worse. Using less short-acting opioid when pain is worse may reflect that the patient is "giving up" or feels despair. If the medicine is not helping, why take more. Using more short-acting opioid when pain is less severe is more difficult to explain and is an intriguing phenomenon that has not been discussed previously in literature.

This supported my finding that related to many reasons not associated with pain behind changing opioid taking behavior. Contrary to Ward and colleagues, [175] my findings show that opioid use and changing opioid taking behavior is not simply related to the reported level of pain.

5. Satisfaction and pain management outcome

This study found a number of important connections between adherence and outcome. Although it is not of direct interest in my study to attempt to describe whether prescribed opioid is related to outcome improvement, a majority of participants reported that taking the opioid according to the prescribed instructions improved the amount of pain relief. Interestingly, some participants reported that adherence with prescribed long-acting opioids helped in improving their pain relief by reducing the frequency and severity of

pain most of the time. However, this relief may not help to keep them to maintain adherence in the future. In contrast, I found that participants who denied any non-adherent behaviors to their short-acting were satisfied with their prescribed opioid. The exact nature of the relationship between adherence and pain management outcome has not been examined in previous research. As a result, the clinical observation that SCD patients with greater alleviation of pain tend to also be more adherent was not supported. This may indicate that reported level of pain in the past may be a sign of future reported behavior.

I found that participants taking the long-acting opioid, who described themselves as experiencing lesser negative effects from opioids, and who attributed their main use of opioid to pain (biological factor), were more likely to be adherent to their short-acting prescribed opioid regimen. In addition, participants taking short-acting opioids who attributed their opioid use to many biopyschosocial factors were more likely not to adhere to their regimen. As a result, the clinical speculation that patients with less reported pain may be more or less adherent with their opioid regimen was not supported. This finding may be due to possible differences in the nature of their pain or may be based upon prior understanding and awareness of how they are supposed to use their prescribed opioids.

Participants that reported autonomous adjustments of their dosages tended to take short-acting opioids. They also were more among participants that attributed behavior to by

psychosocial-spiritual factors such as stress rather than simply biological factors such as pain and side effects.

E. **Erratic and arbitrary behaviors**

Previous research that has shown that failure to adhere to previous treatment regimens is one of the best predictors of future non-adherence. [178] In my study, patients that reported experiencing frequent side effects or fear of addiction reported refraining from taking their prescribed opioid. This finding was more consistent with previous findings that patients were more likely not to take their prescribed opioid if experiencing side effects or if they had certain beliefs about medications. [177]

It is possible that non-adherence or overuse of opioids is partly due to the possibilities that opioids are not effective in providing adequate pain management. This finding is consistent with what was expected.

Arbitrary behavior is an unexpected finding, and it is unclear why a patient would continue to demonstrate such behavior so consistently. It is always a possibility that participants may not have been honest in reporting of non-adherent behaviors, which may account for these unusual findings.

Interestingly, participants that reported experiencing less stress adhered better to their prescribed opioid regimens. This result is consistent with other studies showing that higher levels of depression consistently predicted poorer adherence. [179] It is possible that such findings would have been statistically significant with a larger sample size.

F. **Physician-patient relationship**

In my sample, some SCD participants indicated that adherence to prescribed opioid regimen improved their relationship with providers while others expressed how their providers helped them to improve adherence. The impact of patient-physician relationship on opioid adherence was modeled and studied previously in literature. This body of literature has shown that a strong relationship may promote adherence and improve outcome. [180]

III. Domain 1 Findings: The effect of pain and its consequences on biopsychosocial-spiritual function in patients with SCD

In Domain 1, patients reported their perception of the impact of pain in their lives. Firstly, patients explained that their pain caused mistrust by physicians caring for them (especially in emergency situations). Patients also described their pain differed when they

lived in cities with specialized sickle cell care. This perception could be due to the stress of living in an environment without appropriate facilities or treatments, which are not as advanced or effective as cities equipped with specialized care. As previously described, my qualitative interviews about pain in SCD suggest simultaneous effects of numerous explanatory factors bridging multiple domains from individual care to healthcare policy. The implication of these findings is that interventions affecting numerous aspects of the patient's life will be required to improve the pain of individuals diagnosed with SCD.

IV. Domain 2 Findings: The effect of prescribed opioids on biopsychosocial-spiritual function in patients with SCD

Based on my qualitative study, participants reported positive, negative, or variable effects of prescribed opioids. Here, *variable effects* refer to those effects that may be perceived as positive in one situation and negative in another. The same effect can be viewed differently by individuals in different circumstances. Example is that side effects of medication cause patient to stay home. Some patients view this as positive (not going to the ER), whereas others view it as negative (isolation from friends and family).

Because multiple resources in the literature pertaining to opioid use focus extensively on the biological impact of opioids, [177] there exists a paucity of research regarding the impact of prescribed opioids on other life aspects that affect overall well-being. These life

aspects may be divided into five main domains: Biological, Psychological, Social, Spiritual, and Miscellaneous (Extrinsic Factors). Furthermore, there exists cross-classification (e.g., Psycho-social, Bio-Psycho) for some facets of life. One example of a multi-class life aspect would be work. Work has psychological (sense of achievement on self-esteem), social (sense of camaraderie with coworkers) and miscellaneous (financial) components that may be affected by opioid usage. There are also some strong inter-domain drivers: the *social* stigma of shame and past negative experiences with taking opioids in front of others may drive psychological appraisal of one's illness as well as how they feel their medication is best taken. This would in turn affect their behaviors.

As a note, the Miscellaneous (Extrinsic Factors) domain serves as a gray area placeholder, where the appropriate domain fit is unclear for particular life aspects. These life aspects may still have impact on the other four domains. Financial impetus, for example, may not reside neatly into the biosocial-psychological spiritual categories; however it has a profound impact that changes responses within them.

In defining certain classifications, I recognize that some of these measures might be subjectively brought to attention by patient interviews, or subjectively judged by physicians. This further demonstrates the difficulty of defining a gray area.

One of the reported effects of taking opioids is that personal responsibilities are easier to meet. Although the perceived onset of action differs among my participants, most or all

agree that it lessened the burden and responsibilities of SCD patients.

A negative effect of taking opioids is that these patients must encounter those that abuse medications and their associated stigma. It is very likely that abusers of opioids attempt to use SCD patients for their medication and the SCD patients then are labeled with the stigma of being associated with that group.

A. **The effect of biological factors on other factors**

The physiological effects of opioids appear to be the main mediator of the indirect biopsychosocial-spiritual effects, consequently altering future opioid-taking behavior. Physiological mechanisms serve as the link between opioids and other factors affecting medication taking behavior. For instance, genetic predisposition that aggravates certain side effects may partially influence how an individual perceives his or her medication as well as the actions they take seeking or avoiding social interaction. For all domains, patients may intensify or minimize pain by genetic predisposition. [(181)] Therefore, opioid use is partially dependent on biological factors.

B. **Purity of the Model**

While a theoretical model may not explain every aspect of an individual's life, the domains included in this study can provide a framework for describing opioid taking behavior in SCD patients. Taxonomies serve to improve a general understanding and

classification taxonomy for future research. I believe that some aspects of these domains may fit into multiple domains. For example, vomiting and nausea are common side effects of opioids caused by *biological* stimuli. However, continued experiences with vomiting and nausea may cause an expectation bias that aggravates or reduces the side effects, therefore placing it partially into the *psychological* domain.

To my knowledge, this is the first research based on patient interviews that can inform the debate about the appropriateness of the use of opioids in SCD, and contribute to the foundation of evidence-based practice.

C. **Basis of Patient Responses**

There are four ways that a patient typically responds to a new, life-changing diagnosis and its associated treatment: integrate (blend with existing lifestyle), assimilate (change lifestyle to be like those of others patients), augment (assimilate and do extra treatment), and rejection (reject the treatment and any lifestyle changes).

V. Domain 5 Findings: Advice for providers and fellow patients

The participants were both verbose and consistent in their responses with regard to advice for the healthcare providers responsible for patients with SCD.

According to advice from my interviews; there was a nearly unanimous desire for physicians to *listen* to patients. This advice was presented from biological, psychological, social and environmental perspectives.

One participant stated that patients "know what kind of medications work for them". The perception here is that patients want more attention from physicians because they attest that they know their bodies and experiences best, and believe that their biological needs will be best met when their own opinion is taken into account. From a psychological perspective, there is a high level of self-worth, the patient strongly believes he or she is correct and wants that validation by his or her doctor. Statements like this allude to the possibility that patients are dissatisfied with the relationship they have with their physician, and therefore, do not trust the care-giving environment.

A recurring theme in the interviews is that those experiencing pain are most aware of how much medication they need. One participant suggested that physicians "[u]tilize patients' experiences and perspectives about SCD . . . in prescribing which opioid agent, dose, [and] frequency is most effective for them." Statements like this suggest social and environmental dissatisfaction with the amounts of prescription prescribed by physicians. This also presents the desire to further the patient-physician relationship. Patients furthermore appear to believe that many physicians do not trust them, and fearing drug abuse, limit their prescriptions.

Another common response was that patients want to be trusted by their physicians. Many patients believe that they are not trusted and that they are denied the dosages needed to effectively treat their pain, because physicians believe they will abuse the opioids. Patients attest to this abuse with "stories about selling prescribed opioids" in which patients would relate that other individuals would misuse their prescriptions. Perhaps this is to defend themselves, but the acknowledgement here is that if physicians listened more to what their patients wanted and made accommodations based on individual visits and histories, there would be less abuse than the perceived "blanket dosage" which assumes that standard amounts of narcotics are effective for various individuals with different levels of pain.

In order to improve physician-patient relationships, it would be beneficial to provide more dosage options and reduce outward suspicion towards clients. There appears to be a general consensus among the participants of this study that the people who will be benefitting from taking medication feel that they are under the scrutiny of caregivers. (180)

Interviewed patients were asked to give advice to others living with SCD. Advice was given in the realm of biological, psychological and social domains, with emphasis placed on the effect of medication on one's spiritual life and the interconnectivity of all realms of a patient's life and wellbeing. Responses reflected knowledge of interviewees regarding how their disease worked (presumably from education at the clinic), and was a

reflection of awareness regarding perceived efficacy of reducing pain caused by SCD. Several items were dedicated to urging fellow patients to take medication as indicated.

VI. Other Important Findings Related to Domain 3:

A. **Preferences for taking prescribed opioid based on pain intensity**

Previous studies showed that use of prescribed opioids depended mainly on pain intensity; [49, 50,171, 172] however, in my study, SCD patients vary in their preferences for when to take their prescribed opioids. Some reported they preferred to wait until reaching high levels of pain intensity before taking the initial dose, some will take prescribed opioids for any mild or moderate levels of pain (either for momentary pain or in prevention of pain escalation), while some take prescribed opioids in anticipation of pain. This behavior may be due to a variety of reasons. Some may simply not like taking medications. Others may believe the pain will subside on its own; others may not want to deal with potential side effects at the moment; others may not be thinking clearly because of the pain and medications already in their system. Behaviors may vary from physician and patient expectations even with office visit counseling. Theory and practice may rarely coincide so the physician and researcher may want to anticipate such behavior as normal. Understanding this may help practitioner avoid frustrations of what may seem to abuse or abnormal behavior. Also this will help the researcher design and implement educational programs for physicians and patients.

B. **Beliefs about how opioids work**

Some patients, who reported taking prescribed opioids upon initially feeling mild pain, believe that taking the medication immediately will provide more rapid relief than when taken at a later point in time or upon more severe pain. In contrast, other patients that reported waiting some period of time before taking prescribed opioids believed that they do not yet need them and consider taking opioids upon early pain onset as misusing them.

This belief may be derived from the concept of loading doses in the initial stages of pain management to prevent severe pain later: as indicated by one patient, a nurse taught them to "nip pain in the bud". The concept of loading dose is common in areas where effective drug doses have a narrow therapeutic index (anticonvulsants, aminoglycosides, etc) but not in pain management. [182] Anecdotally, I have observed the benefits of administering high doses at the beginning of pain to decrease opioid use later. This may also lead to decreased medical costs (decreased ED/hospital visits) and increased quality of life.

A pain management researcher may adapt this concept in hospital and ED setting. A practitioner may consider this in the hospital/ED and may encourage patient in outpatient settings within prescribed guidelines use the concept of loading dose when crisis hit.

C. **Intentional non-adherence in taking prescribed opioids when severe pain arises**

Patients reported deliberately not adhering to their prescribed opioid regimen by taking more when having excruciating pain. These patients openly admit to non-adherence with respect to their prescribed opioid regimens and justify their actions as normal behavioral responses to pain. This may indicate a common practice in which patients are not concerned about possible negative repercussions because they know themselves better than the physician. As stated earlier, the combination of pain and medications in patient's system may prevent logical thinking. Practitioner may need to understand SC pain is different from other non-cancer pain in quality, regularity, and intensity, thus these behaviors are not indicative of aberrant behavior. A researcher may consider future research to explore this behavior and how to use it effectively.

While this is not the effective dose, patients preferred having higher strength of prescribed opioids in order to avoid prematurely running out of their medication and/or to exert more precise control in adjusting their dosage.

D. **Taking Several Short-Acting Medications Simultaneously**

Observed clinically and supported by my qualitative interviews, patients typically classify pain by severity and may ask clinicians to prescribe additional, alternative opioid medications by type of pain so that they may tailor their pain management plan of using prescribed opioids. As a result, routine practices of pain clinicians in my clinic involve prescribing multiple opioid medications so that patients may somewhat individually tailor

which agent to use based on intensity of pain, in order to allow for personalized, patient-centered care. For example, clinicians may advise patients to use Percocet for mild to moderate pain and save Dilaudid for severe pain. Based on pain severity and their preferences, many participants autonomously adjust their use of different opioid agents. Interestingly, my interviews revealed that some SCD patients take various short-acting prescribed opioids simultaneously. This is due to the mistaken belief that different prescribed opioid agents will work synergistically in relieving pain. The converse is true; these short-acting medications compete mainly for the same opioid receptors. Thus, patients decrease overall efficacy of their prescribed opioids. Although there is no theory to support taking more than one short-acting med simultaneously, patients report pain relief not achieved with one or the other medication individually. The practice may be due to subjective effect attributed to the combined effect of the short acting medications. All opioids work the same in theory but patient response varies for a number of reasons. Again, further basic and clinical research may be required to explain this observed finding. A practitioner may want to be aware that patients may explore unconventional regimens and are achieving successful outcomes.

E. **Use of OTC and herbal medications in addition to prescribed opioids**

In my study, some SCD patients reported using over-the-counter (OTC) medications, such as Advil, Motrin, and Tylenol, along with prescription opioids for different reasons. First, these patients want to avoid the negative biopsychosocial side effects associated with taking high doses of prescribed opioids. Second, some patients are aware that OTC medications work using different mechanisms and wish to attain more complete pain relief by using a combination of OTC medications and prescription opioids. Third, some patients exhibit a negative attitude toward prescription opioid use, so they try to use OTC medicines in minimizing use of opioids (though they must occasionally use prescribed opioids despite their reservations). Previous studies have shown potential interaction between opioids and herbal medications. Effects of one or the other may be intensified or decreased. Practitioners may want to have this information readily available for their patients that take herbal or OTC medications. In practice, a table may be developed to insert in patient chart to assist practitioner and patient. A researcher may help develop table of the most important interactions with the most commonly prescribed opioids.

F. **Efficacy and satisfaction of prescribed medications**

Throughout the interviews conducted, patients exhibited various levels of satisfaction with their prescribed opioid regimens. Most patients felt satisfied with their daily regimen with exception of times of excruciating pain, while a few were partially dissatisfied and

suggested changes to their prescribed opioid regimen. Based on my sample size, I would not claim that that this is a valid, reliable and representative method of measuring the satisfaction of opioid efficacy in the general SCD population. Nevertheless, from my data we reached the following conclusions: a) opioids are working in this subset of patients, b) their regimens are effective, and c) practitioners are meeting the patients' needs. While few patients were unsatisfied, it is important to understand why in such cases. Usually it is because the regimen is not working. The cause of the ineffectiveness should be determined and addressed by practitioner. It is also possible that patient expectations are too high, that side effects have increased, their bodies have become tolerant, or other reasons. Accordingly, practitioners may need to routinely evaluate the efficacy of the regimen. Continued research is important to explore better ways of measuring satisfaction and reasons for satisfaction.

G. **Initial responses to pain**

SCD patients in my sample expressed different ways of initially responding to pain. Most patients would prefer to take their prescribed opioids simultaneously with home remedies (heat, bath, sleep, deep breathing, etc.) because they attribute their practice to "nipping pain in the bud." This refers to their practice of stopping the pain before it escalates and becomes unbearable. Some prefer trying alternative remedies (such as herbal supplements and OTC medications) before resorting to stronger medication such as prescription. A few patients addressed waiting until reaching severe pain because either

they misjudged the quality, escalation, and type of pain or they are not ready to take the medication due to pending duties or responsibilities. Very few patients reported taking prescribed opioids first due to past experiences of failure with the other initial responses to pain. Future research needs to determine why SCD patients responded differently to initial pain and determine whether it is attributed to genetic, biological, or psychological etc. factors. With proper research, I could predict how people may respond to pain allowing practitioners to better prescribe effective regimens including opioid and non-opioid therapies.

H. **Reasons for Waiting for Initiating Medication Use**

SCD patients in my qualitative phase conveyed reasons for waiting in initiating medication use. Often there was dislike with regards to biological side effects (e.g., hallucinations and uncharacteristic/atypical actions). Several patients indicated safety concerns (e.g., driving while experiencing hallucinations) as a reason for deferring medication use, while others indicated reluctance in becoming a burden to family members (i.e., family members have to give more attention to the patient). It is possible that reasons for delaying initial use of meds has more to do with avoiding side effects and negative consequences than achieving pain relief. Sometimes patients consciously choose to endure pain in order to continue working, driving or to fulfill other duties. Further drug research may be indicated to discover agents with the efficacy of opioids but free of side effects. Perhaps modifications of a current entity or a new moiety altogether

will help. When prescribing, practitioners may consider sometimes pain management may not be the patient's primary goal. Depending upon the intensity and quality of pain, pain management may be secondary to other responsibilities and duties. The ultimate goal of therapy (drug or other) is to increase quality of life. It should not be assumed that quality of life is increased only by decreasing pain when so many other factors may be involved.

I. **Refraining from Taking Prescribed Opioids When Having Mild Pain:**

Some participants in my study considered taking prescribed opioids for mild pain as an unsafe nuisance whose disadvantages outweighed the benefit of alleviating mild pain. They would express annoyance at how opioids would change their "system" (biological, lifestyle, behavioral, psychological, and social life norms) and present more of a danger than a safeguard. Reasons as reported by participants for such behavior were: a) fear of opioid dependency, b) concern about side effects and toxicity, c) wariness about taking the medication earlier than prescribed and being perceived as an opioid abuser, d) excessive worry about harmful effects of opioids, e) believing the opioid needs more time to take effect, and f) having a negative attitude towards taking opioids. For example, some participants repetitively expressed, "I'm not the type of person who takes medication easily." As stated previously, other factors are involved in patient's quality of life not pertaining to pain relief. Researchers may want to further define these factors in future research. For example, "What is quality of life and what factors contribute to in in

patients with SCD?" It is easy for practitioners to focus on pain relief and may lose sight of these other factors when prescribing. Practitioners may want to have such a conversation with their patients periodically and use the results to help develop individual regimens.

J. **Reasons for Waiting Before Taking Subsequent Doses:**

Some participants in my study described a number of unusual (curious) behavior in which they try to maximize the interval between doses by waiting as much as they can tolerate until they reach the level of unbearable pain and feel "really need it [medication]." The reasons behind this behavior were similar to reasons mentioned for refraining from using prescribed opioids. Those participants who exhibited such negative attitude often described reluctance, hesitation, or avoidance to taking their medication at all.

K. **Reasons for Taking More Prescribed Opioids in Terms of the Recommended Interval between Doses**

On the other hand, some participants will increase their intake of prescribed opioids during periods of unbearable/intolerable pain due to the stress of being in pain for a long time. They may perceive excessive pain as a medical emergency that triggers a 'fight-or-flight' response and fight the pain using more of their medication. Some of the

interviewees justified decreasing regularity of the time intervals between doses of opioids by pitting the severe, excruciating pain against beliefs that more frequent dosage of medication would not cause more harmful/toxic effects and side effects experienced would be tolerable/acceptable. These participants were much more at ease with modifying their drug regimen and were more liberally lenient with their prescribed opioid use. As discussed earlier, excruciating pain in combination with effects of meds already in patients system may lead to unclear thinking. Patients that would not normally take frequent doses may do so under the influence of pain and meds. Researchers may consider trying to determine at what point does pain relief becomes the determining factor in quality of life in patients with SCD. Such research may help explain these unusual behaviors. If practitioners had this information readily available, individualizing therapy may become easier.

L. **Self-Gratification and Taking Advantage of Opioids (Self-Enabling Behavior)**

Some participants hold a flexible range to themselves about the acceptable amount of medication that they may take because of the availability and accessibility of their prescribed medications through their physicians, and because of looser personalities. They try to self-gratify their want to be painless without exerting self-control or constraint and show inconsideration towards clinicians' instructions and their health. This epicurean/self-enabling behavior may occur without physical craving to taking medication. Some SCD patients use their disease as a justification for taking opioids.

Their experience has shown them they are capable and may even require a higher dosage than a "normal" person. Some patients exhibit pride in the ability to take more meds than others. It is similar to the pride some have at being able to "drink others under the table." Some of this is tolerance, while some may be a psychological issue peculiar to SCD patients. Research may be indicated to ascertain how this relates to appropriate treatment of SCD.

M. **Impact of Prescribed Opioids on Family Members**

SCD patients reported different stories and anecdotes regarding how they became a burden to their families while under the influence of the prescribed opioids. Additionally, they described this bothersome nature; some said that their families felt scared, concerned, and anxious about their medication use. A lot of time is spent educating patients and practitioners about appropriate therapy when using opioids. My results show the possible need to educate families also. Little research has been are done on the effects of opioid use on family members. On the surface, the effects seem similar to that of family members of addicts and alcoholics. On a deeper level, the sources of shame, for example, are different because addiction may involve illicit activities. US culture looks down upon addicts or alcoholics for various reasons. Some may be shared by family members of SCD patients, while other reasons are unique to this subset. Though sickle cell disease is recognized as a disease (some still argue the point regarding addiction), the African American community has its own issues of shame concerning this disease. If

SCD patients are not taking their opioids appropriately because of the reaction or perceived reaction of family members, investigators may want to examine these phenomena more closely. Practitioners may want to take into consideration family dynamics when developing patient regimens. Similar situations exist with other disease states. For example, new diagnosed diabetics may have family members trained to administer insulin if the patients are considered unable to give themselves the medication. The same may be true for some SCD patients and their families.

N. **Downward Social Comparison**

Some of my SCD participants exhibited the phenomenon of *downward social comparison*. This refers to their tendency to compare themselves to others whom they believe are in a worse situation in terms of health status in order to separate themselves from perceived stigmas associated with other SCD patients and improve their feelings about themselves and their health condition. This concept was introduced by Wills in 1981 [ref]. For example, some participants took a moral high ground, repeatedly stating that they would not abuse or take advantage of their prescribed opioids like other SCD patients, and assert or claim that many other SCD patients typically *do*. The shame of SCD in the African American community was mentioned in detail in earlier point. If SCD patients are not taking their opioid med appropriately due to this phenomenon, research may be indicated. Promising oneself to never abuse opioids to prevent appearing as someone who is an abuser or perceived abuser may make oneself feel better

than someone else. The fact is, no one plans to become tolerant/dependent/addicted. It is easy to promise oneself never to take opioids inappropriately when one is well but it may be more difficult during a crisis. I have already mentioned the effects of excruciating pain and the effects of meds in the patient's system on adherence. I have also briefly discussed the stigma within the African American community. These may be issues for psychologist/sociologist to examine further in hopes the results may guide practitioners.

O. **Comparing Personal Use of Opioids to Others**

In addition to asserting their differences to other SCD patients, some interviewees also cited similarities and comparisons to other SCD patients, cancer patients, and patients with non-cancer pain. When asked about whether they perceived they take higher or lower doses of prescribed opioids than cancer patients, many participants said they were prescribed similar drug regimens. Meanwhile, others stated that they felt or thought they took more pain medicine relative to any other set of patients with cancer or non-cancer pain. I am not sure why some perceived their dosage more different than other subsets of opioids users and what they are basing their responses on. Possibly, it is an assumption about how they perceived their health status. It is also possible that they have a relationship with someone in those other subsets of SCD patients who use less or more of prescribed opioid. It is possible that it is the result of downward social comparison or other phenomenon. This may be an issue for psychologist or sociologist to examine in hopes of guiding practitioners.

P. **Prescribed Opioid Consumption During Crisis Days**

Although many SCD patients inconsistently consume prescribed opioids along typical days with or without pain, most of the prescribed opioids are heavily consumed during unpredictable crisis days. The BPSS situations may be the source of this inconsistency in medication use. Further research need to investigate the in detail the full description and the source of the inconsistency during typical days. Researchers may need to address the allowable consumption of opioid during crisis days.

Q. **Uncertainty of How to Use Medication as Prescribed**

Along my interviews, I asked participants to recall the written instructions on their pill bottles and the doctor's verbal instructions. I found that many patients were uncertain about the number of pills to be taken per dose, the frequency of doses per day, the interval of time required between doses, the maximum allowable doses per day, and the acceptable agents to be used concomitantly. This could imply that the non-adherence found in my sample to pain medicine regimens could be attributed to this partial uncertainty of how to use the medications.

Non-adherence due to patient’s inability to follow practitioner’s instructions is not uncommon. I am not sure if these issues any different than patients of other disease

states. Therefore, I cannot attribute the problem to SCD. Researchers need to further investigate if these issues are different in other disease population. In future research, I can determine the rate of non-adherence due to lack of understanding practitioner's instructions in this population and compare it to other studies.

R. **Variability of prescribed Immediate-Release Opioids**

In my sample, the highest frequency (number of times a day) of taking immediate-release opioids reported was 12 times a day, the lowest frequency reported was 0 times a day, and the average frequency was 8 a day, which does not correspond to the average number of times actually prescribed. This variability represents a form of non-adherence. This form of non-adherence may be attributed to different pain severity and experience among participants.

S. **Changing Regularity of Taking Prescribed Opioid**

Regularity of taking medication is defined as a description of a way of taking medication with regards to taking medication as-needed or on a fixed schedule. Surprisingly, some participants naïvely use their as-needed opioids on a regular, fixed schedule instead of taking them as required (based on their episodic judgment and perception of level of pain).

1. Misunderstand, "dunno"

For some of those patients who reported taking their as-needed medications with set intervals of time between doses, this behavior could be attributed to their lack of knowledge in how their immediate-release opioid should be used. Moreover, such unawareness could happen as a result of miscommunication among physicians, pharmacists, nurses or patients. This may be due to past experience. If patient knows opioid will last 4 hours, they may naturally set-up a schedule of taking medication every four hours to prevent the possibility of future pain. Has anyone asked the patients why they do this?

2. Pain Avoidance and Pain Anticipation (Premonition)

For some other patients, as-needed pain medication was taken regularly in anticipation of pain. Whether this anticipation was as a result of feeling an "aura" and preceding signal, fear of unpredictable pain, fear of consequences of pain, or other fears (e.g., nosophobia, thanatophobia), the result of such feelings was exaggerated pain avoidance leading to overuse of immediate-release opioids.

3. Dependence

Unknowingly, some patients may start to become dependent on their prescribed opioids through the nature of sickle cell anemia pain in terms of quality, intensity, regularity, and frequency, as well as the physical dependence on taking opioids for pain management over an extended period of time. This emerging dependence behavior may be naively founded on good intentions by the patient in coping with the unique characteristics of SCD pain.

T. **Knowledge and Perception of Prescribed Opioids and Adherence**

My findings in this study indicate that patient knowledge and awareness may cause different adherence behaviors. As an aside, there is a cultural (familial, community, and governmental) show of little effort regarding attentiveness to medication and its most practical applications. Embodiment of this sentiment may ultimately result in sub-optimal care, lowered attentiveness from both patients and providers, and lower awareness of correct prescribed opioid usage. Some patients are aware of the risks involved with taking opioids, including side effects, toxicity, and risk of dependence, and some pharmacological aspects (onset and duration of action). Practitioner may want to keep in mind the role of different source of knowledge in non-adherence. How many to take, how often to take and the impact of opioids? Non-adherence in SCD may be due to different reasons than that of non-symptomatic disease states such as diabetes and/or hypertension. For example, the pain of SCD is a reminder for the patient to take their pain meds. If a diabetic forgets their oral medications, they probably will not have

symptomatic signs to remind them to take the meds. Practitioners may want to keep in mind not only the typical causes for non-adherence but also the motivation provided by the desire for pain relief plus the unwillingness to endure side-effects as mentioned earlier. Therefore practitioner needs to educate their patients of the importance of taking their meds as instructed especially during a crisis.

U. **Types of Patient Attitudes**

Based on my qualitative study, participants exhibited attitudes towards two facets of taking opioids: (1) general associations with medicines, and (2) specific associations with opioid medicines. An ambivalent to negative attitude was prevalent among general associations with medicines, as participants would describe wanting to limit the amount of (harmful/unnatural) chemicals going into the body. This attitude was extended towards physical aspects, such as difficulty in swallowing the large opioid tablets, or social aspects, such as public and self-perception of dependency on a drug. On the other hand, specific associations with opioid medicines imparted much stronger positive or negative outcome attitudes. Experiences with biopsychosocial effects, for example, drowsiness and possibility of addiction, daily functioning, and social stigma, often polarized participants' attitudes.

Ultimately, associations with both prescribed opioids and medicines in general, such as those outlined above, form an overall opinion towards taking prescribed opioids. This, in

turn, may affect patients' final opioid-taking behavior until new experiences alter existing attitudes.

My participants showed 4 different types of overall attitudes towards prescribed opioids:

(1) Positive (mild to extreme)

Ex: I have no problem using prescribed opioids and medicine in general, and favor use of prescribed opioids for their biopsychosocial effects.

(2) Negative (mild to extreme)

Ex: I do not like using prescribed opioids or medicine in general, nor do I support use of prescribed opioids for their biopsychosocial effects.

(3) Ambivalence (weakly or strongly)

Ex: I do not like using prescribed opioids and am OK with using medicine in general, but do not mind use of prescribed opioids and medicine in general because I need them to function.

Ex: I am OK with using prescribed opioids and using medicine in general but do not like their biopsychosocial effects. However, I do not mind use of prescribed opioids because I need them to function.

(4) Apathy

Ex: I feel indifference towards prescribed opioids and medicines in general.

Interestingly, my qualitative results show that the positive, negative, and ambivalent attitudes affected opioid-taking behavior among my participants. I observed that positive

and ambivalent attitudes were more likely to stay strictly adherent to the prescribed regimen. Regardless, these behaviors were still prone to non-adherent behavior (overuse and/or underuse). Some participants with positive attitudes tended to experiment with their opioid-taking behavior, while some participants negative attitudes tended to abstain from opioid-taking behavior. Furthermore, some participants expressing ambivalent behaviors were prone to erratic opioid-taking behavior, sometimes taking more and sometimes abstaining from prescribed opioids.

V. Origins of Differences in Attitude Regarding Prescribed Opioids and Adherence

Many participants showed a negative and hesitant attitude towards prescribed opioids, while a few had a greatly positive and enthusiastic attitude towards taking prescribed opioids. On the other hand, many participants also described different attitudes among healthcare providers. Further research is needed to investigate the reasons behind differences in attitude among SCD patients.

W. Frequent Episodic Judgment and Mental Fatigue

Frequent decision-making may result in mental fatigue in SCD patients. Because SCD patients must cope with chronic pain on top of daily activities and life events, the process of judging whether or not to take pain medicine is a complex one that stresses mental

faculties. The strain of constantly having to make such decisions based on a variety of factors (e.g., to take medication or not, judge the level of pain, which medication to take, how it will affect other activities, amount of prescribed opioids left, etc.) may lead to a hands-off approach in which SCD patients use their as-needed medication on a regular, timed schedule in avoidance of continued decision-making. As an additional note, this is a misuse of medication and form of non-adherence to doctors' instructions.

Decisions of this type may also be clouded by desperation to lessen pain, due to the unique nature of SCD pain (i.e., excruciating pain over an extended period of time without break). Such pain may cloud judgment when making decisions, and create situations in which the patient may become unreliable or careless when determining which medication to use, or whether or not to use opioids. Furthermore, use of opioids may itself cause judgment impairment through its possible side effects (feelings of euphoria, vomiting, etc.) that positively or negatively affect personal bias towards using prescribed opioids for pain. Other effects of opioids and excruciating pain may cause patient to forget when they took the last dose. If patient cannot remember when they took the last dose and they are still in unbearable pain, they may take a dose earlier than prescribed. I must also consider the fact that some patients may be using illicit drugs to control pain or other reasons which play a role in inhibit the appropriate thinking process.

X. **Wanted vs. Unwanted Euphoria**

Surprisingly, I found a contrast within my sample in which some participants desired the euphoria that sometimes accompanies opioid use, while others disliked it and found this euphoria as an annoyance or hindrance that negatively affected their norms of living. This may be attributed to the various forms in which different people experience euphoria. [177] Unsurprisingly, because some patients enjoy their feelings of euphoria, they may be either diverging their opioid use or at risk of diverging. Although euphoria is a well-known signal used in assessing aberrant behavior, patients may begin unintentionally associating feelings of euphoria and painlessness and create a behavior in which habitual pain management is linked to a habitual high. Patients may also perceive that they deserve the painlessness that is common among people who do not experience SCD pain. Furthermore, because there is variation in descriptions and desire of euphoria, use of euphoria in assessing aberrancy is questionable as a determinant signal.

Y. **Routinization of Taking Medicine**

Many of the interviewed participants reported routinization (i.e., linking use of medication with a specific habitual time, environment activities of taking their medicines. For instance, some participants would take long-acting medicine upon waking, getting home from work, while watching television, before going to bed, or taking the long-acting medicine concurrently with short-acting medication. Routinizations were generated by different situational prompts: time-specific (e.g., in the morning), context-specific (e.g., when in more pain than usual, while watching television), or situational-

time-specific, a mix of the two (e.g., in the evening after work or at the end of the day with few responsibilities). Interestingly, short-acting medicine received much of the same treatment; the same type of routinization took place based on time, context, or a mix of the two: taking medicine upon waking, getting home from work, while watching television, before going to bed, while taking long-acting medicine. Routinization of both medicines (long-acting and short-acting) may imply habituation of taking prescribed opioids as a perceived means to remind and guarantee proper opioid taking behavior/adherence and decreased need for frequent pain judgment that would result in mental fatigue. Routinization of long-acting opioids will eventually reduce the use of short-acting medication.

Z. **Prompts for Taking Medications**

Some patients may not routinize the medication-taking behavior, but they may unintentionally link spontaneous or habitual events to medication. Overtime, they condition themselves to associate particular circumstances with taking medication, similar to Pavlov's experiments regarding reflexes and conditioning (Pavlov's dog). For instance, many of my participants would link medication to waking the morning. Likewise, awakening in the middle of the night would trigger one participant from my study to take a dosage of medication whether or not the wakefulness was due to pain. This may be linked to past experiences when they did not take their meds after awakening in the middle of the night but later suffered a crisis. As for taking upon

awakening, it is possible that some patients may feel as though they been without it all night and need to get it into their system to feel normal to prevent feelings of withdrawal.

AA. **Behavioral and Physical-Chemical Experimental Non-adherence**

Participants described different ways of modifying/altering their medication-taking regimen; I have classified these methods under two main groups: physical-chemical non-adherence and behavioral non-adherence. Physical-chemical non-adherence refers to altering the physical and/or chemical characteristics of the dispensed dosage form of the prescribed opioid. This can be further sub-classified into the context of the alteration: pre-, post-, or during administration. Participants reported crushing long-acting tablets before swallowing the tablets (pre-administration), applying heat to skin after putting on Fentanyl patches (post-administration), or swallowing tablets with alcohol or any other solution that may change its physical-chemical properties (during administration). Behavioral non-adherence refers to the deviant patterns of taking medication as prescribed. For example, participants would report taking more or less pills per dose or changing their frequency of taking medicine from what was prescribed. It is possible that some patients express the need to "boost" the effects of their opioids. Whether this phenomena is physical or behavioral remains to be determined. It may be different for each patient. It may also be some combination of physical-chemical and behavioral. "Boosting" the opioid may be an indicator of addiction or ineffective pain management.

BB. **Types of Behavior**

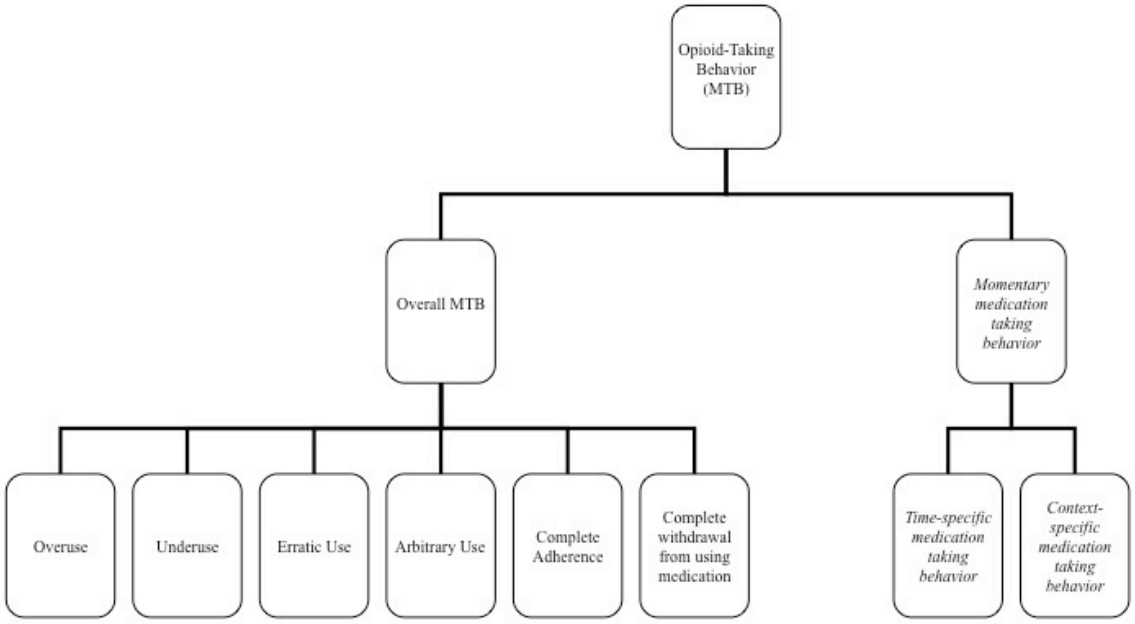
Qualitative thematic analysis uncovered several patterns of opioid-taking behavior and several related biopsychosocial-spiritual phenomena, some hypothesized and some not. The main three phenomena are 1) SCD patients exhibited various opioid-taking behavior patterns including adherence, overuse, underuse, and erratic use 2) A wide variety of biopsychosocial-spiritual factors hindered or motivated opioid use: pain intensity; side effects; fear of addiction; perceived stigma or judgment by others; senses of responsibility, productivity, hopelessness, or obligation; stress; social role pressure; social desirability; bullying; and anticipatory fear of adverse outcomes; and 3) Behaviors varied based on the time of day, week, month, or year, and based on context at times of doses.

My results raise the hypothesis that, for opioid use in SCD, either of these behaviors (overuse or underuse), and presumably all six categories of behavior, including erratic use, overuse, underuse, adherence, erratic, arbitrary, and complete withdrawal, may be intentional or unintentional. But I found few if any references describing unintentional and intentional use in all six behaviors I discovered in my qualitative study. For example, aberrancy has been defined as "Taking medication in a manner that is not prescribed, which may be because of addiction, pseudoaddiction, chemical coping, or diversion" [(51)] and also has been defined as "A behavior outside the boundaries of the agreed-on treatment plan which is established as early as possible in

the doctor- patient relationship. [52, 179] While non-adherence has been defined as "Any use of a medication by the individual to whom it was prescribed where the medication was not taken in accordance with prescription directions or where any additional specified conditions of treatment were not met". [52] Most of the adherence literature focuses on underuse while most of studies of opioid use focus on overuse. Further, medication-taking behaviors may be intentional or unintentional. Most of the adherence literature focuses on unintentional underuse while most of the addiction literature focuses on intentional overuse.

Another explanation for this finding could be that patients reported themselves to be more or less adherences than they actually were. Patients may have had a tendency to consciously and/or unconsciously want to show their treating physicians that they are adherent. This dissertation research probed for whether these six behaviors can be classified as intentional or unintentional, but the instrument I intend to develop will not itself be designed to determine unintentional vs. intentional behavior (See Figure 15).

Figure 15: Taxonomy of Opioid Taking Behavior in SCD



CC. **Forms/Ways of Behavioral Non-adherence**

Patients reported several ways of noncomformity when using their prescribed opioids. Their forms of noncomformity may be grouped in terms of (See Figure 16):

1) Amount per dose: increasing or decreasing number of tablets per dose
2) Duration of therapy: overall time period over which the medication is supposed to be taken

Ex: Taking long-acting prescribed opioids for 2 days a week

3) Frequency: number of times per day medication is taken

Ex: Taking long-acting medication 4 times a day instead of every 12 hours or taking the short-acting opioid 12 times a day instead of 6 times a day as needed

4) Time interval between doses

Ex: Participant would shorten wait-time before next dose of short-acting opioid (waits 1-2 hours instead of the recommended 3-4 hours)

Ex: Participant would lengthen wait-time until feeling excruciating, unbearable pain before taking medication (extreme time interval between doses)

5) Maximum allowable dose per day

Ex: Instead of maintaining a maximum of 12 tablets per day of Percocet or Tylenol III, participants will sometimes take 16 tablets, which exceeds the 12-tablet maximum allowable dose

6) Regularity: Changing the pattern or periodicity of fixed-schedule medication to use it as needed for excruciating pain, or using as-needed medication on a fixed schedule regardless of pain intensity

Ex: Establishing a fixed-schedule for short-acting (as-needed) medication; e.g., taking Dilaudid every 4 hours a day

Ex: Using long-acting opioids as-needed

7) Substituting: replacing a more efficacious medication for another

    1. Changing the type of prescribed opioid agent

Ex: Taking Dilaudid for any pain anticipation or mild pain instead of reserving Dilaudid for strong pain

Ex: Insisting on taking Tylenol III for excruciating, unbearable pain and refusing to receive stronger oral or IV opioids

2. Changing the class of pain medicine: There are different classes of pain medicine such as opioids, NSAIDs, and other classes of pain medicine

Ex: Using 400mg ibuprofen for severe, excruciating pain instead of using any type of opioid

3. Changing to a non-pain medicine: Changing from any class of pain medicine to other non-pain classes (e.g., adjunctive medicine) of medication to manage pain

Ex: Using antidepressants, anticonvulsants, muscle relaxants, alpha-2-adrenergic agonists, anesthetics, and/or steroids for excruciating, unbearable pain instead of opioids

8) Taking inappropriate, other prescribed, or OTC medications concomitantly with opioids

1. Two opioid agents concomitantly

Ex: Taking Dilaudid and Percocent concomitantly

2. One opioid agent and one non-opioid pain medicine concomitantly

Ex: Taking prescribed ibuprofen concomitantly with prescribed opioids

3. One opioid agent and one non-pain medicine concomitantly

a) Adjunctive pain medicine (e.g., prescribed gabapentin, carbamazepine

Ex: Taking tricyclic antidepressants (e.g., amitriptyline) concomitantly with prescribed opioids

b) Non-adjunctive pain medicine

Practitioner may want to keep in mind that SCD patients may have other ailments being treated by other practitioners. Therefore other meds used to treat other ailments may be in their profiles. It should not be assumed to be aberrant behavior. Practitioner should have a clear history of their drug history including meds written by other practitioners.

Ex: Taking cyclobenzaprine (Flexeril) concomitantly with prescribed opioids

4. Using herbal remedies, dietary supplements, and non-pain OTC medications concomitantly with opioids

Ex: Taking Capsaicin concomitantly with prescribed opioids

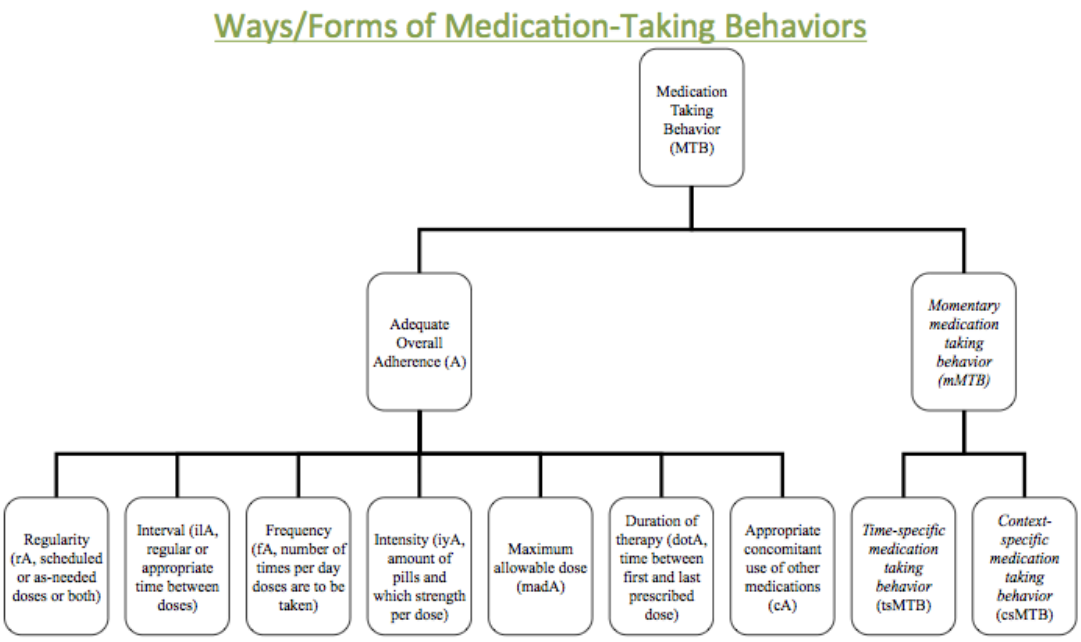
9) Off-prescription use

Ex: Valium or sleep-aid medication

10) Type of pain medicine prescribed

1. Various opioid agents with variable potencies,
2. Use of ER for pain management
3. OTC or non-prescribed non-opioid pain medicine [ex: Motrin, Advil]

Figure 16: Ways/ Forms Medication- Taking Behaviors



Some of the above forms of non-adherence may be due to factors previously discussed. e.g. pain and use of opioid may impair patients ability to make decisions. I found that adhering to all aspects of opioid prescription is problematic, with waiting interval period between doses being the most difficult to follow.

DD. **Medication Adherence and Forgetfulness**

Most patients reported different variety of situations of forgetfulness with regards to taking their medications. Sometimes they would forget to carry their pain medication on

outings, to fill the prescription, where they placed their medication, or to follow the fixed-schedule for their long-acting opioids.

1. Frequency of Forgetting

When I asked participants how frequently they forgot to take their medicines, I heard a variety of responses. Some of them said that forgetting is something they would never do, some said that forgetting was something that happened more often than not, and then some would say that forgetting was an occasional or rare occurrence.

2. Reasons/Context for Forgetting

Participants dealt with two main types of reasons for forgetting: activities-oriented and stress-oriented. Activities-oriented refers to forgetfulness that comes with rushing in anticipation of work or home duties, planned or unplanned business (e.g., appointments, meetings), or temporary situations of increased activities in which medication-taking habits are disturbed. Stress-oriented reasons dealt with extremes of stress. Any stressor (e.g., financial) would trigger forgetfulness; in contrast, extreme relaxation and merry or distracted (e.g., family gatherings, church) would also cause forgetfulness.

Another context of forgetting, some individuals not only forget to take their medicine, but rather they forget to have their medication on hand at all. These individuals may go for

days or weeks without filling their prescription. SCD patients must balance self-duties and self-satisfaction, but they may create an imbalance in which they push their personal needs to the side. An example of this is setting familial priorities (e.g., babysitting, driving relatives, or working) over self-care priorities (e.g., scheduling an appointment or driving to a faraway pharmacy ahead of time to fill his/her prescription). Such procrastination may lead to exhaustive pain, consequently leading to ER visits or hospitalization. This may also be due to patients being out of habitual contexts (e.g., on vacation) that would remind them of their medicine, or an untroubled behavior as result of negligence, carelessness, or absentmindedness. Thirdly, patients sometimes underestimate the amount of medication they need or overestimate the amount of time, prescriber availability/flexibility, and market availability of medications they have, leading to poor planning and medication management.

c. Most Common Time of Day

Participants repeatedly reported that morning time (i.e., getting ready for the day) and evening time (i.e., upon returning from work) were the most common times of day during which forgetfulness occurred.

d. Most Common Situation/Context

I found a common thread among situations of forgetfulness: Rushing. Throughout the day, sickle patients said that when they were rushing to appointments/meetings/work or having unplanned activities, they would forget to either use/utilize or carry their

medications. Patient may forget to take pain meds when they are not having pain. The pain could be a reminder to take opioids.

3. Strategies after Forgetting to take a dose

After forgetting to take a dose of prescribed opioids, participants exhibited four strategies with four subsets each. The four strategies are as listed:

1) Overcompensating: Increased dosage to "catch-up"

2) Undercompensating: Decreased dosage to ease medication back to steady levels of opioid amounts within the circulatory system

3) Taking no medication: Taking no dosage for an extended period of time

4) Maintaining same dosage: No change in dosage amount.

Each strategy varies with time of realization of the missed dose and time of the subsequent dose, creating four subsets. For instance, a patient may overcompensate upon realizing a missed dose, then either overcompensate, undercompensate, maintain, or altogether reject the subsequent dose. Additionally, patients who use the fourth strategy, maintaining the same dosage, may take two paths upon not taking the next dose: either wait until the succeeding dose to take the same dosage, or shift their entire fixed medication schedule to maintain time intervals between doses.

EE. Psychological and Emotional Aftereffects of Missing a Dose

Though missing a dose of medication may be a careless behavior, SCD patients in my sample often reported various feelings upon missing a dose: indifference, feeling "bad" (possibly guilt), and stress (fear and anxiety of the consequences).

FF. Effect of Anxiety, Fear, and Aura on Medication-taking Behavior

1. Classification and Differentiation

It is common knowledge that an "aura" sometimes precedes a migraine or epileptic seizure after a prodrome (early symptom or stage indicative of a disease before the disease actually occurs). Prodromes typically include feelings of being "off": for example, cravings, fatigue, happiness/sadness, upset GI symptoms. Auras for migraines or seizures are changes in perception: visual, auditory, motor-related, some emotional disturbance (e.g., fear), or an unexplainable feeling. For migraines and epilepsy, an aura follows the prodromal phase just before the actual migraine or seizure. However, such distinct phases with unique signs and symptoms for SCD may not be as exclusive as those for other diseases. Though any prodromal states and auras before crises have not been explicitly described or surveyed among adult SCD patients, participants in my study included an occasionally heightened signal when describing the timeline of a pain crisis. Despite a lack of visual and auditory "aural" symptoms among my participants, distinct

feelings of fatigue, weakness, nausea, mild pain, anxiety, or "still before the storm," an unexplicable "feeling," were described as signals before pain onset, mirroring auras of migraines and seizures. Prodromal symptoms and signs do exist: yellow eyes, pallor, enlarged spleen, sweating, fatigue, etc. Some signs may be those easily recognized by patients and their close support network, and some may be more recognized by their providers before the crisis. Furthermore, I could not classify some participants' descriptions as prodromal or aural (e.g., fatigue lasting for weeks before a crisis or within the half-hour before a crisis).

Like described prodromal auras for migraines and seizures, not all auras progress to crises and not all crises are preceded by auras. I will differentiate between those that do not progress as *independent auras* (as in the literature) and "true" auras that progress to pain crisis.

As with some other non-cancer (or pain-related diseases), fear is a central component to patients. My SCD participants reported fear of medicine, fear of opioids, fear of pain before, during, and/or after taking part in activities, fear of pain in general, fear of having a crisis, fear of consequences including fear of death, and fear of recurring pain.
Fear, as described above, may also be part of a patient's aura.
SCD patients sometimes panic based on the quality of pain due to anxiety and anticipation of severe pain. Some patients may also have a fear of opioids' side effects: one patient attributed the onset of a crisis and acute chest syndrome to taking prescribed

opioid medication. This may, however, also be linked to opioid-induced hyperalgesia, in which patients may experience heightened pain sensation and may imprint false feelings of impending pain.

In my sample, many participants described feeling anticipation, which is the expectation of pain based on the following: pain intensity, planned activities, type of activities, level of exhaustion, previous experience, unplanned activities (during the activity), and auras. Constant levels of anticipation are also common due to the recurring, chronic nature of SCD pain. However, while fear and anticipation do not necessarily go hand in hand and may be experienced singly, anticipation may stem from fear or unnecessary, exaggerated fear.

2. Effects on SCD patient behavior

i. Instantaneous pain vs. planning

Anticipation may be used by SCD patients to plan their day if they know they can trigger pain (e.g., doing yard work may cause physical exertion, and, consequently, pain) and treat accordingly, or may negatively affect SCD patients by scaring them into taking excessive opioids out of fear of crisis and/or nonproductively or, in contrast, into taking less or no opioids out of fear of addiction, abuse, medicines, or side effects, as well as productivity.

ii. Adherence vs. non-adherence

Opioid-taking behavior may be influenced strongly by auras, fear, panic and anticipation as patients may reason a holistic balance for themselves based on the different aspects of their lives. Fear and panic impact how a patient perceives medications, allowing one to rate a prescribed opioid as good or bad and act accordingly. Auras and anticipation may then alter how a patient plans ahead. Accordingly, the degree of alteration to prescribed opioid instructions may vary based on a feeling of what may come and what needs to be done to manage one's pain with regards to momentary and projected biopsychosocial circumstances. This ultimately results in adherence or different non-adherence behaviors, such as overuse and underuse.

Despite the influence of social desirability on reported adherence with regards to their provider (good doctor-patient relationship), reasons for adherence may also be strongly influenced by fears. Fear of termination from the clinic, fear of change, fear of addiction, fear of side effects, etc. may work in conjunction to steer individuals to strictly adhere to their given prescription whether or not the techniques of self-adjustment of pain using prescribed opioids is optimal (i.e., individuals resist the notion of dosage self-adjustment with regards to prescribed opioids).

GG. **Impact of Insurance 'prior authorization' on Patient Care:**

Some participants express inability to adhere to prescribed pain medication regimen because insurance refuse to approve the type and amount of medication necessary for treatment.

Prior authorization is a cost driven program that may apply to any type of prescription medications. Prescription medications subject to the prior authorization program require insurance approval before the insurance company will pay for the medicine.
Review and pre-approval Prior authorization programs are supposed to help encourage the appropriate use of medications and supposed to reduce the chances of unnecessary drug treatment and help contain overall healthcare costs. In addition, some insurance companies claim that by reducing the amount of pills approved per month they lessen the risk of overdose (intentional or accidental), misuse, abuse, diversion and addiction. The process of authorization delays the appropriate treatment for the patients. Continuation of current treatment is disrupted. Also, initiation of new treatment may be aborted. Both of these may result in visit to the ED and/or hospitalization.

Patients, who have an intolerance to multiple medications, even when they are from different classes of drugs, are more likely to be sensitive to a new medicine. The question remains: Why should a patient be forced to try a different pain medication just

because it is on the insurance company's formulary or available at a certain tier level so patient has a lower co-payment?

A change in the usual prescription for the patient's pain medications (including a change in the drug, the type of medication, the dose, or the quantity allowed for the month) may lead to an increase in the number of ED visits, hospitalizations, and misuse of their medicines. It also may lead to the development of drug-seeking behavior and a need to experiment with illegal substances in order to control their pain.

VII. Reasons for Momentary Change in Opioid-Taking Behavior (Reasons for Self-Dose Adjustment)

For those participants who took less or no prescribed opioids continuously or episodically, reasons from refraining from opioid use are listed in Tabel.1.

Here I found that SCD patients self-adjust opioid dose to control pain and attain a higher quality of life. Self-dose adjustments include medication adherence, taking more, taking less or a combination of both (overuse and underuse), or refraining or stopping taking medication. Patients' attentiveness in controlling their medication behavior and adherence to their medication regimen as well as consequences of non-adherence and opioid effects, that was clear in themes related to concern for personal safety, and change in lifestyle issues when using opioid. An explanation for my results is that patients receive adequate counseling about prescribed opioid. I believe this is the case in local

practices. Most providers spend adequate time discussing opioid adherence and physical side effects. They also discuss other psychosocial-spiritual and safety issues related to SCD pain.

A. Biological

1. Pain Severity

Escalating pain severity from any level to an unbearable state often led to increased medicine use. This was done through increased frequency (shorter time intervals than typical medicine use) or through increased quantity (number of pills or number of medications).

Less pain than that on a typical day often led to neglecting long-acting and short-acting medication. Participants were often more willing to bear with the pain than to use medication in order to avoid future pain.

Pain projection also played a role in judging medication-taking behavior. Individuals would often vary their medication behavior over the day, based on either anticipation of future pain escalation based on prior experience(s), or based on the experienced pain progression up to when a medication judgment was made. Additionally, changes in weather or environment also played a role in determining

how individuals decided to take their medicine. Though many did not realize that these changes would affect their medicine-taking behavior, interviews revealed that several participants avoided changes in weather, took prescribed opioids in conjunction with changing weather/environmental patterns, or noted a previous experience where they should have taken pain medicine in response to a temperature change but did not.

A marked "warning pain" that signaled incoming severe pain was also indicated to be a notable factor when judging pain and its future course. Similar to the aura experienced by migraine patients, individuals who experienced and categorized this milder pain as a signal would often make a special effort to take short-acting medicine in anticipation and to ward off possible crisis-level pain.

Pain persistence marked by a long duration and no overall change either led to increase in medicine-taking behavior (greater amount, frequency, or shorter intervals), or to a state where individuals might simply endure the pain in hopes that it would go away rather than visiting a healthcare provider for an opinion after a couple of days. Extended duration of pain also sometimes led to disbelief in potency of the medicine --individuals experienced that their medication was no longer working or that they had acquired a tolerance for their prescribed opioid medicine.

Seeking comfort from pain was a primary driver when study participants tried different pain treatments. For those more willing to experiment, intentional non-adherence sometimes occurred when individuals tried physically altering their medication (ex: crushing), or taking multiple short-acting medicines simultaneously. These present a problem from a pharmaceutical point of view -patients either increase the rate of uptake of strong medicine into their body or unnecessarily use medicines that, instead of working synergistically, work in competition and reduce the efficiency of medicines used. Additionally, many participants were more willing to use increased amounts of over-the-counter medicines like Tylenol and Motrin rather than increase any dosage their opioid medicines in circumventing biopsychosocial effects of opioids, using the OTC medicines synergistically with prescribed opioids, or minimizing overall prescribed opioid use.

Most patients tried many methods of home remedies, including heat (ex: showers, hot water bottle, heat rubs), herbal remedies (ex: capsaicin), and rest, as an attempt at decreasing pain before resorting to prescribed opioids or in combination with prescribed opioids. This often occurs at the onset of pain, if circumstances allow, so that individuals may "nip the pain in the bud."

2. Effectiveness

Throughout the interviews conducted, participants exhibited various levels of satisfaction concerning the efficacy of their prescribed opioid regimens. Most individuals felt satisfied with their daily regimen with exception to times of excruciating pain, while a few were partially dissatisfied and suggested changes to their prescribed opioid regimen. Perception of "working" prescribed opioids also depended largely on biological effects of the medication. Participants reported an opioid not working if great side effects occurred with little pain relief, while most participants agreed that a short-acting medicine was easily felt when working (through pain relief and side effects like euphoria, disorientation). Long-acting medications were reported by most patients as probably working, but not easily felt. This often led to decreased use of long-acting medication, or non-adherent use of short-acting medicine instead of long-acting medicine.

3. Side Effects

Side effects played a great role in participant's willingness to use their medications at all. Most side effects experienced are fairly severe (ranging from euphoria to vomiting), and led to most participants' hesitancy but eventual use towards using medication. Uncertainty towards how a medication might change a participant's physical and mental faculties also led to decreased use as many individuals stressed over the possibility of tolerance, dependence, and/or addiction with continued prescribed opioid use. Overall,

however, participants regarded prescribed opioids as a necessary means of pain relief despite its drawbacks.

4. Drug-drug and Food-drug Interactions

Most individuals were at least somewhat aware of proper prescribed opioid use and possible drug-drug or food-drug interactions. Decreased possibility of dependence and higher levels of comfort with OTC medicines led to many participants preferring to use OTC or prescribed non-opioid medicines before beginning use of short-acting prescribed opioids. In addition, use of OTC medicines in conjunction with prescribed opioids was often used as a more comprehensive approach to pain relief, as they pain medicines work on different receptors. Many individuals who were comfortable with some amount of leniency in their prescribed opioid regimens were more likely to use combinations of OTC medicine, non-opioid pain medicine, and prescribed opioids to combat different levels of pain. This sometimes led to aberrant behavior, though typically combinations of pain medicine were used with prudence.

Most participants also reported taking prescribed opioid medicines with water only, while a few individuals occasionally took prescribed opioids with alcohol or herbal teas.

5. Other ailments

Some participants described taking prescribed opioids to combat pains from other symptoms (ex: arthritis pain), stress, and other symptoms, as they did with sickle cell pain. Other study participants described saving opioid medicine for sickle cell pain only, using other prescribed pain medicines, OTC medications, and home remedies to deal with more bearable pains.

B. Social

1. Accomplish school, work or household tasks

Accomplishing necessary tasks for school, work, and/or a household were often a high priority for study participants. This often led to decreased opioid use, as many individuals felt drowsy, sick, or euphoric as well as less focused after their short-acting medications took effect. This was a momentary judgment, however, as participants would sometimes take short-acting in order to focus on tasks at hand should they not be able to manage pain using sheer will, home remedies, or non-drowsy OTC medicines.

2. Maintain responsibilities/obligations - schedule/time management

Increased or adherent use of opioids was used to maintain ability to do necessary responsibilities and obligations such as babysitting or driving others. Many participants

would schedule initial or later doses with flexibility within their prescribed regimen to maintain work or schools schedules, or routinize their medication taking-behavior such that they described aberrant behavior without realizing it. For many participants, routinization of long-acting opioids was typical, while routinization of short-acting opioids was common among many, and often triggered by things like getting to work on time or upon arrival back home after work.

3. Rushing, Spontaneous Events

Many participants reported forgetting to take prescribed opioids with them when rushing to a social event or activity. Others reported that having to often rush to events or work led to keeping a stash of prescribed opioids with them at all times, or keeping them with others who would typically go to similar events (ex: mother). In addition, spontaneous events were also a cause for forgetfulness or this rushing sensation, leading to decreased opioid use (choosing to instead bear the pain) or keeping a separate stash of prescribed opioids at all times common to many individuals.

4. Social Gathering Dynamics and Judgment

While at a social event, changing group dynamics and possibility of judgment of character often led to changes in time interval of opioid taking behavior, or staunch opposition to any person who would suggest changes in opioid taking behavior. Many participants talked about taking opioids before a social event to prevent the possibility of pain or to avoid judgment by friends or workers who might see them. A few other

individuals strongly defended their apathy towards what others thought and defended their stance on taking medication wherever they went, so long as they adhered to proper opioid taking behavior as prescribed or as necessary for the pain.

i. Influence of others and resistance to lifestyle changes

In this study, I noted that many SCD individuals tried to present a more "normal" lifestyle to society, using OTC medicines like others, or by maintaining a lifestyle they see others doing (ex: taking no note of weather, doing heavy manual labor, etc.). This led to resistance in overall lifestyle changes for SCD (for some), or decreased or erratic use of long-acting medication due to feeling little to no difference. Many individuals were prone to comparing their medicine use to non-SCD family members or friends and using that as a key in judgment on whether or not to take medicine. Additionally, a few participants reported being reprimanded by family members on taking or not taking prescribed opioids as prescribed, leading participants to either rebel against suggestions or take them regardless of how the opioids impacted them or as prescribed. This, in turn, led to divergent increased or decreased opioid use.

ii. Response to life events

Noted earlier, prescribed opioids were used by very few participants to deal with stressful life events or emotions. For those participants who indulged in use of prescribed opioids in response to life events, increased use was momentary until normal schedules were reintroduced.

C. Psychological

1. Fear of future negative consequences (medical, side effects/behavior), future pain, or going to ER

Based on my qualitative study, participants exhibited attitudes towards two facets of taking opioids: (1) general associations with medicines, and (2) specific associations with opioid medicines. An ambivalent to negative attitude was prevalent among general associations with medicines, as participants would describe wanting to limit the amount of (harmful/unnatural) chemicals going into the body. This attitude was extended towards physical aspects, such as difficulty in swallowing the large opioid tablets, or social aspects, such as public and self-perception of dependency on a drug. On the other hand, specific associations with opioid medicines imparted much stronger positive or negative outcome attitudes. Experiences with biopsychosocial effects, for example, drowsiness

and possibility of addiction, daily functioning, and social stigma, often polarized participants' attitudes.

Many participants, females in particular, seemed to describe much more fear or worries regarding future negative consequences of opioid medication potency, side effects, odd behaviors, and negative stigma that could be imparted to their person or to their families. A few mentioned strange or behaviors or others taking advantage of them, and these patients ultimately less pain medicine/chose longer time interval between doses.

2. Mental Fatigue

Frequent decision-making may result in mental fatigue in SCD patients. Due to the constant necessity of revising pain and pain relief plans daily, many SCD patients reported routinizing their prescribed opioid taking behaviors. This is an increased use of short-acting, as-needed opioids and possibly builds unnecessary tolerance within individuals to their medications. Mental fatigue may also cloud judgment in patients, as many already expressed dislike towards having to deal with taking their strong, short-acting medication and were less inclined to make careful, cautious decisions regarding prescribed opioid use when in pain.

3. Perception of physician disbelief/misunderstanding

Many participants who distrusted physicians' opinions or felt that physicians were not listening to their points of view were more prone to experimenting with their regimens and taking more or less medication. These individuals tended to have a heightened sense of themselves (or felt they had a better understanding of their bodies) and often conducted independent research, typically on the internet, to better understand why their physicians prescribed certain medications and any possible adverse effects.

4. Need for strict adherence

For those participants who were more wary of overuse and possibility of addiction, and feared so, many reported strictly adhering to doctors' order. However, these mentalities also often led to increased use of prescribed opioids through routinization, or through underuse in thinking that "as-needed" was for only the most severe pain.

5. Availability, transportation, cost ($), insurance, or ER cost

Availability was a huge factor in participants deciding to hoard, use medication differently than prescribed, or take little to none of their prescribed opioid medication. Difficulties in transportation, affording prescribed opioids, lack of insurance, and the fear of an ER visit/cost often led to participants increasing use in effort to avoid an ER visit at any cost. Other patients would take less medication or cut tablets in half in order to make their medications last longer, often hoarding medication when close to running out (5-10

tablets from empty) or if having trouble reaching a medical provider or pharmacy. Notably, several patients did as directed by their prescribers and went to the ER if their medication did not work within 2-3 consecutive doses without improvement in pain level (adhered to their drug regimen).

6. Flexibility

For patients who were willing to experiment or were comfortable adjusting their medications as prescribed by healthcare providers, "common sense" was used in judging whether to take or not take prescribed opioids. This common sense varied among participants, leading some to take more in prevention of increasing pain (overuse), while leading others to only take pain medicine as a last resort (underuse). These patients also often consulted the internet or family members for judging pain medicine use and for more knowledge about pain medicine, rather than their physicians. For very few patients, extreme comfort with drugs and prescribed opioids led to accidental overuse incidents in which unbearable pain led to exaggerated use of opioids prior to an ER visit.

7. Forgetfulness

When I asked participants how frequently they forgot to take their medicines, I heard a variety of responses. Some of them said that forgetting is something they would never do, some said that forgetting was something that happened more often than not, and then some would say that forgetting was an occasional or rare occurrence. Depending on how individuals felt towards their memory and how to cope with rare (or uncommon) cases of

forgetfulness led to divergent responses. For those that routinized medications, memory was out of the question as they used external cues to judge whether or not to take pain medicine. For those that did not routinize their short-acting opioids, level of pain upon remembering was often the factor used to take or not take a dose of pain medicine. Finally, for those very relaxed about prescribed opioids and strong medications, some might take the medication in warding off possible future pain. Long-acting prescribed opioids, for those that had them, were reported as almost never missed, as most participants would take their long-acting medications upon waking or prior to work or school.

8. Feelings of security with provider, safety or comfort

Needing a feeling of security from pain often led to participants holding pain medicine with them at all times, though not necessarily overusing their medication. A sign of aberrant use, holding multiple medicines together, was sometimes noted, but participants often made a point to remember to take medication with them. Should medication be forgotten, participants recalled either dealing with pain, or remembering for the next time. Additionally, some participants did take extra medication prior to social events or obligations so that they might not forget during the event (if they had routinized medication-taking behavior). This extra dose of prescribed opioid was used as a safety net in preventing future pain.

Some study participants described taking underusing medication to maintain open and comfortable connections with their healthcare providers. Most participants were wary of the necessity of being addiction- or dependence-free to maintain good standing to maintain use of prescribed opioids and would underuse to maintain a facet of being able to handle pain without pain medicine. Underuse of prescribed opioids was also reported in order to pacify the negative stigmas towards SCD patients that they perceive from their healthcare providers.

9. Morality of strong pain medicine - overall opinion of medicine over time

Many participants were morally against putting foreign chemicals in their bodies, instead opting for home remedies or no medication, or underusing their prescribed opioids. Some participants described opioids as a necessary tool for pain relief in making typical life obligations, as comparable to non-SCD individuals, possible, and tended to underuse prescribed opioids, or withdraw completely for more independence.

10. Stress

As mentioned before, stress was a factor among a few of the interviewed participants when deciding to take a dosage of prescribed opioids. For the few individuals that would use prescribed opioids to combat stress, intentional non-adherence was noted through overuse (using prescribed opioids not as indicated by a physician).

11. Boredom, depression, fearlessness

Boredom, depression, and fearlessness were factors that influenced more open-minded study participants to take larger doses of prescribed opioids by physically altering or changing other use aspects (frequency, interval, and amount). Very few individuals reported intentionally experimenting for the sake of seeing how their medicines affected their bodies. Very few participants also reported taking their prescribed opioids for depression instead of for sickle cell pain.

12. Judgment

Some interviewed sickle cell patients did alter their medicine-taking behavior in response to judgment from others. Whether for fear of their "strange" actions under the influence of strong opioids or for respect to relatives' experience, many participants would underuse their prescribed opioids on their own. For some participants, urging of their family members led them to take more prescribed opioids, to appease these members as well as to avoid pity from others. Social comparison led many participants to learn from prior experience as well as observed experiences of others in taking less medication. Additionally, many participants that experienced others telling them about strange actions were prone to underusing their medications in attempt to preserve how they wanted other to see them.

i. Independence

Many participants experienced much comparison to non-SCD individuals and felt that taking such strong medication on a daily basis was abnormal. This led to increased feelings of a need for independence from chemicals, and thus led to decreased opioid usage.

ii. Beliefs towards opioids

Many participants disliked having to constantly use opioids for pain control but felt that, over time, opioids preserved a certain mode of life with which they were comfortable. Changes in behavior were not often noted unless different experiences were felt by individuals leading to increased or decreased opioid use based on positive or negative experiences, respectfully.

iii. Perception of disease & sick role

When interviewed, some participants sought use of prescribed opioids to take a rest from daily activities (e.g. work). Depending on their perceptions of sick roles of SCD patients, some participants reported underusing prescribed opioids to maintain outward perception of being like "everyone else", underusing prescribed opioids because their sickle cell

anemia was "more mild than others", overusing because strong medicine is part of the identity as a sickle cell patient, or overusing to gain pity from others. Most participants, however, disliked feeling any sense of pity from non-SCD relatives or friends.

D. **Spiritual**

i) Religious reasons/morality obligations & duties -

Many participants in this study reported religious reasons for preemptive use of prescribed opioids in order to fulfill church obligations. This led to unintentional overuse of prescribed opioids in prevention of pain during a religious obligation or duty.

1. Religious events

When interviewed, many participants denied changing prescribed opioid use for typical social events and gatherings. However, church or other religious events and obligations were often a priority for participants, especially with family involved, and many reported preemptively taking medication before or during church activities. This sometimes led to mild non-adherence in that individuals did not take short-acting medication as needed, but as planned for working around a religious event.

VIII. Conceptual Framework

Strength of framework varies from person to person. However, I built a conceptual framework of opioid taking behavior based on my qualitative findings and the prior related literature to inform current and future search strategy. Most of the determinant and barriers of prescribed opioid adherence explored in this study fit into the categories created in the conceptual model. See Figure 17 for a conceptual framework of factors of overtime (overall) opioid taking behavior. See Figure 18 for a conceptual framework of factors of momentary opioid taking behavior.

Figure 17: A conceptual framework of factors of overtime (overall) opioid taking behavior.

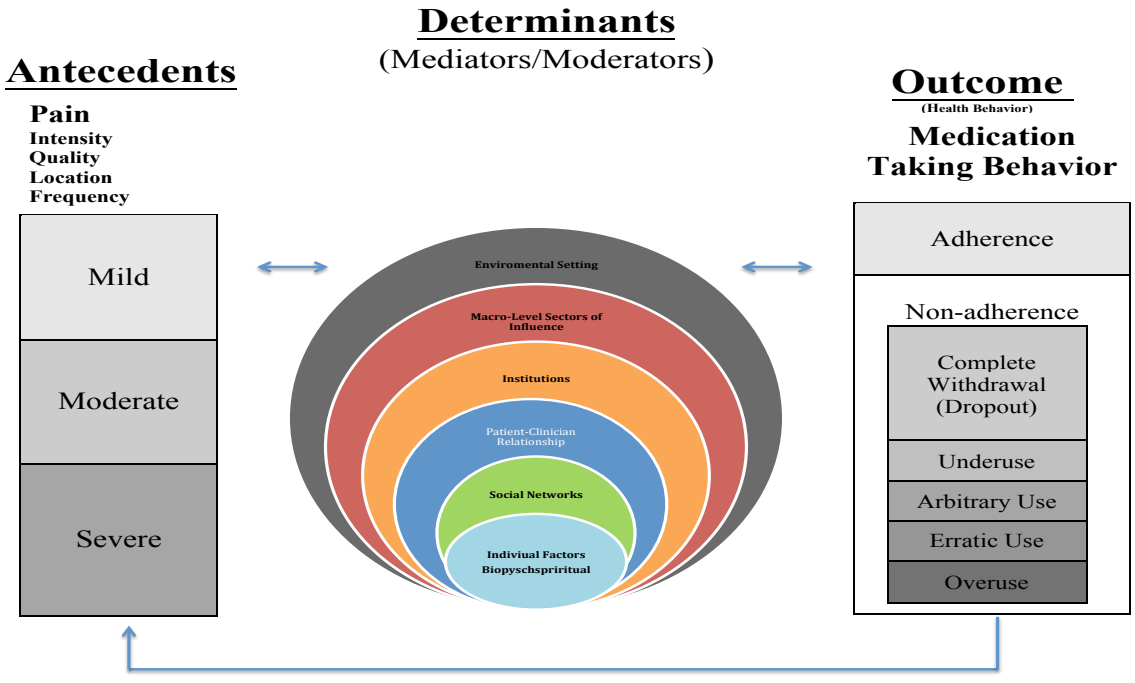
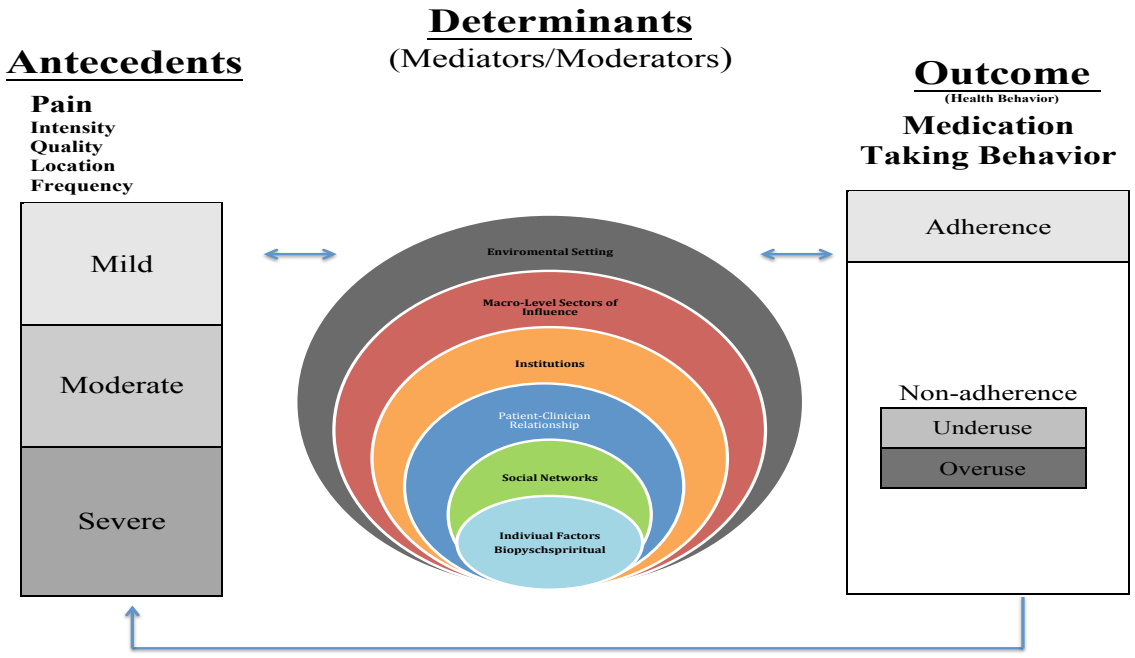


Figure 18: a conceptual framework of factors of momentary opioid taking behavior.



IX. AOTBA Scale

Various disease-specific and general (Morisky et al.) scales have been developed to assess medication adherence. However, I found no sickle cell disease (SCD)-specific measures of opioid taking behavior and adherence, especially for as-needed medication. The objective of my study therefore was to develop a disease-specific research instrument describing prescribed opioid adherence and opioid taking behavior in patients with SCD.

As part of a multiphase, mixed-method study, I used an adaptation of several published methods to construct 20 sequential, chronological steps for developing a new scale. I then customized these steps for relevant SCD opioid taking domains. I report here on steps 1-6, which included wide-ranging quantitative and semi-structured, qualitative interviews of 11 male and 10 female African-American adults with SCD (average age = 36 years). I used a grounded theory approach to analyze the qualitative data. Next, I used a priori procedures for domain specification and survey item delineation, specifically a linguistic-transformation approach (53, 54). I used a posteriori procedures to conduct a preliminary appraisal of translational (content and face) validity.

Almost all the items have I-CAV equal 1.00. Also, the S-CVI index was 0.989 for relevancy and 0.971 for clarity. Both these readings (findings) are very acceptable for content validity and indicate that AOTBA scale has exceptional high content validity.

The development of the Assessment of Opioid Taking Behavior Adherence (AOTBA) scale led to the inclusion of a new concept: momentary medication taking behavior, which is not previously described in the literature. The scale was also able to capture concrete patterns of adherence for as-needed medication in addition to scheduled medication regimens. Lastly, it has given expression to a number of conceptual domains that explain observed opioid taking behavior. These domains can be categorized under a biopsychosocial-spiritual schema. Domains include (but are not limited to): forgetfulness, carelessness, social stigma, fear of addiction, side effects, cost of medication, excruciating pain, maintaining functionality at work/ school, meeting life obligations.

The emerging draft scale demonstrates that adherence and opioid taking behavior in SCD is not characterized by chaos, but rather appears too driven by underlying discernible behavior patterns. Additionally, the scale reflects new concepts of medication adherence. These concepts challenge current theories and models of medication taking behavior and adherence.

X. Strengths of the study

There are several unique strengths to this study. There was only one refusal for this study. In addition, these patients did not differ on demographic variables suggesting that the participants were highly representative of the population. In addition, this study involved a diverse sample with male and female participants from urban and suburban areas and various socioeconomic backgrounds.

This study allowed for evaluation multiple aspects of adherence and many different reasons of non-adherence behaviors. This study also allowed for the identification of many important factors that may not have been included in a study with a more narrow focus. Instead of asking participants whether they were adherent, various domains of adherence were explored. Participants were asked a number of questions regarding opioid use and possible overuse and underuse and other questions designed to assess adherence to other aspects of specific opioid recommendations.

In previous adherence studies, many researchers have relied upon dichotomous ratings when evaluating adherence and have not attempted to assess multiple domains of adherence separately. In addition, this study obtained a heterogeneous distribution and range of adherence ratings, particularly for the adherence to other behaviors. This allowed for better holistic description of adherence.

To my knowledge, this is the first study attempt to describe adherence to prescribed opioid and factors of adherence in SCD. No published studies describe pattern of opioid

use to prescribed opioid in SCD patients nor do any explore the possible relationship of adherence to biopyschscoical-spiritual factors. It is also the first study that attempted to develop a scale for assessing adherence to prescribed opioid in non-cancer pain including SCD. Self-report measures of adherence are more likely to be accessible for researchers because they are very convenient choice for certain study designs.

In addition, the adherence measures in my survey and interview questions in this study are capturing and differentiating between patients' level of adherence with the use of regularly scheduled versus as needed opioids which usually ignored in assessing adherence to opioid use in cancer patients. Also, analyzing the data with multiple investigators prevented the data from being subjected to subjective analysis of one person. Lastly, in this study, I used mixed method (qualitative and quantitative) design, which gave me deep insight and understanding of adherence, patterns of opioid use and their reasons in SCD.

XI. Limitations of the findings

It is important to point out the limitations of my study. There were several limitations to this study. First, the primary limitation of the research is the small sample size, sampled using non-random sampling, from a single clinical site at one geographic location limiting generalizability of findings and the statistical power to detect significant relationships. The selected site was a major academic medical center and may have

reflected a high standard on pain education and management that reduced variation. Additional interviews with SCD patients conducted at other sites with larger sample size may give different results than my findings. My investigation did not assess adherence and pattern of opioid use over time. The study design was cross-sectional, so causal relations between factors cannot be determined. Participation was restricted to SCD patients who had been prescribed opioids and did not address the experience of patients who do not report pain or who refuse opioids. Further, the research was on individuals. It is acknowledged that other influences people with SCD pain in their surroundings. Both family members and providers influence patients' analgesic use. However, in this beginning research project the focus was on intra-subject factors.

This study relied on self-report assessment of adherence and outcome. Self-report has been shown to have limitations and problems. Based on previous research, self-report assessment of adherence are subject to measurement bias such as social desirability, recall bias and response bias.

It is unclear how valid and reliable self-report is. For example, patients may overestimate adherence in an attempt to present themselves in favorable light to their healthcare practitioner. It is possible that participants in this study wanted to please the investigator with reports of minimize the bias of patient report utilizing suggestions to obtain an adherence-oriented history and to assure patients that their responses will remain anonymous and confidential. Actually, I ensured the confidentiality of disclosed

information by participants, which may encourage honesty. Although self-report may have caused the patients to be reluctant to respond in an open and honest manner, I believed that this was minimized through careful explanation that participants' comments would not be communicated directly to their physician and the importance of their honesty to the final results of the study.

I have also explained that their treatment would not be altered in any way by their participation; the only potential benefit of participation was to help advance research in this area. Thus, participants may have motivation to be honest in their reporting. Furthermore, care was taken to question participants in non-threatening manner designed to elicit honest responding.

For example, it was always made clear up front that the investigator was not a medical healthcare professional, but was a student reviewing the pain management program and its efficacy. This made it easier to avoid direct questions regarding opioid adherence. In order to determine if a patient was overusing medication or using medication inappropriately, I might approach questioning in a curious manner and say something like, “I am not sure as familiar with the opioid that you are taking. How often can you take that opioid?" Participants seemed to respond well to this type of questioning and often did not seem aware of the contraindications to using the opioid in the manner they subsequently described.

The complicated nature of this study coupled with the limited resources of the investigator necessitated the use of self- report. In addition, it was believed that more patients would agree to participate in this study because it was perceived as involving very minimal work.

This study could have been improved by the inclusion of at least one objective measure of adherence such as pill counts, the use of pharmacy records, or both. Returned pill counting has been traditional used as an objective measure of adherence. However, recent evidence indicates that this method is inadequate for adherence assessment. Utilizing a system such as the Medication Event Monitoring System to record each time a pill bottle is opened or closed would have been an ideal way of assessing medication adherence, particularly for symptomatic medication. However, the problem with such measurement is the cost associated with it. Additionally, such as a method would prove more difficult if used to assess abortive medication use.

I made every effort to make the study a positive experience for the patients by being accommodating regarding the timing of the call as well as being extremely polite and friendly. It was believed that this approach would elicit more honest and open responding and greater cooperation with the study.

In addition, the findings of this study are limited by the fact that the results are based on a sample of patients who received three prescription of opioid in the last 12 month and

reported more than 29 % pain days in the last month. These patients likely experienced more frequent and severe pain than what may be found in a more general sample of SCD suffers. This has important implications for the results of the present study.

In addition, this study was exploratory in nature; with no previous hypotheses. Quantification and validation of the significant findings in another larger sample of the SCD population is necessary to demonstrate of statistical the relationships. I believe that if these results do replicate, then this research has several research and clinical implications.

Although one limitation of this method is its participant bias, instrument specificity, sensitivity, validity, and reliability, the ease of administration and reduced resource burden are worthwhile considerations. This is particularly true when compared with other approaches such as electronic monitoring, pill counts, pharmacy record surveillance, or biological assays. Finally, finding of this study must be interpreted in light of the limitations of this research project.

CHAPTER 6: CONCLUSION

I. Overall Conclusion

I carried out a mixed method multiphase study that explored opioid taking behavior in patients with SCD. The project demonstrated that each day, a variety of situations might change opioid taking behavior in these patients. The evidence from this study suggests that biopsychosocial-spiritual and other factors may be reasons for overall and momentary non-adherence. More research needs to be carried out to help clarify the issues that this study raises.

I found that pain in SCD has significant biopsychosocial-spiritual consequences. Prescription opioids may minimize theses consequence by providing pain control which in its turn may create new consequence. Non-adherence to prescribed opioid regimens may be one of many reasons for pharmacotherapy plan failure. In light of the consequences that I have explored here, it is very important to appropriately understand and assess patients' medication adherence. It is difficult for researchers and clinicians to readily identify patients who are non-adherent to opioid regimens. When broken down, the act of adhering to opioids is a complex process, influenced by societal, provider, and patient issues. The complexity of assessing adherence to prescription opioids suggests the

need for more innovative and convenient self-reported measurements of adherence. Additionally, the multifaceted nature of the *momentary construct* makes defining adherence to opioids a complex task. Therefore, to learn more about this facet of opiate taking behavior, it was important first to develop new instruments that not only measure adherence and opioid taking behavior, but also identify predictors of these behaviors. It was then important to develop a scale covering several multifaceted constructs dependent on a range of physical, social, economic, and psychological considerations. Also, it was important to consider the interplay of these factors in assessing opioid taking behavior. I developed a scale to assess adherence to prescription opioids within a context of overall and momentary adherence, autonomous dose adjustment, and chemical coping. I generated many items incorporating multidimensional biopsychosocial-spiritual determinants of opioid taking behaviors as important constructs in the scale. I hope by following this approach to yield meaningful results of the scale in the future.

One important finding of this study is that patients with SCD have several healthy and unhealthy lifestyle changes to cope with their pain and opioid effects. This study highlights that other non-pain factors should not be ignored. Regular discussions with patients could include coping with dependency, stigma, inadequate sleep, and stress. In my sample of patients with SCD, I found that opioid-taking behaviors should be an area of emphasis during patient interactions.

My results raise the hypothesis that, for opioid use in SCD, all six categories of behavior, including erratic use, overuse, underuse, adherence, arbitrary, and complete withdrawal, may be intentional or unintentional. But I found few if any references describing unintentional and intentional use in all six behaviors I discovered in my qualitative study.

This dissertation research probed for whether these six behaviors can be classified as intentional or unintentional, but the instrument I plan to develop will not itself be designed to determine unintentional vs. intentional behavior.

Together, my results suggest that the accepted terminology, which is based on current models and theories of medication adherence, does not accurately describe all medication taking behaviors. I found that contextual factors may drastically affect opioid taking behavior. Further, these newly described phenomena raise new hypotheses that may challenge current theories and models of medication taking behaviors and methods of assessing adherence. These hypotheses call for a new round of research on opioid taking behavior, and should be rigorously tested in future research.

II. New concepts with expanded framework

Like all of human behavior, opioid-taking behavior is an intriguing and complex phenomenon. Existing concepts, terminology, and measures of medication taking behavior seem inadequate to actually improve behavior when improvement is warranted. This dissertation introduces a new framework containing concepts of medication taking

behavior that, integrated with traditional ones, may inform theory and practice. The framework emphasizes patient-oriented terminology, which better acknowledges that medication taking requires patients' cooperation and insight. The framework also emphasizes not only longer-term but also momentary adherence assessment. Applying the new, combined framework may uncover previously ignored or unmeasured aspects of adherence, may answer many old questions about how to improve adherence, and may reveal contextually rich, more accurate information and substantive insights regarding medication-taking behavior. My research groups are currently working to develop formulas and methods of measurement for each of the concept I have described in my new framework. I was also exploring whether current theories about behavioral determinants of medication adherence fully explains and is completely consistent when tested using my newly framework

Based on the findings of this project, my research group will continue working to develop formulas and methods of measurement for each of the concept I have described in my new framework. I was exploring whether current theories about behavioral determinants of medication adherence fully explains and is completely consistent when tested using my new framework

Accordingly, emerging methods of assessment may allow this new framework to be better applied to medication taking behavior data. Meanwhile, this framework underlines the challenges and opportunities currently associated with obtaining and using current

medication taking behavior data. It is my hope that the scientific, practice, and policy community can adopt and apply this framework, moving this field ahead.

The findings of this project elucidate the importance of finding new measures of adherence. It proposes a new framework containing more inclusive concepts and more standardized terminology that not only describes adherence in more detail, as well as more specific measures of various sub-categories of adherence, but also describes all medication taking behavior. It argues for the integration of and measurement of behavior associated with specific medication types or dose schedules. Last, it describes promising research enabled by the new framework that, if implemented, might lead to improved adherence. They suggested that improving concepts and methods of adherence assessment is key to improving adherence outcomes.

III. AOTBA Scale

The objective of my multiphase, mixed-method studies was to develop a disease-specific patient-reported outcomes (PROs) scale for prescribed opioid taking in patients with SCD. The newly developed scale is completely built on patient-reported experience. I started by collecting all experiences qualitatively, in the patients' voice. I then continued to involve patients in successive (total of 3) phases of scale development. The resulting draft scale is aimed to capture patient values, patient-centered decision making, patient characteristics, patient preferences, and practical considerations related to prescribed opioids, rather than physician-judged outcomes or outcomes of biomedical assays related

to prescribed opioids. It is focused on symptoms, function, satisfaction, and quality of life. This patient-centered approach challenges current theories and models. For example, models and measures of medication-taking behavior and adherence have generally not focused on patient judgments or perspectives. This research relied on PROs to uncover a new general concept of medication adherence—momentary medication-taking behavior—not previously described in the literature. This concept captures concrete patterns of adherence for as-needed medications as well as for scheduled medications.

Patients reported positive and negative effects of prescribed opioids on biopsychosocial-spiritual outcomes in SCD. To my knowledge, this is the first hypothesis-generating research that can inform the debate about the appropriateness of the use of opioids in SCD, and form the basis for evidence-based practice. My resulting draft scale reflects underlying discernible behavior patterns of adherence and behavior in opioid taking for SCD, rather than chaos. Third, the scale documents and measures newly uncovered general concepts of medication adherence.

I believe that application and wide use of this scale may predict and improve all the above high-impact PROs, not just capture them. The mechanism of improvement of PROs should be through improved physician-patient communication and improved prescribing, as well as provision of a more concrete basis for behavioral and self-management interventions in patients.

IV. Implications for clinical practice

Although the implications of this study for clinical practice are preliminary because of the small sample size and single-site design, Findings from this study may have the several important clinical implications. However, because some findings were consistent with previous research in pain, cautionary recommendations can be made. Health care providers can recommend that patients keep a diary of their opioid use, particularly if new opioids are prescribed or in adequate pain relief is reported.

Given the problems with adherence noted qualitatively during this study, recommendations for improving SCD patient adherence to opioid prescriptions can be offered. First, I recommended that the biopsychosocial-spiritual factors identified as reasons of adherence in the present study be routinely assessed within the context of a multidisciplinary setting in order to determine which patients need specialized attention to maximize adherence. It is possible that healthcare practitioners may increase adherence rates among their patients if they routinely screen for a history of different situations, negative effects, and non-adherence attributions and make specific treatment recommendations as a result.

Second, patient education may be a useful intervention for those patients with excruciating pain. I recommend that SCD specialty clinics routinely follow up with their patients by telephone approximately 1 month after their visit. Numerous patients

communicated difficulty understanding of their opioid regimen or other treatment recommendations that could have been easily clarified over the telephone. For example, one patient stated that he had to take long-acting only when he is pain. This patient believed that he had been prescribed long-acting opioid for as-needed basis. (Perhaps you do not need to cite any specific examples since this is the conclusion?) In addition, many patients often communicated little awareness of how to take their medication despite being provided this information in writing from the physician. A follow-up telephone call could provide patients with the opportunity to ask questions and clarify any misunderstandings that may have occurred during the practitioner-patient interaction.

Patients with a history of opioid overuse may require more patient education from either the physician or another healthcare practitioner. Such patients may benefit from a follow-up telephone call two weeks after their clinic appointment to monitor their opioid use and determine if any changes can be made to their prescribed opioid regimen to enhance their medication adherence, such as changing the type of short-acting opioid to reduce a particularly bothersome side effect.

Patients endorsing biopsychosocial-spiritual attributions for their non-adherence should be given special attention as well. It is recommended that these patients be allotted additional time with the healthcare practitioner during their routine visit. A careful adherence history should be taken with such patients to determine the possible associations between their history and non-adherence. It may be the case that the reasons

represent a defensive or hopeless state that warrants further consideration. Patient education regarding appropriate opioid use may be helpful with these patients, particularly if specific causes for previous non-adherence are discovered.

Further research should be conducted to identify improved measures of both adherence behavior and its underlying causes. Such variables may account for larger portions of the variance of adherence. The results of exploratory analyses provided in this study can provide useful information to guide the researcher. For example, future studies may seek corroborating information on adherence behaviors from family or friends. Other self-report measures might provide stronger and more consistent relationships as well.

Patient satisfaction with treatment and the doctor-patient relationship is another variable that might be interesting to examine in future studies. A longitudinal study would be particularly helpful, so that the course of this critical relationship could be understood more clearly.

Furthermore, assessing adherence can help to customize appropriate analgesics regimen and clinical interventions. Additionally, investigating adherence in prescription opioid use can assist clinicians in designing more effective and better therapeutic pain plans that address patient priorities. Activities of daily living, particular situations may require adjustments in adherence to the analgesic regimens. Such studies are necessary to understand factors that affect adherence in this population and to serve as the foundation

for the development of more effective strategies to improve adherence. Hopefully, the findings may help clinicians to plan better care for patients who may underuse or overuse on the prescribed opioid. Recognizing factors will help to find solutions that may help the clinician to identify patients at risk and intervene appropriately. Providers who are able to overcome the obstacles to adherence will improve the lives and outcomes of their SCD patients.

On a broader level, especially given the magnitude of the epidemic of non-cancer pain, improving adherence to pain management has very widespread public health implications. The quantitative survey of this study may serve to predict which subjects would be adherent to long-acting opioids or short-acting opioids. Finally, a broad taxonomy of patterns of opioid use and barriers to adherence can be created for patients with SCD and patients with non-cancer pain. This taxonomy can be used to assist medical providers in developing interventions designed to optimize patient education and problem solving with regard to prescription opioid regimens. The taxonomy may also help to develop and evaluate the efficacy of specific analgesic regimens.

Although I learned many things during the course of carrying out this study, two major areas worth special attention. First, this study did not directly address physician-patient relationship, which could have helped to clarify some important relationships and to help understand how patient education could be improved. Clinical observation suggests that this is an important area for consideration. More time should be spent with SCD patients

to help them understand their role in managing their pain and their responsibility to remain adherent to their opioid regimen.

Secondly, this population represents a group of patients that is very difficult to treat successfully for a number of reasons, including the significant biopsychosocial-spiritual factors discussed here. This is also well known in the literature and in healthcare settings. It is believed that the multidisciplinary team approach is the best model for treating these patients. Inclusion of a pharmacist as a team member is essential to educate patients about their prescribed opioid and ensure their awareness of appropriate use.

V. Future Research directions

There is much work to be done in the area of adherence to prescription opioid regimens in SCD and non-cancer pain to better characterize the nature of pain. It is critical to determine and understand the underlying causes of adherence or non-adherence. In this area, future studies can address the possible relationship of adherence with different biopsychosocial-spiritual factors. A prospective longitudinal study describing and assessing adherence is the logical next step. For example, using other adherence assessment such as an electronic pill monitoring system and electronic E-diary to measure adherence, detect patterns of opioid use and to assess reason for use will be very practical and useful way of adherence monitoring especially for PRN medications.

In addition, ensuring reliability and further validation steps (explained in chapter 3) are needed in the future to validate and start using AOTBA scale in research.

There were several ultimate objectives of this line of research, beyond the scope of this dissertation research. These include: 1) completion of the steps of validation of the research instrument to describe adherence and opioid taking behaviors in SCD adults, both over time and at particular times and their related contextual factors; 2) adaptation of the validated SCD opioid taking behavior instrument and completion of a similar validation process to describe opioid taking behavior in chronic non-cancer pain, and; 3) revision of the instrument(s) so that it (they) is (are) useful to practitioners to enhance communication with their chronic non-cancer pain patients. Although we are not sure that this instrument would validate in other non-cancer pain populations, we have designed the instrument to be adaptable to other non-cancer pain populations.

For future work, the quantitative survey was shaped based on the findings of Phase I. For example, several hypotheses could expand to comparative hypotheses; depending on whether both multiple opioid taking behaviors and multiple contexts related to those medications behaviors.

There is a need for further research to determine how, when, and where in the course of SCD do patients need to be educated on all aspects of their disease to improve adherence to their prescribed opioid regimens. The physician's role in adherence should be

thoroughly investigated to establish strategies that improve adherence. The data from such a study can be transformed into a measure of the most common and frequently occurring pattern of opioid use and the problems associated with it (i.e., categories of problematic situations in such population). Data about time and context specific-adherence can be used to develop a more accurate and useful measure of adherence to opioids especially for PRN short-acting opioids. This measure can serve to provide outcome data for interventions to improve adherence not only in SCD patients but also for patients with non-cancer pain. Prospective studies or predictive models can also determine which factors are significantly related to adherence to opioid of use and whether patients' outcomes differ based on the patterns of opioid use. Improving measurement of PRN medication adherence should allow the adherence researcher to get on the development and evaluation of adherence-improving interventions with tested adherence measures.

E. **Computing a Total Score**

Currently, I do not have a clear idea about calculating a score for adherence using this new scale. I will consider the calculations for scoring adherence using this scale. I will try to preserve the ability to calculate an overall adherence score. I will calculate a total score for each respondent, by summing the values of all items. Suppose respondent X will have the following response pattern for 5 items. The total score computed for respondent X would be:

4 + 4 (Negative item) + 5 + 3 + 4 (Negative item) = 20/25

The score report (indicate) that the level of non-adherence reported by the participants. The item was worded so that "always" indicated an unfavorable behavior (more of non-adherence). For ease of comparison with other items, scores will be made so that higher values indicate more unfavorable responses (higher level of non-adherence). I will calculate the mean subscore for the items in each Assessment of opioid-taking behavior and Adherence (AOTBA) dimension.

For statements indicating perfect adherence, the scoring is reversed so that 'always' would be scored as '1', and so on, with 'Never' being scored as '5'.

VI. Other Types of Reliability and Validity

For the next phase of instrument development and validation, several steps should be used in the assessment of this new instrument, future research should add to the other assessments of translational validity (content validity and face validity), construct validity, reliability testing (internal consistency, and test-retest), and criterion validity. Although these steps of validations needed large sample size, and therefore it beyond the scope of this dissertation project, however, I will report preliminary psychometric results related to construct, criterion validity and internal reliability. I do not consider these results as completion of validation steps 11-20.

A. **Criterion Validity**

For criterion validity, I need an external gold standard assessment of medication adherence or another measure generally accepted as a more accurate or criterion variable that correlates with my proposed new measure. However, in the field of medication adherence measurement, it is rarely if ever that a perfect 'gold-standard' measure exists against which to test the validity of new adherence measure. Perhaps the only untarnished gold standard is recorded observation of each prescribed dose of therapy. However, this method is not feasible and practical. Instead, a number of more indirect approaches are recommended to judge instruments' validity of adherence measure. Many treat these approaches as a practical and feasible gold standard, even though they each have

limitations. Thus, with all these limitation, selecting an appropriate and meaningful criterion measure can be a challenge for medication adherence.

I also realized that monitoring prescribed opioid therapy could be done by pharmacokinetic measures (e.g. predicting oral or IV morphine doses using serum or urine morphine concentration. [157] Other methods of monitoring pain and prescribed opioid are functional magnetic resonance imaging [158] and vascular inflammatory markers. [159] Likewise, these measurements are costly and often impractical.

For validating a new self-report measure of medication adherence with concurrent measurement most would suggest using a MEMS cap. However, because MEMS technology is expensive, a less costly measure, such as pill count or refill records, therefore, I will instead use pill count and the validated Morisky adherence scale [160] to provide evidence of criterion validity.

B. **Construct Validity**

Construct validity refers to the degree to which the items on an instrument relate to the relevant theoretical construct. [135, 136] It refers to the degree to which the intended independent variable (construct) relates to the proxy independent variable (indicator). [135, 136] For example, in the AOTBA, dose-self-adjustment (chemical coping), pain intensity, and pain relief from prescribed dose will be used as proxy indicators of non-adherence.

When an indicator consists of multiple items, factor analysis is used to determine construct validity.

Future construct validity studies can measure whether the adherence measures tap the constructs I intend, by measuring correlation with related concepts. Opioid use is well known to be correlated with pain intensity in SCD. [4] Thus I expect that overusers should have more pain than erratic users, since they in general should have more opioid use. Similarly, erratic users should have more pain than underusers, since they should have more opioid use. Besides pain, I expect that pain relief should be correlated with opioid use, i.e. patients with more use (overusers) should have more pain relief than erratic users or underusers. Similar relationships should exist for use and emergency department utilization and hospital utilization.

Satisfaction with provider in term of drug regimen may have a complex relationship. Given the unclear standards about appropriate prescribing (quantity of opioids), "stingy" prescribers may be alternately seen as satisfactory or not depending on patients' attitudes about opioids and tendency toward overuse or underuse. However, it is possible to measure agreement (satisfaction or dissatisfaction) of patients with prescribed doses. I expect that underusers may be quite satisfied, whereas overusers may be quite dissatisfied, distinct from whether the satisfaction is appropriate.

I will use the commonly statistical method known as Factor Analysis in order to cluster items into common factors, interpret each factor according to the items having a high loading (measure of association between an item and a factor on it), and summarize the items into a small number of factors. [135, 136, 161, 162] I define a factor as a list of items that belong together. Related items define the part of the construct that can be grouped together. Unrelated items, those that do not belong together, do not define the construct and should be deleted. [135, 136, 161, 162]

I will use the commonly statistical method known as exploratory factor analysis (EFA) to: a) explore the hypothesized dimensions; b) examine the relationships among variables; and c) helps us define the construct based on the theoretical framework, which indicates the direction of the measure [135, 136] and identifies the greatest variance in scores with the smallest number of factors. [135, 136, 161, 162] All items will be loaded as predicted on the hypothesized dimensions. To further purify the measure, a Confirmatory Factor Analysis on the final numbers of items will be performed in order to assess the psychometric properties of the scale developed in this study. [135, 136, 161, 162]

C. **Reliability**

Once the preliminary validity procedures are completed, the final draft version of the AOTBA will be examined to assess its reliability. Reliability refers to the ability of a questionnaire to consistently measure an attribute and how well the items fit together,

conceptually. [135, 136] Two estimators of reliability are commonly used: internal consistency reliability and test-retest reliability: both will be used to examine the reliability of the AOTBA.

Internal consistency examines the inter-item correlations within an instrument and indicates how well the items fit together conceptually. [135, 136, 161, 162] In addition, a total score of all the items will be computed to estimate the consistency of the whole questionnaire. Internal consistency is measured in two ways: Split-Half reliability and Cronbach's alpha correlation coefficient. [135, 136, 161, 162]

Cronbach's alpha is the most frequently used reliability statistic to establish internal consistency reliability, [135, 136, 161, 162] therefore, I will compute the Cronbach's alpha to examine the internal consistency of the AOTBA, where the average correlations of all items that measure the same construct are computed. If an instrument contains more than one subscale, Cronbach's alpha will be computed for each subscale as well as the entire scale. A measure of internal consistency or composite reliability is a composite alpha value. For reliability analyses of several factors from this instrument, Cronbach's alpha will be calculated (in order to determine whether any items need to be recoded and/or deleted to make a stronger subscale). I will create scale scores for each of the factors and compute the bivariate correlations among the scales. Finally, I will create confidence intervals around the estimates of reliability. Construct reliabilities, average variances extracted, means, standard deviations, and correlations for all latent variables will be are

identified. Construct reliability coefficients should all exceed the .70 (lower limit), to conclude good reliability. [135, 136, 161, 162]

Future reliability studies can measure test-retest reliability, which is estimated by administering the same tool to the same sample on two different occasions on the assumption there will be no substantial change in the construct under study between the two sampling time points. [135, 136, 161, 162] I believe opioid taking behavior is stable characteristics over two weeks that a high correlation between the scores at the two time points (15 days of administration). The duration of time between the two tests is critical. The shorter the interval the higher the correlation between the two test. [135, 136] Longer interval than two weeks can affect the results because of changes in participants or their environment. Currently, there is no definite evidence about the best time interval to allow between the test and the retest for medication adherence. To make an appropriate decision about the time interval between tests, I need to consider factors such as the effects of time on health status such as deterioration or improvement in health. I hope to see no significant differences between the two tests (test and retest in two weeks).

D. **Additional Survey Tools**

In addition to the above draft survey, I will co-administer several other items and pre-validated surveys, scales, and instruments, to enrich my understanding of the draft survey's construct and criterion validity. These include the Morisky Adherence Scale,

[160] BPI Pain Scale, [48] the McGill Pain Scale, [48] PiCES Pain Diary, [4] and baseline assessment of psychosocial variables inclusive of the Coping Strategies Questionnaire [163, 164] to assess coping skills, and the Pain Medication Attitude Questionnaire (PMAQ) [156] attitudes about opioid use.

E. **Pilot Testing the Draft Survey**

I plan to identify problems with items or responses by pilot testing my draft survey with colleagues and a few SCD patients. These pilot tests will help identify redundant or poor questions and provide an early indication of the reproducibility of the responses. For example, I may rewrite or drop an item if it confuses several respondents. I plan at least two pretests, and with each revision, the will likely become shorter.

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APPENDICIES

Appendix A

Pre-Screening Form

Pre-Screening Eligibility Criteria through Chart Review

- Is patient's age between 18-64?
  - If less than 18 or more than 64, exclude
- What is the race/ethnicity of the patient?

Caucasian African-American Asian Hispanic Other

  - If not African-American, exclude
- Did the patient receive three outpatient prescriptions for at least one (Schedule II or Schedule III) opioid medications from Virginia Commonwealth University Health Care System (VCUHS) within the previous 12 months? YES NO
  - if No, exclude
- Does the chart show evidence of patient dependence on any psychoactive substance or history of drug use problem YES NO
  - If yes, exclude
- Serious psychiatric diagnosis (by chart review and electronic medical record (EMR) system). YES NO
    - If yes, exclude

Appendix B

Recruitment Form and Script

"Hello, my name is Abdulkhaliq Alsalman and I am a PhD student working under the supervision of Dr. Wally Smith from the sickle cell anemia research team in the Department of Internal Medicine at Virginia Commonwealth University. The reason I'm talking to/contacting you is that I am currently conducting research on pain medicine use in sickle anemia. As part of my dissertation research; I am conducting interviews with sickle cell anemia patients to discover their ways of using prescribed opioid and their perspectives on why they use their pain medicines in that ways. I am recruiting participants for that reason. This research will hopefully lead to a better understanding of how physicians should prescribe opioid and eventually be used to guide and teach sickle cell anemia patients to use their pain medicine in more effective and safe ways especially when they have special circumstances and situations. I am contacting you because you are scheduled to have an outpatient medical appointment in sickle cell anemia clinic. We are currently seeking volunteers from the adult sickle cell anemia clinic patients as participants in this study and I wondered if you would be interested in hearing more about it. Is this a convenient time to give you further information about the interviews?
[IF YES] provide some more information regarding the interviews that will be conducted
(Continue on page 2)
OR No, could you talk back later (agree on a more convenient time to contact person back). With your permission, I would like to email/mail/fax you an information letter which has all of these details along with contact names and numbers on it to help assist you in making a decision about your participation in this study and If you are not interested in the study, then I will destroy the personal information you give me.
May I call you in 2 or 3 days to see if you are interested in participating study?
Yes (get contact information from potential participant i.e., phone/mailing address/fax number).
[IF NO] Thank you for your time. Have a good day. Good-bye.
"Participation in this study involves coming into a private room and having interview. If you volunteer as a participant in this study, you will be asked during the interview to talk about your pain, how and why you use your pain medicine, filling out a questionnaire about your pain, saying words and personal memories out loud. Participation in this study would take approximately 1.5 hours of your time and would be arranged for a time convenient to your schedule. Involvement in this interview is entirely voluntary and there are no known or anticipated risks to participation in this study. You may decline to answer any of the interview questions you do not wish to answer and may terminate the interview at any time. With your permission, the interview will be tape-recorded to facilitate collection of information, and later transcribed for analysis. All information you provide will be considered confidential. The data collected will be kept in a secure location. If you have any questions regarding this study, or would like additional

information to assist you in reaching a decision about participation, please feel free to contact Dr. Wally Smith at 804-828-6938. After all of the data have been analyzed, you will receive an executive summary of the research results. In appreciation of your time commitment, you will receive $45. I would like to assure you that this study has been reviewed and approved by the VCU Office of Research IRB.
However, the final decision about participation is yours.
Would you be interested in participating?"
[If NO] Thank you for your time. Good-bye.
[IF YES] Thank you; we appreciate your interest in my research! If you are interested in participating, please fill out one of the individual confidential recruitment cards* and I will be in touch with you. Alternatively, you can come to Ambulatory Clinic building, 4th floor and see me. Thank you. (Schedule a mutually agreeable time to come to the interview room.) "
Now, let me give you some important information about the study. Have you got a pen and piece of paper? The name of the study is Understanding Adherence to Prescribed Opioids in Sickle Cell Disease, and my name is Abdulkhaliq Alsalman. "The study is being conducted in the Clinical Research Service Unit (CRSU) in the 8th floor of the North Hospital building on the MCV campus at Virginia Commonwealth University. On the day of your appointment, please meet me in the Ambulatory Clinic Parking lot. We will provide you with a parking pass or cover any needed parking costs. Please plan to arrive in the waiting area on the 1st floor of the Ambulatory Clinic building five minutes before the time of your appointment. Also, if you wear glasses or contact lenses to correct your vision, or if you use a hearing aid, please bring them with you to the session." "The day before your session, I will phone you to make sure that you are still able to make it. If you have to cancel your appointment, you can call the research team at (804) 728-9803 to contact me or leave a message on the answering machine. I look forward to meeting you on [day and time of appointment]. Thank you very much for helping us with my research!" Once again, if you have any questions or concerns, please do not hesitate to contact me at my research office number 804-728-9803. Thank you very much for your time.
* Individual Confidential recruitment cards: please request the following information to be completed by potential participants:

Name
Email
Fax number
Phone number
Best Days and Times to call you
Best Days and Times to interview you (if agree to participate)
* If you are not interested in the study at anytime, then I will destroy the personal information you give me.

Appendix C

Appendix C

Screening for Eligibility

MINI-MENTAL STATE EXAM

Participant study number: _____

Date of Exam:

The Mini-Mental Status Examination offers a quick and simple way to quantify cognitive function and screen for cognitive loss. It tests the individual's orientation, attention, calculation, recall, language and motor skills.

Each section of the test involves a related series of questions or commands. The individual receives one point for each correct answer.

To give the examination, seat the individual in a quiet, well-lit room. Ask him/her to listen carefully and to answer each question as accurately as he/she can.

To score, add the number of correct responses. The individual can receive a maximum score of 30 points.

Right / Wrong? - 30 questions for 30 points

ORIENTATION – 10 points

Ask the following questions:

1. What is today's date?
2. What is the month?
3. What is the year?
4. What day of the week is it today?
5. What season is it?
6. What is the name of this clinic (place)?
7. What floor are we on?
8. What city are we in?
9. What county are we in?
10. What country are we in? Orientation subtotal = /10

IMMEDIATE RECALL – 3 points

Ask the subject if you may test his/her memory. Then say "ball", "flag", "tree" clearly and slowly, about 1 second for each. After you have said all 3 words, ask him/her to repeat them - the *first* repetition determines the score (0-3):

11. BALL
12. FLAG
13. TREE Recall subtotal = /3

ATTENTION – 5 points

NB PERFORM SERIAL 7S OR 'WORLD' BACKWARDS BUT NOT BOTH!

A) Ask the subject to begin with 100 and count backwards by 7. Stop after 5 subtractions. Score the correct subtractions.

14. "93"
15. "86"
16. "79"
17. "72"
18. "65"

B) Ask the subject to spell the word "WORLD" backwards. The score is the number of letters in correct position. For example, "DLROW" is 5, "DLORW" is 3, "LROWD" is 0.

"D"
"L"
"R"
"O"
"W" "DLROW" or Serial 7s subtotal = /5

DELAYED VERBAL RECALL – 3 points

Ask the subject to recall the 3 words you previously asked him/her to remember.

19. BALL?
20. FLAG?
21. TREE? Delayed verbal recall subtotal = /3

NAMING –2 points

Show the subject a wrist watch and ask him/her what it is. Repeat for pencil.

22. WATCH
23. PENCIL

REPETITION – 1 point

Ask the subject to repeat the following :"No ifs, ands, or buts"

25. REPETITION

3-**STAGE COMMAND** - 3 points

Give the subject a plain piece of paper and say, "Take the paper in your hand, fold it in half, and put it on the floor."

25. TAKES
26. FOLDS
27. PUTS

READING – 1 point

Hold up the card reading, "Close your eyes", so the subject can see it clearly. Ask him/her to read it and do what it says. Score correctly only if the subject actually closes his/her eyes.

28. CLOSES EYES

WRITING 1 point

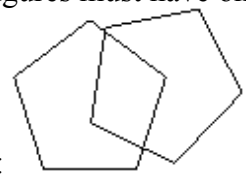
Give subject a piece of paper and ask him/her to write a sentence. It is to be written spontaneously. It must contain a subject and verb and be sensible. Correct grammar and punctuation are not necessary.

29. SENTENCE

Language subtotal = /8

COPYING – 1 point

Give subject a piece of paper and ask him/he to copy a design of two intersecting shapes. One point is awarded for correctly copying it. All angles on both figures must be present, and the figures must have one overlapping angle.

Example: 

30. PENTAGONS **Pentagon subtotal = /1**

TOTAL MMSE = /30
(MMSE maximum score = 30)

- What is the MMSE score at screening? (See below for MMSE exam)
  - Is patient incapable of being interviewed (e.g., dementia, mental retardation, illiteracy)? YES NO If yes and MMSE less than 23, exclude
- How much pain are you experiencing today? If 0 is ‘‘no pain’’ and 10 is the ‘‘worst pain imaginable’’
  - If more than >7, exclude
- In the last month, how many days did you feel pain?
  - Circle one:
    - ≤ 8 days (≤ 30% of days), exclude
    - 9-14 days (> 30-50% of days)
    - > 14 days (> 50% of days)

Appendix D
Baseline Information

Appendix D: Baseline Information and Data Collection Form (after signing the consent form and being eligible)
IRB protocol HM13946 Principal Investigator: Dr. Wally R. Smith, MD

Project Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease	
Pt Study_ID: _____	**Assessment Date:** ___ ___ / ___ ___ / 2 0 ___ ___ (d d m m y y y y)
Assessment Type: Baseline (interview)	

Is the participant eligible for the study based on Inclusion and Exclusion criteria? ☐Yes ☐No **(If no leave the rest of the form blank) If yes:** Date enrolled (met all eligibility criteria): _____/_____/_____ (dd/mm/yyyy)

Does you have a medical or surgical history, current or resolved, of any of the following?

MEDICAL HISTORY	Yes / No	Unknown	If Yes, Explain	Current / Resolved
1. Head, Eye, Ear, Nose, Throat	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
2. Respiratory	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
3. Cardiovascular	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
4. Gastrointestinal	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
5. Genitourinary	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
6. Musculoskeletal	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
7. Neurological	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
8. Endocrine-Metabolic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
9. Blood/Lymphatic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
10. Dermatologic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
11. Psychiatric	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
12. Allergy	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
13. Other, specify: _____	☐ Yes ☐ No	☐		☐ Current ☐ Resolved

Project Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease	
Pt_ID: _____	**Assessment Date:** ___ ___ / ___ ___ / 2 0 ___ ___ (d d m m y y y y)
Assessment Type: Baseline (chart review)	

Record all past and/or concomitant medical conditions or surgeries. Record only one condition or surgery per line using the codes provided in the table. When recording a condition and surgery related to that condition use one line for the condition and one line for the surgery.

01 Head, Eye, Ear, Nose, Throat	06 Musculoskeletal	11 Psychiatric
02 Respiratory	07 Neurological	12 Allergy
03 Cardiovascular	08 Endocrine/Metabolic	91 Other
04 Gastrointestinal	09 Blood/Lymphatic	
05 Genitourinary	10 Dermatologic	

ICD9 Code	Condition/Disease (one item per line)	Start Date dd/mm/yyyy	Current / Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved
			☐ Current ☐ Resolved

Project Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease

Pt_ID: _____

Assessment Date: ___ ___ / ___ ___ / 2 0 ___ ___
d d m m y y y y

Assessment Type: **Baseline** (chart review)

Prior and Current Medications

Were any prior or current medications taken by the participant __ days before or during the study? Yes (If so record below)☐ No☐

Medication	Indication	Start Date (dd/mm/yyyy)	Stop Date (dd/mm/yyyy)	Ongoing
1.				☐
2.				☐
3.				☐
4.				☐
5.				☐
6.				☐
7.				☐
8.				☐
9.				☐
10.				☐

Project Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease	
Pt_ID: _____	**Assessment Date:** __ __ / __ __ / 2 0 __ __ (d d m m y y y y)
Assessment Type: **Baseline**	

Study Completion

1. **Date of study visit and interview:** ___ / _____ / _____ (dd mm yyyy)

2. **Primary reason for terminating participation in the study:**

- ☐ Completed study
- ☐ Participant was determined after enrollment to be ineligible (Provide Comments)
- ☐ Participant withdrew consent
- ☐ In the Investigator's opinion it was not in the participant's best interest to continue. (Provide Comments)
- ☐ Adverse Event

  If checked, complete the AE form
- ☐ Other (specify): _____
- ☐ Unknown

COMMENTS:

Date Informed Consent Signed: __ __ / __ __ / 2 0 __ __ (d d m m y y y y)

PI Signature: _____ Date: _____

Appendix E

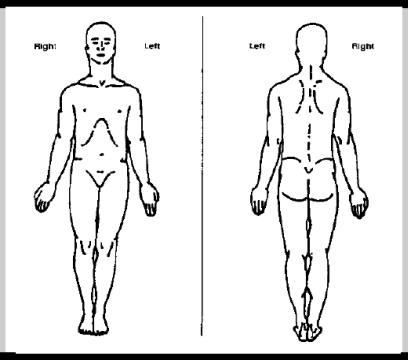
Appendix D: Baseline Information and Data Collection Form (after signing the consent form and being eligible)
IRB protocol HM13946 Principal Investigator: Dr. Wally R. Smith, MD

Brief Pain Inventory (Short Form)

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

   1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one nuimber that best describes your pain at its least in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No Relief										Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

Appendix F

Appendix D: Baseline Information and Data Collection Form (after signing the consent form and being eligible)
IRB protocol HM13946 Principal Investigator: Dr. Wally R. Smith, MD

McGill Pain Scale with Drawing (Short Form)

1- Instructions: Since you have reported that one of your problems is physical pain, the purpose of this checklist is for you to give us an idea about what your physical pain feels like. Each of the words in the left column describes a quality or characteristic that pain can have. So, for each pain quality in the left column, check the number in that row that tells how much of that specific quality your pain has. Rate every pain quality.

PAIN QUALITY	NONE	MILD	MODERATE	SEVERE
1. Throbbing	(0)_____	(1)_____	(2)_____	(3)_____
2. Shooting	(0)_____	(1)_____	(2)_____	(3)_____
3. Stabbing	(0)_____	(1)_____	(2)_____	(3)_____
4. Sharp	(0)_____	(1)_____	(2)_____	(3)_____
5. Cramping	(0)_____	(1)_____	(2)_____	(3)_____
6. Gnawing	(0)_____	(1)_____	(2)_____	(3)_____
7. Hot-burning	(0)_____	(1)_____	(2)_____	(3)_____
8. Aching	(0)_____	(1)_____	(2)_____	(3)_____
9. Heavy	(0)_____	(1)_____	(2)_____	(3)_____
10. Tender	(0)_____	(1)_____	(2)_____	(3)_____
11. Splitting	(0)_____	(1)_____	(2)_____	(3)_____
12. Tiring-exhausting	(0)_____	(1)_____	(2)_____	(3)_____
13. Sickening	(0)_____	(1)_____	(2)_____	(3)_____
14. Fearful	(0)_____	(1)_____	(2)_____	(3)_____
15. Punishing-cruel	(0)_____	(1)_____	(2)_____	(3)_____

Descriptors 1-11 represent the sensory dimension of pain experience and 12-15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0= none, 1= mild, 2 = moderate, 3 = severe.
S = /33 A/E = /1

2- The below scale is the visual analogue (VAS) pain scale, a tool which helps you to provide a measure of your overall pain intensity scores. Please indicate by circling a number on the line above the intensity of your pain. The left end of the line indicates no pain at all. The far right end indicates worst pain possible.

3- Please check the one descriptor below that best describes your present pain intensity (PPI)

0	No Pain	❑
1	Mild	❑
2	Discomforting	❑
3	Distressing	❑
4	Horrible	❑
5	Excruciating	❑

4- Is your pain? (Check one word)
❑ Brief
❑ Intermittent
❑ Continuous

Appendix D: Baseline Information and Data Collection Form (after signing the consent form and being eligible)
IRB protocol HM13946 Principal Investigator: Dr. Wally R. Smith, MD

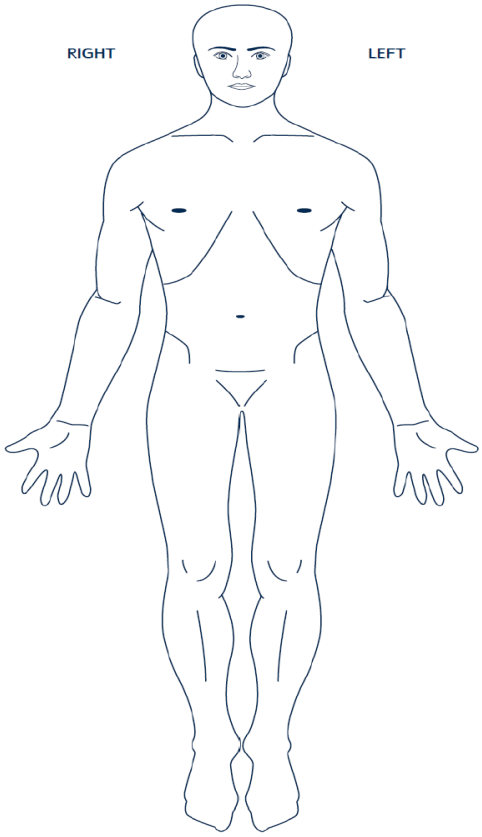
Please mark the drawing where you feel the following sensations:

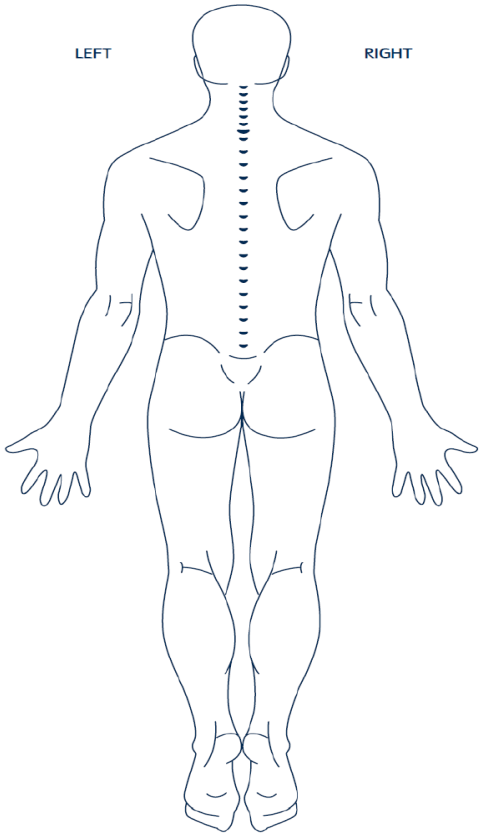
1. Numbness: //////////
//////////

2. Pain: XXXXXXX
XXXXXXX

3. Pins & Needles: ....
....
....
....

4. Ache: 00000000
00000000





Appendix G

Semi-Structure Interview Guide

Project Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease
Arrival
Welcoming patient and having some informal chat in order to put them in their ease and make them feel comfortable. **Opening Questions:** How are you today? How is [school] [Work]? "Please tell us your first and last name."
The following statement is to be read to the participants before each interview.
"Thank you so much for agreeing to participate in this study. What we would like to do today is talk about issues connected with sickle cell disease pain. We will be discussing how you manage your pain, drawing on your experiences. We want to learn from you to help other people in the future. We have a number of areas we would like to cover, including how patients use their medicine and other ways of pain control. At any time if you think of any comments or experiences, we would very much like to hear them, even if that's not what we are talking about right then. We want to understand the different ways people cope with their pain."

Introduction

Medication adherence: "As I mentioned before, the first thing we will ask you is a series of questions about your experience with pain and how it made you feel. Then we will ask you a series of questions about how patients take their prescribed pain medicines. I am interested in things that people do that affect their ways of taking their pain medicines. The purpose of the study is not to judge whether your ways of taking pain medicine are good or bad. The purposes of the study are to just learn exactly how pain affects you and what you do about it. That includes what medicines you take, and how you take them, regardless of how they are prescribed. Please try and answer each question with as much detail as possible."

Sickle Cell Anemia and Pain (generally)

1) **Beginning the interview:** I'd like to start out this interview by hearing a little bit about your experiences with Sickle Cell Disease. Can you tell me how you usually experience your disease?

   Probe:
   a) *How has your sickle cell disease pain affected your personal life? Think about when you are in pain–during that time, how are your family, life style, daily activities affected?*

2) Please tell me all the medical problems that cause you pain.

   Explore:
   a) *Follow-up questions (f/u): Of all the problems you have that are causing you pain, which one is the worst?*

3) What medicines are you currently taking for your pain? (Please tell me all you can remember, regular or occasional, prescription or over the counter).

Explore:

a. *(f/u): How well do these medicines work for you?*

In the following questions, I would like to know about how you use your strong pain medicine like Morphine, MS Contin, Tramadol, Tylenol III, Codeine, Darvocet, propoxyphene, Percocet, OxyContin, oxycodone, Vicodin, Lortab, hydrocodone, Dilaudid, hydromorphone, or Pain patches (Fentantl), prescribed by a doctors. But from now on I will just say pain medicine for strong pain medicine. Let's talk now about that.

Adherence to Prescribed Opioid: To Identify Actual Behavior of Use

4) It sounds like you are taking (select appropriate phrase according to above) [both] [short-acting] [and] [long-acting] to manage your pain. Thinking back over the last 30 days, how did you use your pain medicine?

Probes:

a. *Do you usually use as needed and/or scheduled pain medicine every day?*
b. *How often do you take them? How many pills do you take each time? How many times are you supposed to take pills each day?*

Explore:

a. Typically, how long do you wait to take your next dose of pain medication? What factors influence your decision?
b. How long does it take you to get comfortable after taking your medication?
c. Do you ever take your medicine in a different order or dosage than prescribed by your doctor? Why? What factors influence your decision?
d. Have you ever stopped using your medicine for any reason? Can you tell me a little bit about that?

Reasons for Underuse, Overuse, Erratic, and Quitting

5) The following questions below depend on answer to this question # 4) [For Adherent what was it that made you want to keep taking your pain medicine as prescribed?] [For Non-adherent: Why did you decide that you wanted to quit using your pain medicine?] [For Erratic User: You mention that you sometimes use more and sometime use less of your pain medications that your doctor than prescribed of your strong pain medicines; what is the reason? What made you use it that way?]

6) I know that many doctors prefer to treat sickle cell pain with a combination of as-needed and scheduled pain medicine or a number of different medicines at the same time. How do you know which kinds of medicine to use? How did you decide to take them?

7) Besides using your pain medicine to help with pain, what other methods do you use, such as home remedies?

Explore:

a. *(f/u) If you use more than one method, how do you choose which one to use when? How do you combine methods?*

8) Thinking about a typical day (with pain or without pain), tell me how you usually take your prescriptions during that 24 hour period.

Probes*:*

a. *When do you usually take your pills?*
b. *Are there any times of day (or night) when you take more or less of your medications?Why?*
c. *How would your medication usage vary on an atypical (unusual) day? What does an atypical day look like for you? Why would you change the way you use your medicine?*

9) Do you agree with the amount of pain medicine your doctor prescribes for your sickle cell pain?

Probes:

a. *Do you think that your doctor has you on the right medicines?*
b. *What changes would you make to your drug regimen if it were up to you?*

10) Regimen Complexity Do you take your pain medication the way that your doctor originally prescribed it? Have you ever had any problems understanding how to take your medications? (If so) Tell more me about it.

General Factors Affect Adherence (Motivations and Difficulties) Over the Time or Episodically

Transition: Next, I would like to ask you some questions about your experiences with pain medicine

11) Motivations or Factors for Use: What factor influence, encourage, or motivate you to use your pain medicine (scheduled pain medicine or as-needed pain medicine)?

12) Barriers, Challenges or Difficulties of Adherence to Pain Medicine at Home: Sometimes SCD adults find it difficult to take medicines as the doctor has ordered. What are some things that make it difficult to continue taking your pain medicines as prescribed? Why?

Explore:

a. *(f/u) Describe a time when you experienced difficulty taking your scheduled or as-needed pain medicine. How did these challenges affect your ways of using pain medicine?*

13) Family or Friends Concern of Opioid Use: Think of your environment. By environment I mean the physical and social world around you. How does your environment affect the way you take your medicine?

Probe:

a. *How do your family and friends affect how you take (or don't take) your pain medicine? Share with us about how people in your life play a role in taking your medicine?*
b. *(f/u) How does society affect how you take your pain medicine? Do you feel you must be "responsible" to yourself or to others?*
c. *How does the weather affect how you take your pain medicine? If you can, share with us what kinds of weather change the way you take your pain medicine.*

14) Reasons for Underuse: There are many reasons why SCD patients use less pain medicine than prescribed, don't use pain medicine for a time, or choose not to use it. Thinking about the last three months, please tell me a story of a time when you took less of your medicine than you usually take or took less than you thought you needed?

Explore:

a. *(f/u) What were the reasons for each of the times that you needed/wanted to use pain medicine, but didn't use? Describe those reasons in detail.*

15) Reasons for Overuse: There are many reasons why SCD patients use more pain medicine than prescribed or there are times when they don't need or want to use pain medicine, but they choose to use it anyway. Thinking about the last three months, please tell me a story of a time when you took more of your medicine than you usually take or took more than you thought you needed?

Explore:

a. *(f/u) What were the reasons for each of the times that you didn't need/want to use pain medicine, but used more or used it anyway? Describe those reasons in detail.*

Using Opioid for Symptoms/Reasons Other than Pain

16) Some SCD patients may use pain medicine for reasons other than pain. Thinking about the last three months, please tell me a story of a time you used your pain medicine for reasons or symptoms other than pain. How would you describe these reasons?

17) Forget or Missing Doses: People have a lot of different feelings about how medicines work and what the results are if they miss a dose. Thinking about the last three months, please tell me a story of a time you missed a dose or several doses of pain medicine.

Explore:

a. *(f/u) How did you feel you when you missed a pill or several pills?*
b. *(f/u) How important is it to you to take your medicines as prescribed? Please explain.*
c. *(f/u) What do you do when you realize you miss/forget to take a dose of your prescribed medicines? Take more, take less? Describe.*

Reasons for Episodic and Temporary Change in Adherence

Using Opioid while in Pain when Feeling Worse than Usual

18) Think back to when you were **feeling worse** pain than usual or when you having crises. What, if anything, did you do differently to get rid of your pain?

Explore:

a. *Why do you think yo**u chose to us**e your pain medicine in this way, in this situation?*
b. *(f/u) What did you do when the pain was not relieved (you **were sti**ll feeling pain) after you took your pain medicines? Did you use your pain medicine differently then? Did you use more or less than prescribed?*
c. *(f/u) What made you decide to use the medicine in such a way?*
d. *(f/u) Did the location of pain affect your way of using pain medicine?*

Using Opioid while in Pain when Feeling Good

19) When you are feeling good, how do you use your medicine?

20) Think back when you are/were feeling better after you took your pain medicines, how did you use your medicine then?

Probes:

a. *Did you ever stop taking your scheduled or as-needed medicines when you were feeling good? If so, tell more about that.*

21) Describe a time for me when you were having no/little SCD pain (or you felt better) but still chose to take more pain medicine?

Explore:

a. *(f/u) Why do you think you chose to use your pain medicine in this way, in the situation you explained to me?*

Psychosocial Factors

Using Opioid while in Pain and Having Social Activities, Special Events, Circumstances, or Situation

22) How do you use your pain medicine before, after, or during some special social event, activity or special situation?

Explore:

a. *(f/u) To what extent are you able to use your medicine as prescribed during this time? Do you change your routine?*

Using Opioid while in Pain and Having Stress or Other Psychological Components

23) How does stress in your life relate to your pain? Which usually comes first, the stress or the pain?

Explore:

a. *(f/u) How do you cope with the stress when you are in pain?*
b. *(f/u) Do you change your routine (I mean the way in which you take your medicine) when you are in stress and in pain?*
c. *(f/u) Do you change how you use your pain medicine when you are under stress?*

Ending the Interview

24) Recommendations: Based on your experience, what information do you think is important for other patients and healthcare providers to know about pain medicine?

Probes:

a. *What advice would you give a person who is considering maintaining his/ her pain medicine as prescribed or improving his /her way of taking pain medicine?*

To wrap up: We have come to the end of the interview. You explained before how you use your pain medicine and the reasons for using them. In light of what we have just been discussing (medicine use and reasons for use), I'd like to ask you if you have any additional, final comments, or anything that you think we should have talked about but didn't? This concludes ends the interview. As we conclude, I would like to thank you for your assistance with this research project. You have been most helpful in responding to the questions. Thank you for taking part in this interview and for responding to the questions so thoroughly. I appreciate your time, interest, and openness. How do you feel about the interview we have just had? May I call you if I need to clarify or add to any information you have provided? Is there anything that you would like to ask me? I am happy to answer any questions that you may have.

Appendix H

Phase 1: Preliminary Survey (to be administered after the interview)

1) In general, how did you take your pain medicine during the last seven days?"
   a) Regularly took all pain medications.

   b) Regularly took some prescribed pain medications.

   c) Took all prescribed pain medications after an increase in pain

   d) Took some medications after an increase in pain.

   e) Did not take prescribed pain medication most of the time.

2) Which of the following statements best describes the way that you take your **as-needed (short-acting)** pain medicine?
   a) Over the last month, I usually took my medication as prescribed.
   b) Over the last month, I usually took LESS medicine than prescribed.
   c) Over the last month, I usually took MORE medicine than prescribed
   d) Over the last month, I sometimes took MORE medicine than prescribed and sometimes LESS medicine than prescribed.
   e) Over the last month, I usually took my medicine more than prescribed when I had little pain and less than prescribed when I had more pain.
   f) Over the last month, I stopped taking my medicine without consulting my health care provider.

3) Which of the following statements best describes the way that you take your as-**needed (short-acting)** pain medicine?
   a) Over the last month, I usually used my medication according to the directions on the bottle.
   b) Over the last month, I usually took LESS medication than the directions on the bottle said I should take.
   c) Over the last month, I usually took MORE medication than the directions on the bottle said I should take.

d) Over the last month, I used both MORE and LESS medication than the directions on the bottle said I should take.

4) If you are taking long-acting medicine, which of the following statements best describes how you take your **scheduled (long-acting)** pain medicine?
   a) Over the last month, I usually took my medication as prescribed.
   b) Over the last month, I usually took LESS medicine than prescribed.
   c) Over the last month, I usually took MORE medicine than prescribed.
   d) Over the last month, I sometimes took MORE medicine than prescribed and sometimes LESS medicine than prescribed.
   e) Over the last month, I usually took my medicine more than prescribed when I had little pain and less than prescribed when I had more pain.
   f) Over the last month, I stopped taking my medicine without consulting my health care provider.

5) If you are taking long-acting medicine, which of the following statements bests describes how you take your **scheduled (long-acting)** pain medicine?
   a) Over the last month, I usually used my medication according to the directions on the bottle.
   b) Over the last month, I usually took LESS medication than the directions on the bottle said I should take.
   c) Over the last month, I usually took MORE medication than the directions on the bottle said I should take.
   d) Over the last month, I used both MORE and LESS medication than the directions on the bottle said I should take.
   e) Over the last month, I usually took my medicine more than prescribed when I had little pain and less than prescribed when I had more pain.
   f) Over the last month, I stopped taking my medicine without consulting my health care provider.

6) Some SCD patients may take medicines because they worry about having more pain and other complications in the future. How frequently do you take your medicine because you have this feeling?
   a) Never
   b) Rarely
   c) Sometimes
   d) Often
   e) Always

7) While in pain, some SCD patients may want to continue moving and doing their daily activities, such as work, social activities, housework, or attending school, but the fear of movement or injury keeps them from doing such things. How frequently do you take your medicine because you have this feeling?
   a) Never
   b) Rarely
   c) Sometimes
   d) Often
   e) Always

8) Some SCD patients may use more pain medication when they are dealing with difficult situations, like family, relationship, or financial problems, or other kinds of stressors. How frequently do you take your medicine to escape of avoid these kinds of feelings?
   a) Never
   b) Rarely
   c) Sometimes
   d) Often
   e) Always

9) Some SCD patients may change the way they take their medication to deal with temporary situations, like taking exams, finishing assignments, or dealing with specific work duties. How frequently do you INCREASE your medicine when you are in this situation?
   a) Never
   b) Rarely
   c) Sometimes
   d) Often
   e) Always

10) Some SCD patients may change the way they take their medication to deal with temporary situations, like taking exams, finishing assignments, or dealing with specific work duties. How frequently do you REDUCE your medicine when you are in this situation?
   a) Never
   b) Rarely
   c) Sometimes

d) Often
e) Always

11) SCD patients told me that because they were rushing off to appointment/ meeting or having unplanned activities, they chose to take less or more of pain medicine or they forgot to take their medicine. How frequently you take LESS pain medicine because you have this situation?
a) Never
b) Rarely
c) Sometimes
d) Often
e) Always

Background Information Form

Lastly, I would like to gather some demographic information about you. Fill in the blank or check the response that best fits you as an individual

Partnership status (Are you married, single, or in a relationship?

___Married
___Widowed
___Separated
___Divorced
___Single
___Unknown
___Others: Partnered

Living arrangement:

___ live alone
___ live with partner/spouse
___ live with roommate (how many ____)
___ live with parents
___ other (explain_____)

Education: What is the highest level of education that you have obtained?

___Less than High School
___High School Graduate
___Some College
___College Graduate

What is your yearly household income?

___ No income
___ $1 - $25,000
___ $25,001- $50,000
___ $ 50,001 - $75,000
___ $75,001 - $100,000
___$ 100,001+

What are your sources of income? What is your current employment status?

Do you have health insurance? ___Yes ___No **If so, what kind?**_____
How much do you spend on your medicine (per prescription)?
$3 to $5.00 per pain prescription
$6 to $29 per pain prescription
$30.00 to $50.00 per pain prescription
More than $ 100 per pain prescription
Do you drink alcohol? ___Yes ___No
When you do, how much do you drink per day? _____
Do you smoke cigarettes? ___Yes ___No

Appendix I

IRB Approval

VCU Memo
Virginia Commonwealth University

Office of Research Subjects Protection
BioTechnology Research Park
BioTech One, 800 E. Leigh Street, #114
P.O. Box 980568
Richmond, Virginia 23298-0568
(804) 828-3992
(804) 827-1448 (fax)

DATE: November 7, 2011

TO: Wally R. Smith, MD
Internal Medicine
Box 980306

FROM: Lisa M. Abrams, PhD
Chairperson, VCU IRB Panel B
Box 980568

RE: **VCU IRB #: HM13946**
Title: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease

On November 7, 2011, the following research study was ***approved*** by expedited review according to 45 CFR 46.110 Categories 5, 6, and 7. This approval reflects the revisions received in the Office of Research Subjects Protection on November 3, 2011, and supporting document received on November 7, 2011. This approval includes the following items reviewed by this Panel:

RESEARCH APPLICATION/PROPOSAL: None

PROTOCOL (Research Plan): Understanding Adherence to Prescribed Opioids in Sickle Cell Disease, received 11/3/11, version 3
- VCU IRB Study Personnel Roster, received 11/3/11, version 1, dated 8/29/11
- Pre-Screening Form, received 11/3/11, version 3, dated 11/3/11
- Screening Form: MINI Mental State Exam, received 11/3/11, version 3, dated 11/3/11
- Baseline Information and Data Collection Form (Brief Pain Inventory – Short Form, McGill Pain Scale with Drawing – Short Form, Prior and Current Medications, and Study Completion), received 11/3/11, version 2
- Interview Guide, received 11/3/11, version 2
- Bibliography, received 9/22/11, version 1

HIPAA PROCESS:
**The following pathways for accessing and/or using PHI have been approved:*
- Partial Waiver of Authorization for Recruitment
- Signed Authorization combined with Informed Consent

CONSENT/ASSENT (attached):
- Research Subject Information and Consent Form, received 11/3/11, version date 11/3/11, 5 pages

ADDITIONAL DOCUMENTS (attached):
- Recruitment Invitation Letter, received 11/3/11, version date 11/3/11
- Contact Information for Recruitment, received 11/3/11, version date 11/3/11

(Continued...)

Please Note: The VCU IRB acknowledges receipt of the revised/final VCU IRB Appendix A: HIPAA for Research form, on November 7, 2011.

This approval expires on October 31, 2012. Federal Regulations/VCU Policy and Procedures require continuing review prior to continuation of approval past that date. Continuing Review report forms will be mailed to you prior to the scheduled review.

The Primary Reviewer assigned to your research study is Elizabeth Ripley, MD, MS. If you have any question please contact Dr. Ripley at eripley@mcvh-vcu.edu and 828-1955; or you may contact Jennifer Rice, IRB Coordinator, VCU Office of Research Subjects Protection, at irbpanelb@vcu.edu and 828-3992.

[Attachment – Conditions of Approval]

Recruitment Invitation Letter

Dear Patients,

I am contacting you because you are listed and scheduled to have a medical appointment today (or recently) in the Adult Sickle Cell Anemia Clinic at the Ambulatory Clinics Building at Virginia Commonwealth University Health System. We would like to invite you to consider participating in a new study called "Understanding Adherence to Prescribed Opioids in Sickle Cell Disease." that I am conducting.

Are you interested in hearing about this study? If yes, here is a brief description of this new study. This study is designed to find out about ways and patterns of prescribed opioid use at home in patients with sickle cell disease and to find out about the reasons of using prescribed opioid in different ways and different pattern. You are being asked to participate in this study because you have a medical appointment in the sickle cell anemia clinic, and may meet the study entry requirements. If you are interested and eligible to participate you will be interviewed today, or at any another convenient date/time. If you are interested, I will need to ask you some questions to determine your eligibility."

I am looking for 30-40 people who have sickle cell anemia to join in this study. The study involves some screening questions, then some pain assessment questions, collecting some medical history from your medical records and an interview for 1.5 hours.

I am including my contact information for you to contact (phone, mail) to indicate if you are interested in having me contact you to participate in this study. Indicating "Yes" does not mean that you have any obligation to join the study; it simply means you would like to receive more information.

If you have questions or need more information about this study, please feel free to contact me, Abdulkhaliq Alsalman, at the hospital during weekdays, (804) 728-9803.
Sincerely yours,

Principal Investigator signature Date:

Principal Investigator
Dr. Wally R. Smith
Wally R. Smith, MD
Professor of Medicine
Virginia Commonwealth University
1200 E. Broad St. Rm W10W-403
Box 980306
Richmond, Virginia 23298-0306
Ph 804-828-6938
Fax 804-828-4862

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Understanding Adherence to Prescribed Opioids in Sickle Cell Disease
VCU IRB NO.: HM13946
INVESTIGATORS: Dr.Wally Smith, Dr. Donna McClish, Amy Belo-Nichols, and Abdulkhaliq J. Alsalman,

This consent form may contain words that you do not understand. Please ask the study staff to explain any words that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY
The purpose of this research study is to find out about patterns of medication use in patients with sickle cell disease and to find out about the reasons patients use prescribed opioids in different patterns (if they exist). You are being asked to participate in this study because you have been diagnosed with sickle cell disease, and may meet the study entry requirements.

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT
If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered and understand what will happen to you. Any information gathered from you will only be used for research purposes. Approximately 40 subjects who have sickle cell anemia will participate in this study.
Information from your medical records will be collected. The information to be collected includes type of sickle cell, history of ER visits, medications, past medical history, visit history, and sickle cell related complications. In this study you will be asked to participate in a single interview. In this interview, you will be asked a series of questions about your medication use. The interviewers will ask you questions about your treatment experiences as a sickle cell patient. Answering these interview questions will take approximately one hour and a half. You may take a brief break mid-way through the interview if you need to. Before, during, or after the interview, we will offer juice and/or water if you need it. The interview will be tape recorded so we are sure to get your ideas, but no names will be recorded on the tape.

RISKS AND DISCOMFORTS
You may find some of these questions to be of a sensitive nature. You may feel uncomfortable answering them. You may refuse to answer any question(s) for any reason. Sometimes talking about these subjects causes people to become upset. Several questions will ask about things that have happened to you that may have been unpleasant. You do not have to talk about any things you do not want to talk about, and you may end the interview at any point. If you become upset, the study staff will give you names of counselors to contact so you can get help in dealing with these issues.

USE AND DISCLOSURE OF PROTECTED HEATLH INFORMATION

Authority to Request Protected Health Information
The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Research Collaborators
- Data Safety Monitoring Boards
- Others as Required by Law
- Study Sponsor
- Institutional Review Boards
- Government/Health Agencies

Authority to Release Protected Health Information
The VCU Medical Center (VCUMC) may release the information identified in this authorization from my medical records and provide this information to:

- Health Care Providers at the VCUMC
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Others as Required by Law
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released
The following types of information may be used for the conduct of this research:

☒ Complete health record	☒ Diagnosis & treatment codes	☒ Discharge summary
☒ History and physical exam	☒ Consultation reports	☒ Progress notes
☒ Laboratory test results	☐ X-ray reports	☐ X-ray films / images
☐ Photographs, videotapes	☐ Complete billing record	☐ Itemized bill
☒ Information about drug or alcohol abuse	☐ Information about Hepatitis B or C tests	
☒ Information about psychiatric care	☐ Information about sexually transmitted diseases	

☐ Other (specify):

Right to Revoke Authorization and Re-disclosure
You may change your mind and revoke (take back) the right to use your protected health information at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you must write to the Principal Investigator.

APPROVED

11-7-11 /EBR/JR

BENEFITS TO YOU AND OTHERS
This is not a treatment study, and you are not expected to receive any direct medical benefits from your participation in the study. The information from this research study may lead to a better understanding of treatment in the future for people with sickle cell disease. Please be aware that the research team and the University may receive money to conduct this study.

COSTS
There are no costs for participating in this study other than the time you will spend in the interview and filling out questionnaires.

PAYMENT FOR PARTICIPATION
You will be offered $45.00 for your time and effort to complete this study. Tax laws now require us to have you complete a W-9 tax form that says you received your money. In addition, you will receive cab/bus vouchers (if you need it).

ALTERNATIVES
This is not a treatment study. Your alternative is not to participate in this study.

CONFIDENTIALITY
Personal information about you – including your medical records and personal research data gathered in this study – will be kept private and safe.
Information about you that will have your name will consist of interview notes and recordings of interviews, and information from the medical record. Information is being collected only for research. Your information will be identified by ID numbers and birthdates, not names, and codes for this will be stored separate from your medical record in a locked research area. We will password-protect your information. The codes to identify you will be deleted after we complete the study on all participants. Access to all data will be limited to study personnel. The didgital recording will be destroyed after transcription and the completion of the study. The de-identified data may be kept indefinitely.
We will not tell anyone the answers you give us; however, information from the study and information from your medical records and the consent form signed by you may be looked at or copied for research or legal purposes by Virginia Commonwealth University. Although results of this research may be presented at meetings or in publications, your name or medical record number or anything that can identify you will not be disclosed.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

You do not have to participate in this study. If you choose to participate, you may stop at any time without any penalty. You may also choose not to answer particular questions that are asked in the study. Your decision will not change your future medical care at this site or institution.

APPROVED
11-7-11 / EBR / JR

Your participation in this study may be stopped at any time by the study staff without your consent. The reasons might include:

- the study staff thinks it necessary for your health or safety;
- you have not followed study instructions;
- Administrative reasons require your withdrawal.

QUESTIONS

In the future, you may have questions about your participation in this study. If you have any questions, complaints, or concerns about the research, contact:

Abdulkhaliq J. Alsalman, M.S.
PhD Student
Department of Pharmacotherapy and Outcome Sciences
School of Pharmacy/Virginia Commonwealth University
410 N. 12th Street, PO Box 980533
Richmond, VA 23298-0533
(804) 728-9803
Fax: (804) 828-8359

OR, call the Principal Investigator,

Wally R. Smith, MD
Professor of Medicine
Virginia Commonwealth University
1200 E. Broad St. Rm W10W-403
Box 980306
Richmond, Virginia 23298-0306
Ph 804-828-6938
Fax 804-828-4862

If you have any questions about your rights as a participant in this study, you may also contact:

Office for Research
Virginia Commonwealth University
800 East Leigh Street, Suite 113
P.O. Box 980568
Richmond, VA 23298
Telephone: 804-827-2157

You may also contact this number for general questions, concerns or complaints about the research. Please call this number if you cannot reach the research team or wish to talk to someone else. Additional information about participation in research studies can be found at http://www.research.vcu.edu/irb/volunteers.htm.

APPROVED
11-7-11 /EBR/JR

CONSENT

I have been given the chance to read this consent form. I understand the information about this study. Questions that I wanted to ask about the study have been answered. My signature says that I am willing to participate in this study and I have not waived any of the legal rights or benefits, to which I otherwise would be entitled. I will receive a copy of the consent form once I have agreed to participate.

Participant name printed	Participant signature	Date

Name of Person Conducting Informed Consent Discussion / Witness [3]
(Printed)

Signature of Person Conducting Informed Consent Discussion / Witness — Date

Principal Investigator Signature (if different from above) — Date [4]

APPROVED
11-7-11/EBR/JR

Appendix J

Assessment of Opioid Taking Behaviors and Adherence Scale (AOTBA)

"Hello. My name is Abdul. I'm a graduate student working with Dr. Smith. I'd like to ask you some questions about your pain medicine(s) As you may know, you are participating in a research study designed to learn more about pain medicine(s)and how it works in order to help health care providers to better prescribe for their Sickle Cell Disease (SCD) patients. I also want to remind you that the information you give me will be completely confidential. It will be used only for my research, and we will not share it with anyone outside my research project. Some of these things you may know about and some you may not. Just give me the best information you can, and let me know if you're not clear of what I'm asking. Do you have any questions before we begin?"

Part 1: Background Information

First, I would like to gather some demographic information about you. Fill in the blank or check the response that best fits you as an individual

4. **How would you describe your racial or ethnic (origin) background?**

   - ○ American Indian/Alaskan Native
   - ○ Hispanic
   - ○ Asian/Pacific Islander
   - ○ White (non-Hispanic) Caucasian
   - ○ Black African American (non-Hispanic)
   - ○ Other_____ (Please specify.)

5. **Are you:**

   - ○ Female
   - ○ Male

6. **How old are you?** _____ years old

7. **Relationship status (Are you married, single, or in a relationship?**

- Married
- Widowed/ Widower
- Separated
- Divorced
- Single
- Unknown
- Partnered
- Others:

8. Living arrangements (mark best answer):

- House
- Apartment
- Other

With whom: (mark all that apply)

- I live alone
- I live with my partner/spouse
- I live with roommate(s) (if so, how many? ____)
- I live with my parent(s)
- I live with my children
- I live with parent, partner/spouse and/or children
- other (explain_____)

9. County of residence: _____ Zip Code: _____

10. How long have you lived in this county?

- Less than one year
- One to two years
- Two to five years
- Five to 10 years
- Ten years or longer

11. What is the highest level of education that you have completed?

- Grade school
- Some high school
- High School Graduate
- Some College
- Associate degree

- College Graduate (Bachelor's degree)
- Professional degree

12. If you have children, how many children do you have?
..... Child (ren)

13. If you have children, how old are they? (Mark all that apply.)

- I do not have any children
- 0-4 years
- 5-9 years
- 10-14 years
- 15-17 years
- 18-21 years
- Over 21 years

14. What is your total household income from all sources, before taxes?

- ___ No income
- $10,000 or less
- $10,001 to $20,000
- $20,001 to $30,000
- $30,001 to $40,000
- $40,001 to $50,000
- $ 50,001 - $75,000
- $75,001 - $100,000
- $ 100,001+

15. What are your sources of income?

_____
_____
_____

16. What is your current employment status?

_____

17. Do you have health insurance?

___Yes ___No

If so, what kind? _____

18. How much do you spend on your pain medicine(s)(per prescription)?

- ○ $3 to $5.00 per prescription
- ○ $6 to $29 per prescription
- ○ $30.00 to $50.00 per prescription
- ○ $51.00-100.00 per prescription
- ○ More than $ 100 per prescription

19. Do you drink alcohol? ___Yes ___No

20. When you do, how much do you drink per day? _____

21. Do you smoke cigarettes? ___Yes ___No

22. Do you use illicit (illegal) drugs? ___Yes ___No

23. Place of permanent residence:

- ○ In-state
- ○ USA, out of state
- ○ Other country

Part 2

19. At what age did you first take prescribed pain medicine? (Mark an X in the appropriate columns and fill the blank)

	As-needed Short acting pain medicine	**Scheduled long-acting pain medicine**
I have never used prescribed pain medicine	☐	☐
I have started taking prescribed pain medicine(s)at age	.....	.....

Type of Pain Medicine(s)

20. Health care provider(s) prescribe the following strong pain medicine(s) Which of the following medicine(s)do you take? Mark an X in one box for each type of prescribed pain medicine(s)that you take.

	I currently take this medicine(s)	I've tried it a few times (at least once)	I've cut down my use	I have regularly used this pain medicine(s) in the past but no longer.	I have never used this medicine(s) at all.	Why? (E.g. if stopped, Why Stopped?)
Morphine IR (short-acting)	☐	☐	☐	☐	☐	
MS Contin (long-acting Morphine)	☐	☐	☐	☐	☐	
Ultram (Tramadol)	☐	☐	☐	☐	☐	
Any Tylenol 1-4 (acetaminophen/codeine).	☐	☐	☐	☐	☐	
Codeine	☐	☐	☐	☐	☐	
Darvocet (propoxyphene)	☐	☐	☐	☐	☐	
Methadone	☐	☐	☐	☐	☐	
Oxycodone IR (short-acting)	☐	☐	☐	☐	☐	
OxyContin (long-acting Oxycodone)	☐	☐	☐	☐	☐	
Percocet	☐	☐	☐	☐	☐	
Lortab OR Vicodin	☐	☐	☐	☐	☐	
Dilaudid (hydromorphone)	☐	☐	☐	☐	☐	
Opana (short acting oxymorphone)	☐	☐	☐	☐	☐	
Opana ER (Long acting oxymorphone)	☐	☐	☐	☐	☐	
Pain patches (Fentanyl)	☐	☐	☐	☐	☐	
Demerol	☐	☐	☐	☐	☐	
Other strong prescribed pain medicine(s) Not listed……	☐	☐	☐	☐	☐	

…… ……						

Frequency of Use within the Last Year

21. To the best of your knowledge, in the past 12 months, how often have you used your strong prescribed pain medicine? Mark one column for each medicine(s)you currently take.

	Never	Once/year	Every other month	Every month	Other
Morphine IR	☐	☐	☐	☐	.....
MS Contin LA	☐	☐	☐	☐	.....
Ultram (Tramadol)	☐	☐	☐	☐	.....
Any Tylenol 1-4 (acetaminophen/codeine)	☐	☐	☐	☐	.....
Codeine	☐	☐	☐	☐	.....
Methadone	☐	☐	☐	☐	.....
Oxycodone IR	☐	☐	☐	☐	.....
OxyContin	☐	☐	☐	☐	.....
Percocet	☐	☐	☐	☐	.....
Lortab OR Vicodin	☐	☐	☐	☐	.....
Dilaudid (hydromorphone)	☐	☐	☐	☐	.....
Opana (short acting oxymorphone)	☐	☐	☐	☐	.....
Opana ER (Long acting oxymorphone)	☐	☐	☐	☐	.....
Pain patches (Fentanyl)	☐	☐	☐	☐	.....
Demerol	☐	☐	☐	☐	.....
Other strong prescribed pain medicine(s) NOT listed.....	☐	☐	☐	☐	.....

Frequency of use within the last month

22. To the best of your knowledge, during the past 30 days, how many days have you used your strong prescribed pain medicine? (Mark one for each line)

	0 days	1-4 days	5-9 days	10-14 days	About 14 days	15-19 days	20-24 days	25-29 days	Every day
Morphine	☐	☐	☐	☐	☐	☐	☐	☐	
MS Contin LA	☐	☐	☐	☐	☐	☐	☐	☐	
Tramadol	☐	☐	☐	☐	☐	☐	☐	☐	
Tylenol III	☐	☐	☐	☐	☐	☐	☐	☐	
Codeine	☐	☐	☐	☐	☐	☐	☐	☐	
Methadone	☐	☐	☐	☐	☐	☐	☐	☐	
Oxycodone	☐	☐	☐	☐	☐	☐	☐	☐	
OxyContin	☐	☐	☐	☐	☐	☐	☐	☐	
Percocet	☐	☐	☐	☐	☐	☐	☐	☐	
Lortab OR Vicodin	☐	☐	☐	☐	☐	☐	☐	☐	
Dilaudid (hydromorphone)	☐	☐	☐	☐	☐	☐	☐	☐	
Opana (short acting oxymorphone)	☐	☐	☐	☐	☐	☐	☐	☐	
Opana ER (Long	☐	☐	☐	☐	☐	☐	☐	☐	

acting oxymorphone)									
Pain patches (Fentanyl)	☐	☐	☐	☐	☐	☐	☐	☐	
Demerol	☐	☐	☐	☐	☐	☐	☐	☐	
Other strong Prescription Painkillers Not Listed.....	☐	☐	☐	☐	☐	☐	☐	☐	

Frequency of use within the last week

23. To the best of your knowledge, during the last week, how many days have you used your strong prescribed pain medicine?

	None last week	One day last week	Two days last week	Three days last week	Four days last week	Five days last week	Six days last week	Every day last week
Morphine	☐	☐	☐	☐	☐	☐	☐	☐
MS Contin LA	☐	☐	☐	☐	☐	☐	☐	☐
Tramadol	☐	☐	☐	☐	☐	☐	☐	☐
Tylenol III	☐	☐	☐	☐	☐	☐	☐	☐
Codeine	☐	☐	☐	☐	☐	☐	☐	☐
Methadone	☐	☐	☐	☐	☐	☐	☐	☐
Oxycodone	☐	☐	☐	☐	☐	☐	☐	☐
OxyContin	☐	☐	☐	☐	☐	☐	☐	☐
Percocet	☐	☐	☐	☐	☐	☐	☐	☐
Lortab OR Vicodin	☐	☐	☐	☐	☐	☐	☐	☐
Dilaudid (hydromorphone)	☐	☐	☐	☐	☐	☐	☐	☐
Opana (short acting oxymorphone)	☐	☐	☐	☐	☐	☐	☐	☐
Opana ER (LA oxymorphone)	☐	☐	☐	☐	☐	☐	☐	☐
Pain patches (Fentanyl)	☐	☐	☐	☐	☐	☐	☐	☐
Demerol	☐	☐	☐	☐	☐	☐	☐	☐
Other Painkiller	☐	☐	☐	☐	☐	☐	☐	☐

s Not Listed _____								

Frequency of Use within the <u>Last 24 hours</u>

24. To the best of your knowledge, in the past 24 hours, how many doses of strong prescribed pain medicine(s) did you take?

	5 or more doses in 24 hours	Four doses in last 24 hours	Three doses in last 24 hours	Two doses in last 24 hours	One dose in last 24 hours
Morphine	☐	☐	☐	☐	☐
MS Contin LA	☐	☐	☐	☐	☐
Tramadol	☐	☐	☐	☐	☐
Tylenol III	☐	☐	☐	☐	☐
Codeine	☐	☐	☐	☐	☐
Methadone	☐	☐	☐	☐	☐
Oxycodone	☐	☐	☐	☐	☐
OxyContin	☐	☐	☐	☐	☐
Percocet	☐	☐	☐	☐	☐
Lortab OR Vicodin	☐	☐	☐	☐	☐
Dilaudid (hydromorphone)	☐	☐	☐	☐	☐
Opana (short acting oxymorphone)	☐	☐	☐	☐	☐
Opana ER (Long acting oxymorphone)	☐	☐	☐	☐	☐
Pain patches (Fentanyl)	☐	☐	☐	☐	☐
Demerol	☐	☐	☐	☐	☐
Other Prescription Painkillers Not	☐	☐	☐	☐	☐

Listed……. …….					

25. To the best of your knowledge, during the last week, how much of each type of medicine(s)did you take? What is the average daily use of your strong prescribed medicine?

Name of medicine	Actual-use				
	Strength of pill (How many milligrams/pill)	Average number of pills I take at a time	Average number of pills I take a day	I usually wait ____ hours between doses of medicine(s)	Calculation or comments (to be filled in by investigators)
Morphine	……*mg*	Up to…..pills	Up to…..pills	……	
MS Contin LA	……*mg*	Up to…..pills	Up to…..pills	……	
Tramadol	……*mg*	Up to…..pills	Up to…..pills	……..	
Tylenol III	……*mg*	Up to…..pills	Up to…..pills	……	
Codeine	……*mg*	Up to…..pills	Up to…..pills	……	
Methadone	……*mg*	Up to…..pills	Up to…..pills	……	
Oxycodone	……*mg*	Up to…..pills	Up to…..pills	……	
OxyContin	……*mg*	Up to…..pills	Up to…..pills	……...	
Percocet	……*mg*	Up to…..pills	Up to…..pills	……	
Lortab OR Vicodin	……*mg*	Up to…..pills	Up to…..pills	……..	
Dilaudid (hydromorphone)	……*mg*	Up to…..pills	Up to…..pills	……	
Opana (short acting oxymorphone)	……*mg*	Up to…..pills	Up to…..pills	……	
Opana ER (Long acting oxymorphone)	……*mg*	Up to…..pills	Up to…..pills	……	
Pain patches (Fentanyl)	……*mg*	Up to…..pills	Up to…..pills	……..	
Demerol	……*mg*	Up to…..pills	Up to…..pills	……..	
Other Prescription Painkillers Not Listed……	……*mg*	Up to…..pills	Up to…..pills	……..	

Physician Instructions

26. To the best of your knowledge, what are the instructions on the label of the bottle of your strong prescribed pain medicine?

Name of medicine					
	Strength of pill (How many milligrams/pill)	Minimum and Maximum number of pills to take at a time	Maximum Number of pills to be taken a day (if stated)	I usually wait ___ hours between doses of medicine	***Comments (to be filled in by investigators)***
Morphine	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
MS Contin LA	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Tramadol	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Tylenol III	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Codeine	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Methadone	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Oxycodone	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
OxyContin	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Percocet	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Lortab OR Vicodin	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Dilaudid (hydromorphone)	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Opana (short acting oxymorphone)	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Opana ER (Long acting oxymorphone)	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Pain patches (Fentanyl)	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	

Demerol	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	
Other Prescription Painkillers Not Listed……	……*mg*	___ to ___ pills.	Up to…..pills	……..*hour*	

27. How many days out of the last 30 did you take any pain medicine?

……..days

28. In the last 6 months, how many times did you have to call the doctor for pain medicine(s) before they were due, but you had no more medicine(s)to take, and to get more?

……..times

29. Why did you call early?

……
……
……
……

30. In the last 30 days, how many days were you in severe pain but you did not have your as-needed pain medicine?

…….. days

31. Which of the following statements best describes the way that you take your as-needed (short-acting) pain medicine(s)over the last month? (Please choose one)

h. I usually took my medicine(s)as prescribed

i. I usually took LESS medicine(s)than prescribed

j. Over the last month, I usually took MORE medicine(s)than prescribed

k. Over the last month, I sometimes took MORE medicine(s)than prescribed and sometimes LESS medicine(s)than prescribed.

l. Over the last month, I usually took my medicine(s)more than prescribed when I had little pain and less than prescribed when I had (great) pain.

m. Over the last month, I stopped taking my medicine(s)

n. Other……

32. I receive pills to last a certain amount of time, at the end of the time normally (OR At the end of most (every) month) **I had**

a. For as-needed short-acting strong pain medicine(s)(Please choose one)

- ○ All or most the pills left
- ○ Few pills left
- ○ Taken all the pills in the bottle
- ○ Finished all the pills before the 30 days

b. For scheduled long-acting strong pain medicine(s)(Please choose one)

- ○ All or most the pills left
- ○ Few pills left
- ○ Taken all the pills in the bottle
- ○ Finished all the pills before the 30 days

33. For as-needed short-acting strong pain medicine, if my next prescription is due to start the first week of the month,

a. I normally try to get the medicine:

- ○ Two weeks or more before due
- ○ One week before due
- ○ The week due

- ○ One week late (after due)
- ○ Two weeks or more before due

b. I normally begin taking it (Please choose one)

- ○ First week of the month
- ○ Second week of the month
- ○ Third week of the month
- ○ Fourth week of the month

c. When do you normally finish taking it? (Please choose one)

- ○ First week of the month
- ○ Second week of the month
- ○ Third week of the month
- ○ Fourth week of the month
- ○ Beginning of next month

28. My as-needed short-acting strong pain medicine(s)should last ____ days. They actually last ___ days.

34. During the last 30 days, what influence your decision to take pain medicine(s) other than pain? (Please circle up to 3 of the items)

1. Life situations (e.g. school/work/household tasks, responsibilities,, social gathering)
2. Mood (e.g. stress, boredom)
3. Environmental (e.g. change in weather)
4. Other people: (e.g. family, friends/peers, health care providers)
5. Other:……
6. Nothing

Part 3

Par 3: a. Characterizing Overall Medication Taking Behavior and Adherence with Pain Medicines

35. Which of the following statements best describes the way that you took your pain medicine during the past week? Please mark the one statement below that best describes how you took your pain medicine in the last seven days. Please mark tables, one for short-acting and one for long-acting medication. Please note that "as prescribed" means according to the directions on the bottle. All the statements that list pain medication mean the medication that is prescribed. The word "pain medication" refers to the medicine that is prescribed for you.

	Short-acting Opioid					Long-acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
1. I take LESS medicine than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
2. I take MORE medicine than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
3. I take both MORE medicine than and LESS medicine than	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

prescribed on certain days /occasions.										
4. I take LESS than prescribed when I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
5. I take MORE than prescribed when I have mild pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
6. I take both MORE than prescribed when I have mild pain and less than prescribed when I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
7. My health care	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

provider gives me prescriptio n for pain medicine and I fill them but do not take them.										
8. My health care provider gives me prescriptio n for pain medicines but I do not fill them on time (when they are due).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
9. My health care provider gives me prescriptio n for pain medicine but I do not fill them at all.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
10. 6. I am able to	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

follow exactly the agreement I made with my prescriber about how to take my pain medicine.										
11. I accurately describe the way I take my pain medicine to my healthcare provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
12. I consult my health care providers before making any change.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
13. I follow changes recommended by my health care	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

providers.										
14. I consult and follow my health care providers before making any changes	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
15. I consult and follow my health care providers before making some changes.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
16. I do consult but may NOT follow my health care providers before making some changes	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
17. I stopped taking my medicine	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

without consulting my health care provider.										
18. I choose to NOT take my pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
19. I choose to NOT take my pain medicine because I do not like it.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
20. I choose to NOT take my pain medicine because it reminds me that I have chronic illness.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
21. I cut back or stop taking my pain medicine because	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

its use will be long-term use associated and long-term side effect.										
22. I cut back or stop taking my pain medicine because I worry about addiction (dependence upon the medicine).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
23. I cut back or stop taking my pain medicine because I do not want to become tolerant and have to increase the dose for pain	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

relief.										
24. I cut back or stop taking my long-acting pain medicine because it was too hard to maintain a schedule.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
25. I cut back or stop taking my pain medicine because it interfered with normal every day activities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
26. I have trouble remembering if I have already taken my medication(s).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
27. I have	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

difficulty remembering to take all my medicine.										
28. I take all pain medicines as prescribed for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
29. I took some prescribed pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
30. I take prescribed pain medicine when I have mild to moderate pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
31. I take prescribed pain medicine when I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
32. I take prescribe	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

d pain medications only when I have severe pain.										
33. I am able to rely on myself more today than I was several years ago to manage my pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
34. I rely on myself to manage minor everyday pain with prescribed pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
35. I rely on myself to manage severe pain with prescribed pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
36. I take	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

responsibility for whether or not I take my pain medicine in the way that it is prescribed.										
37. I take my pain medicine even when I am not in pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
38. I manage non-pain symptoms with changes from what is written on the prescription.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
39. I remove my medication from its original bottle for convenience.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

40. I carry some pain medicine with me for emergencies.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
41. I rely on natural means rather than my pain medicine to relive my pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

Par 3: b. Momentarily Medication Taking Behavior and Momentarily Adherence with Pain Medicines
How often was each of the following statements true for you during the past week (the last 7 days)? (How frequently do you take your medicine because you have this feeling?) Mark one number per line.

	Short-acting Opioid					Long-acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
42. I change the prescribed way I take my pain medication when I	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

am dealing with difficult situations.										
43. I change the prescribed way I take my pain medication to deal with temporary situations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
44. I change the prescribed way I take my pain medication when I am dealing with financial problems.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
45. I change the prescribed way I take my pain medication to finish school or work assignmen	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

t.										
46. I change the prescribed way I take my pain medication when I am dealing with any kind of stress.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
47. I change the prescribed way I take my pain medication to finish Household chores /duties.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
48. I change the prescribed way I take my pain medicine in response to my responsibilities/obligations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

49. I change the prescribed way I take pain medicine in response to Family obligations and responsibilities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
50. I change the prescribed way I take my pain medicine in response to social events or activities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
51. I changed the prescribed way I take pain medicine in response to a social gathering.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
52. I change the prescribed way I take my pain medicine	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

in response to opinions of others.										
53. I change the prescribed way I take my pain medicine because of the influence of others.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
54. I change the prescribed way I take my pain medicine in response to life events.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
55. I change the prescribed way I take pain medicine in response spiritual needs or obligations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

56. I change the prescribed way I take my pain medication because I was rushing off to appointment or meeting.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
57. I change the prescribed way I take my pain medication because of unexpected events.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
58. I change the prescribed way I take my pain medication because of unplanned activities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
59. I change the prescribed way I take	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

pain medicine in response to pain severity.										
60. I adjust my pain medicine dosage based on pain level.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
61. I take my pain medicines at the first feeling of pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
62. I take my pain medicine only if I am really suffering.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
63. I take my pain medicine whenever I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
64. I change the prescribed way I take my pain medicine	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

in response to amount of pain relief.										
65. I change the prescribed way I take my pain medicine in response to how I think my pain will change over the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
66. I take my pain medicines whenever I feel any warning sign of pain (before the actual pain begins).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
67. I change the prescribed way I take my pain medicine because it makes me	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

feel better.										
68. I change the prescribed way I take my pain medicine because I am bored.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
69. I change the prescribed way I take my pain medicine because I have I difficulty thinking/concentra-ting with the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
70. I change the prescribed way I take my pain medicine because I experience different outcomes.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

71. I change the prescribed way I take my pain medicine if I experience any side effects.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
72. I change the prescribed way I take my pain medicine in response to the severity of side effects.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
73. I change the prescribed way I take my pain medicine in response to fear worry of negative consequences.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
74. I take my pain medicines whenever I	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

worry about having more pain in the near future.										
75. I take my pain medicines when I worry about having complications in the near future.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
76. I change the prescribed way I take my pain medicine because I used other prescribed medicines.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
77. I change the prescribed way I take my pain medicine because my doctor do NOT believe	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

and understand my pain.										
78. I take my pain medicines whenever I think I need them.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
79. I manage to take my pain medicine in whatever way works for me in my current situations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
80. I take my pain medicine as prescribed in every situation.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
81. I take the same dose of pain medicine as prescribed throughout the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

82. I change the prescribed way I take my pain medicine at different times of the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
83. I take the same dose of pain medicine as prescribed at the same time throughout the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
84. I take the same dose of pain medicine as prescribed every day of the week.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
85. I change the prescribed way of taking my pain medicine on the	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

weekend.										
86. I change the prescribed way I take my pain medication at different time of the day throughout the week.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
87. I take the same dose of my pain medicine as prescribed in every season of the year.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
88. I change the prescribed way I take my pain medication in different season of the year.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
89. I change the prescribed										

way I take my pain medicine because of changes in the weather.										
90. I change the prescribed way I take my pain medication in different geographic location.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
91. I change the prescribed way I take my pain medication whenever I am away from home.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
92. I change the prescribed way I take my pain medicine because I keep my	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

medications in different places.										
93. I change the prescribed way I take my pain medicine based upon the amount of pills available next to me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
94. I change the prescribed way I take my pain medicine because I did not arrange to have the medicine available to me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
95. I change the prescribed way I take my pain medicine because I	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

have no transportation to bring me to my clinic visit.										
96. I change the prescribed way I take my pain medicine whenever I learn about other ways that may work for me personally.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
97. I change the prescribed way I take my pain medicine based upon information I have read and decide what works best for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
98. I try to find the best	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

way to use my pain medicine for pain control and follow it as long as it is work for me.										
99. I control my pain with changes to my daily dose of pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
100. I control my pain with changes from what is written on the prescriptio n.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
101. I have adjusted my pain medicine in different ways at different times in my life.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

102. I manage more of my pain at home instead of consultation with my prescriber.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
103. I rely on myself to adjust the way I take my pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
104. I take responsibility for how I take my pain medicine in different situations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
105. I use common sense to adjust my pain medicine.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
106. I change the prescribed way I take my pain medicine	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

because I have only a few pills left to last for many days.										
107. I change the prescribed way I take my pain medicine because I have no more pills of one of my pain medicatio n.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
108. I change the prescribed way I take my pain medicine because I have only a few pills left to last for many days.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
109. I change the prescribed	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

way I take my pain medicine because of the cost of the pills.										
110. I change the prescribed way I take my pain medicine because my insurance will NOT pay for it.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
111. I take more of my prescribed pain medicine to avoid the need to go the Emergency Department.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
112. I forget to bring along my pain medicine, when I	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

travel or leave home.										
113. I miss taking my pain medicine because I do not want to take it out of my house with me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
114. I miss taking my pain medicine because I feel unsafe carrying it with me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
115. I cut back or stop taking my pain medicine when I feel better but the pain still there.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
116. I cut back or stop taking my pain medicine	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

when my pain is relived completel y.										
117. I cut back or stop taking medicatio ns when I feel worse from side effects.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
118. I cut back or stop taking my pain medicines when does not work and I need to try something for my pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
119. I cut back or stop taking my pain medicine because I do not believe it is morally right for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

120. I cut back or stop taking my medications because I feel worse and need to go the Emergency Department.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
121. I forget to take my medicine because I have to deal with a variety of life situations	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
122. I miss taking my pain medicines for reasons other than forgetfulness.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

Par 3: c. Ways of non-adherence/Ways of Deviation (Aspect of Non-adherence)

	Short-Acting Opioid					Long-Acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
123. I take my pain medicine at the same times daily regardless of pain intensity.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
124. I take every pain medicine only when I have pain or on an "as-needed basis"	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
125. I take the prescribed type of medicine for whatever level of pain severity I have at	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

the moment.										
126. I take every pain medicine prescribed for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
127. I take my long-acting pain medicine only when I have severe pain at the moment.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
128. I take my long-acting pain medicine only during days of severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
129. I take my short-acting pain medicine to prevent any pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

130. I take my short-acting pain medicine to prevent severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
131. I take my short-acting pain medicine until pain severity is at manageable level for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
132. I change the number of pills I take at a time.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
133. I take a different number of pills at a time from the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

134. I take more pills at a time than the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
135. I take fewer pills at a time than the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
136. I take more pills to manage symptoms other than pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
137. I change the prescribed way I take my pain medicine to manage symptoms other than pain (e.g. sleep, anxiety, etc.)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
138. I take my pain medicine at different	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

number of times per day than what is written on my prescription.										
139. I take my pain medicine more often than prescribed	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
140. I take my pain medicine less often than prescribed	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
141. I take my pain medicine more often than prescribed to manage symptoms other than pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
142. I wait to take my pain medicine until it is time for the	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

next dose.										
143. I wait to take my pain medicine until it is time for a dose according to the prescribed schedule.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
144. I wait the required (prescribed) amount of time between doses.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
145. I take my pain medicine until I receive relief.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
146. I wait a shorter amount of time between doses than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

147. I take my pain medicine more frequently than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
148. I take my pain medicine less frequently than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
149. I take my pain medicine at the prescribed time interval (waiting time between doses)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
150. I take my pain medicine and wait the prescribed amount of time between doses.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

151. I take my pain medicine in the time interval (waiting time between doses) that works for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
152. I wait to take my pain medicine until it is time for a dose according to the prescribed schedule.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
153. I wait less than the prescribed amount of time between doses.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
154. I wait more than the prescribed amount of time between	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

doses.										
155. I take more than the maximum number of pills prescribed per day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
156. I take more than the prescribed maximum daily number of pills that contain Tylenol.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
157. I take my pain medicine for the full number of days prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
158. I take my pain medicine for less number of days than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

159. I take more than one type of prescribed short-acting pain medicine at the same time.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
160. I take over the counter products and pain medicine at the same time without consulting my health care provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
161. I take herbals and pain medicine at the same time without consulting my health care provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

162. I take medicine prescribed for other conditions at the same time as pain medicine without consulting my health care provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

Appendix K
Revised AOTBA Instrument

Part 3

Part 3a

36. Which of the following statements best describes the way that you took your pain medicine(s) during the *past month*? Please mark the one statement below that best describes how you took your pain medicine(s)in the last seven days. Please mark tables, one for short-acting and one for long-acting medicine(s)(if applicable). Please note that "as prescribed" means according to the directions on the bottle. All the statements that list pain medicine(s) mean the medicine(s)that is prescribed to you.

	Short-acting Opioid					Long-acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
1. I take LESS pain medicine(s) than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
2. I take MORE pain medicine(s) than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
3. I take LESS pain medicine than prescribed when I have	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

severe pain.										
4. I take MORE pain medicine than prescribed when I have mild pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
5. I fill the pain medicine prescriptions I receive from my doctor but I do not take the medicine(s)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
~~6.~~ I do not fill the pain medicine prescriptions I received from my doctor on time (when they are due).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

~~7.~~ I do not fill the pain medicine prescriptions I receive from my doctor.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
8. I am able to faithfully follow the agreement that I made with my doctor regarding pain medicine(s)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
9. I describe accurately the way I take my pain medicine(s) to my doctor.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
10. I consult my doctor before I make any change in the way I take my pain medicine(s	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

)										
11. I follow the changes recommended by doctor regarding pain medicine(s).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
12. I do consult but may NOT follow my doctor's advice before making any changes to how I take my pain medicine(s).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
13. I stopped taking my pain medicine(s) without consulting my doctor.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
14. I choose NOT to take my	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

pain medicine because I do not like it.										
15. I choose NOT to take my pain medicine(s) because it reminds me that I have a chronic illness.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
16. I cut back or stop taking my pain medicine(s) when I feel worse from side effects.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
17. I cut back or stop taking my pain medicine(s) because I worry about dependence upon the	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

medicine.										
18. I cut back or stop taking my long-acting pain medicine(s) because it was too hard to maintain a schedule.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
19. I cut back or stop taking my pain medicine(s) because it interfered with normal every day activities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
20. I have trouble remembering if I have already taken my pain medicine(s)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
21. I have difficulty	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

remembering to take all my pain medicine(s)										
22. I take all my pain medicine(s) as prescribed for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
23. I take my pain medicine(s) when I have mild to moderate pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
24. I take my pain medicine(s) only when I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
25. I rely on myself to manage minor everyday pain with pain medicine(s)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

26. I rely on myself to manage severe pain with prescribed pain medicine(s)	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
27. I ignore the doctor's advice about how I take my pain medicine because I know better what works for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
28. I ignore the directions on my pain medicine bottle because I know better what works for me.										

29. I take my pain medicine(s) even when I am not in pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
30. I change the way I take my pain medicine(s) to manage non-pain symptoms.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
31. I remove some pain medicine(s)from the original bottle for convenience/ emergencies	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

Par 3: b.
How often was each of the following statements true for you during the *<u>past week</u>* (the last 7 days)? (How frequently do you take your medicine(s) because you have this feeling?) Mark one number per line.

	Short-acting Opioid					Long-acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
32. I changed the way I take my pain medicine(s) when I was dealing with difficult situations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
33. I changed the way I take my pain medicine(s) from the prescribed instructions when I was dealing with financial problems.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

34. I changed the way I took my pain medicine(s) from the prescribed instructions to finish my school or work assignment.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
35. I changed the way I took my pain medicine(s) when I was dealing with stress.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
36. I changed the way I took my pain medicine(s) to finish Household chores /duties.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
37. I changed the way I took my pain medicine(s	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

) in response to Family obligations and responsibilities.										
38. I changed the way I took my pain medicine(s) in response to social events or activities.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
39. I took more of my pain medicine(s) than prescribed in response to opinions of others.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
40. I took less of my pain medicine(s) than prescribed in response to opinions of others.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

41. I changed the way I took my pain medicine(s) in response to spiritual needs or obligations.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
42. I changed the way I took my pain medicine(s) because of unexpected events.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
43. I took less of my pain medicine(s) than prescribed when my pain got better.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
44. I took more of my pain medicine(s) than prescribed when my pain got										

worse.										
45. I changed the way I took my pain medicine(s) in response to amount of relief.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
46. I changed the way I took my pain medicine(s) in response to how I thought my pain would change over the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
47. I took my pain medicine(s) whenever I felt any warning sign(s) of pain (before	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

the actual pain began).										
48. I changed the way I took my pain medicine(s) because it made me feel better emotionally.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
49. I changed the way I take my pain medicine(s) because I was bored.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
50. I changed the prescribed way I take my pain medicine(s) because I had difficulty thinking/concentra-ting with the prescribed	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

dose.										
51. I changed the way I take my pain medicine(s) whenever I experienced complications of SCD.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
52. No matter how bad the side effects, I kept trying to take my pain medicine(s).										
53. I changed the way I took my pain medicine(s) in response to fear or worry of negative consequences.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

54. I took my pain medicine(s) when I worried about having complication in the near future.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
55. I changed the way I take my pain medicines because I used my other prescribed non-pain medicine(s).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
56. I changed the way I took my pain medicine(s) because my doctor does NOT believe my pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
57. I changed the way I took my	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

pain medicine(s) because my doctor does NOT understand my pain.										
58. I take my pain medicine(s) as prescribed in every situation.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
59. I took the same dose of pain medicine(s) as prescribed throughout the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
60. I changed the way I took my pain medicine(s)at different times of the day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
61. I took the same dose of pain medicine(s	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

) as prescribed at the same time every day throughout the week.										
62. I took the same dose of pain medicine(s) as prescribed every day of the week.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
63. I changed my way of taking my pain medicine(s) on the weekend.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
64. I changed the way I took my pain medicine(s) to different times of a given day throughout the week.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

65. I took the same dose of my pain medicine(s) as prescribed every season of the year.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
66. I changed the way I took my pain medicine(s) in different season of the year.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
67. I changed the way I took my pain medicine(s) because of changes in the weather.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
68. I changed the way I took my pain medicine(s) whenever I was away	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

from home.										
69. I changed the way I took my pain medicine(s) based upon the amount of pills available to me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
70. I changed the way I took my pain medicine(s) because I did not arrange to have the medicine(s) available to me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
71. I changed the way I take my pain medicine(s) whenever I learned about other ways that may	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

work better for me personally.										
72. I controlled my pain by taking my pain medicine(s) differently from what is written on the bottle.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
73. I managed more of my pain at home without talking with my doctor.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
74. I changed the way I took my pain medicine(s) because I only had a few pills left to last for few days.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
75. I changed the way I took my										

pain medicine(s) because I lost my pills.										
76. I changed the way I took my pain medicine(s) because I did not get my prescription on time.										
77. I changed the way I took my pain medicine because I ran out of one of them (pain medicines).	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
78. I changed the way I take my pain medicine(s) because of the cost of the pills.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

79. I changed the way I took my pain medicine(s) because my insurance would NOT pay for it.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
80. I took more of my prescribed pain medicine(s) to avoid the need to go the Emergency Department.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
81. I forgot to bring along my pain medicine, when I travelled or left home.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
82. I missed taking my pain medicine(s	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

) because I did not want to take it out of my house with me.										
83. I missed taking my pain medicine(s) because I felt unsafe carrying it with me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
84. I cut back or stopped taking my pain medicine(s) when I felt better even if I still had some pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
85. I cut back or stopped taking my pain medicine(s) when my pain was relieved completely.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

86. I cut back or stopped taking my pain medicine(s) when it did not work.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
87. I cut back or stopped taking my pain medicine(s) because I do not believe it is morally right for me.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
88. I cut back or stopped taking my medicine(s) because I feel worse and need to go the Emergency Department.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

Part 3: c.

	Short-Acting Opioid					Long-Acting Opioid				
	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼	Never ▼	Rarely ▼	Sometimes ▼	Often ▼	Always ▼
89. I take my pain medicine(s) at the same time daily regardless of pain intensity.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
90. I take my pain medicine(s) only when I have pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
91. I change which pain medicine I take	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

according to the level of pain I have at the moment										
92. I take my long-acting pain medicine(s) only when I have severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
93. I take my long-acting pain medicine(s) only during days of severe pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
94. I take my short-acting pain medicine(s) to prevent any pain.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
95. I take my pain medicine(s) to prevent severe	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

pain.										
96. I take my short-acting pain medicine(s) until my pain is manageable.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
97. I take more pills at a time than the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
98. I take fewer pills at a time than the prescribed dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
99. I take my pain medicine(s) more often than prescribed to manage stress.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
100. I take my pain medicine(s) more										

often than prescribed to help me sleep.										
101. I take my pain medicine at different times of day than what is written on my bottle.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
102. I take my pain medicine(s) more often than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
103. I take my pain medicine(s) less often than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
104. I wait to take my pain medicine(s) until it is time for the next dose.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

105. I keep taking my pain medicine(s) until I get relief.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
106. I take my pain medicine(s) more frequently than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
107. I take my pain medicine(s) less frequently than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
108. I wait a shorter amount of time between doses than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
109. I wait more than the prescribed amount of time between	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

doses.										
110. I take more than the maximum number of pills prescribed per day.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
111. I take more than the prescribed maximum daily number of pills that contain Tylenol.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
112. I take my pain medicine(s) for fewer numbers of days than prescribed.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
113. I take more than one type of prescribed short-acting pain medicine(s	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

) at the same time.										
114. I take over-the-counter products and pain medicine(s) at the same time without consulting my health care provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
115. I take herbal medicine and pain medicine(s) at the same time without consulting my health care provider.	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5
116. I take medicine(s) prescribed for other conditions at the same time as pain	☐1	☐2	☐3	☐4	☐5	☐1	☐2	☐3	☐4	☐5

medicine(s) without consulting my doctor.										

Appendix L

Table: Summary of all emergent themes in domain 3 (related to opioid taking behaviors)

1.1 A variety of medications are taken for individuals with sickle cell anemia to cope with pain. Among these are long-acting and short-acting opioid medicines, such as Dilaudid, Percocet, and morphine, used to prevent and lessen pain. Non-opioid over-the-counter medications, such as Tylenol and Motrin, are also used, sometimes in conjunction with home remedies.
1.2 In choosing what medication to take, many patients weigh the intensity of pain, speed of onset of medication, pending responsibilities, availability of medication, and side effects. A few patients would use long-acting medication to dull pain but continue with responsibilities, while short-acting medication would be dedicated to reducing more intense pain when there were few responsibilities.
1.3 Many SCD patients typically use routines for long-acting opioid medications long-acting drugs are typically scheduled, and a scale of as-needed, personal judgment for short-acting opioid medications while short-acting drugs are taken as needed within the limits of a prescribed schedule. Use of short-acting medication is typically includes factors such as pain, time of day, and future tasks while maintaining standard time intervals of at least 2-4 hours apart per dose. Factors that determine short-acting drug use other than pain include time of day, and anticipated tasks.
1.4 Situation, context, and time of day of the SCD individual is often key to routinization of long-acting and short-acting medications. Setting schedules for taking medicine is

often done for habit, to avoid forgetfulness, and avoid the mental fatigue of making pain judgments every few hours.

1.5 A typical day with pain involves scheduled long-acting medications with pain judgments and extrapolation to decide the course of short-acting medicines.

1.6 Over a typical day without pain, most participants continued use of schedule long-acting medication, while decreasing the amount or frequency of the short-acting medicine. More typically, a day without pain meant a day with more bearable pain.

1.7 Reported frequency for taking medications varied from 3-4 times a day to once a day depending on the severity of pain and estimated probability of future pain.

1.8 Unusual intervals between medication doses was more typical with highly severe pain and little to no pain.

1.9 Unusual interval times between doses were usually interpreted by SCD patients to mean shorter time intervals.

1.10 Behaviors towards taking medication varied greatly among study participants. Behaviors depended on routines, context specificity, and participant attitude towards medicine as a whole. Additionally, participants were keen on either being independent of their medicines by taking less than prescribed and using home remedies, or by tolerating the need for opioid medicine to maintain daily normalcy.

1.11 Reported time to comfort after taking medication varied greatly, from less than 20 minutes to never feeling noticeable comfort.

1.12 Time to become comfortable after taking short-acting medication was typically

after half an hour, but sometimes unnoticed during bouts of severe pain.

1.13 Time to become comfortable after taking long-acting was typically a subtle effect, if noticed.

1.14 Many participants were aware of the preventative use of long-acting opioid medicine and has routinized its use.

1.15 Participants' ways of taking medication during a crisis usually included decreasing the time interval between doses, increasing the amount of medicine in the dose, and combining the opioid medicine with other home and over-the-counter medicines. Additionally, number of doses after beginning of the severe pain was counted as a measurable way of knowing when to go to the emergency room.

1.16 Ways of taking medication after a crisis were usually very similar to pre-crisis habits; however, participants were likely to feel increased vulnerability to future crises and were more likely to slightly increasing their opioid medicine dosage.

1.17 Some participants used schedules to keep track of and regulate their medications and dosages. Familiarity with a dosage schedule allowed participants to be more aware of their written instructions while minimizing the possibility of missed doses. Additionally, the constancy of having decreased pain led to more productivity and relief from fears of dependence on the medicine.

1.18 A majority of participants entertained the idea of stopping medication due to a decreased amount of pain, boredom with medicine, or test of pain-bearing skill. However, those that tried stopping either had little consequences or had a stronger

wave of pain.

1.19 Motivation for continuing medicine use was the decrease in pain and decrease in complications from pain.

1.20 Despite the use of at-home pain management, most SCD patients are sensitive to the need for emergency room care should the need arise. A gray area of pain and decreased medicine efficiency leads to confusion for the transfer of at-home to emergency treatment.

1.21 Others who knew or watched a SCD patient sometimes changed how the SCD patient would later act specifically around that individual or around others. Encouragement and discouragement often assisted positive or negative opinions about the opioid medicine. Family and friends of patients also changed their behaviors towards the patient depending on the patients's pain and medication status. However, some patients perceived themselves more distanced from family and/or friends, resulting in a distanced, apathetic view towards others' opinions on the patient's medicine-taking behavior.

1.22 Many patients agreed that opioid medication did not take the sickle cell pain away, instead reducing it to bearable severity.

1.23 Many of the patients interviewed worried about the risks of under-treating their severe pain and were scared of the possible complications that could result.

1.24 Many SCD patients who were prescribed long-acting medicine often ran out due to inability to refill or availability of the medicine.

1.25 Some patients who suffered from other pains (e.g., due to arthritis) as well as SCD pain often used the "feel" and location of pain to determine how to adjust their medication. Ultimately, the nature of the momentary pain led to either taking less than prescribed, taking as prescribed, or taking more than prescribed.

1.26 Participants reported a variety of reasons for running out of medication, including: theft, decreased availability, financial hardship, misplacement, and miscalculation of remaining amount of medication.

1.27 Most patients felt that they did not take advantage of their opioid medication like "other" SCD patients did. Additionally, they also often felt that "others" had worse sickle cell pain than they did.

1.28 Some patients had the flexibility to choose between different prescribed opioids, such as Dilaudid, Percocet, and OxyContin, to most effectively treat varying levels of pain.

1.29 Patients reported preferences for different pains. For severe pain, 1 tablet of Dilaudid every 2-4 hours was preferred, while 1 tablet of Percocet every 4 hours or 1 tablet of OxyContin every 3-4 hours was preferred for moderate pain. Additionally, 2 tablets of oxycodone every 4 hours was used for regular and mild pain, while Tylenol III was used to reduce mild pain.

1.30 Among most patients, usage of opioid medication varied dependent on crisis duration, typically 1-2 weeks per month.

1.31 Many patients time their medications and wait between doses to fulfill

responsibly using their medication and to maintain attention to duties, responsibilities, and other tasks at hand.

1.32 Many SCD patients understand the risk of overdose as too harmful, and many patients are under the impression that the initial dose of medication should take effect in reducing their pain. Additionally, many patients also felt that taking another dosage "too close" to a previous dose would be considered an overdose.

1.33 The main reason reported for not delaying the next dose of medication was to deal with unbearable pain.

1.34 Factors influencing the decision to take medicine involved the severity of pain, difficulty in doing tasks, emotional state, time of the last dose, the location of pain, the want for comfort, adherence to a medication schedule, increased activity, and the anticipation of escalating or future pain.

1.35 When having mild pain, many SCD patients refrain from taking opioids because the pain is tolerable without, they are more able to focus in their working environment and less likely to make mistakes, they have family responsibilities, or they dislike the side effects.

1.36 When having no pain, some SCD patients refrained from taking opioids altogether.

1.37 On average, most SCD patients reported taking more opioids during the day in order to maintain comfort, to work during the day and finish tasks, and to maintain activity throughout the day.

1.38 Many SCD patients agreed that less medication was necessary at night due to the relaxation of sleep.

1.39 For some SCD patients, taking more opioid medicine occurred at night to control the pain prior to bed, to deal with an accumulation of pain from activity throughout the day, and because colder temperatures at night increased pain.

1.40 Some SCD patients took less medication during the daytime because of a need to be more productive, avoid side effects, fulfill familial responsibilities, and because more favorable weather was less associated with severe pain.

1.41 SCD patients reported taking more rest when experiencing an unusual day with stronger pain and taking more medication to avoid escalation of pain. For others, an unusual day was one without pain, in which less or no medication would be taken. However, most participants reported that they would take their long-term medicine without fail.

1.42 A typical day of pain, as described, was with limited activity with mild to no pain that increased in severity as the day passed. Pain would be judged upon waking and a typical medication-behavior route would be taken. Home remedies, such as using heat, were reported as commonly used and preferred over medicine if possible.

1.43 SCD participants agreed that some things would make an unusual day with stronger pain more bearable. They suggested resting in bed, taking medication, sleeping/resting, drinking fluids, and taking slightly more medicine than from a typical day.

1.44 The surveyed patients shared their methods of relieving a crisis on an unusual day of pain. These ways involved taking more medicine, and going to the ER.

1.45 SCD patients had a variety of ways of taking medicine specifically before going to the ER, sometime based on the time of day. For many, they would stop taking their medication after a certain number of doses and go straight to the ER if they realized they had crisis pain. Others would either take more or less medication than they would normally take.

1.46 During a day with crisis, most patients would prefer to stay at home and self-treat than go to a hospital to go to the hospital. Additionally, some SCD patients also felt that they could better treat themselves at home, sometimes taking up to two days self-treating before going to the hospital. Typically more short-acting medication would also probably be taken.

1.47 Most patients would take their prescribed short-acting opioids when in severe pain or when trying to avoid a visit to the ER. However, some would also take it when running out of long-acting medication or when realizing they are out of long-acting medication. Additionally, some patients would take short-acting medication for emotional symptoms (stress, anxiety, etc.), when in colder or unstable environments, or when feeling pain that is perceived as not bettered with long-acting medication.

1.48 Patients with long-acting medication would take additional doses for long-term pain prevention over the day, to avoid extreme pain that would be otherwise unmanageable later in the day, or to get “back on track” to a self-scheduled dosage.

1.49 Patients were mindful of their medication in order to avoid dependency, to prevent overdose, to fulfill different tasks, and to prevent damage to their livers and kidneys.

1.50 Some patients felt that during some crises, they were not receiving full care, not being admitted to, or being discharged early from the ER and sent home.

1.51 Some patients did not take proper care of their medication duties by not going to the clinic or by not keeping up with appointments.

1.52 On a typical day without pain, patient would take their long-acting medication, rarely take their short-acting medication, or take their short-acting and long-acting medication together.

1.53 Patients reported taking more short- and long-acting medications in both frequency and amount of pills per dose when experiencing a day with pain. Additionally, one patient reported crushing their tablets and mixing it with tea, although most patients did not report any special medication behaviors for days they experienced pain.

1.54 Factors encouraging medication use (as prescribed and take more than prescribed) were the severity of pain, a need for comfort, social encouragement by family and peers, perceived lack of pain relief, the location of pain, having access to medication, anticipation of pain (feeling an “aura” or otherwise), and fear for biological safety and preventing complications.

1.55 Factors that make it difficult to take pain medicine included forgetting the exact

physician instructions, lack of understanding of when to take their medications, lack of availability, needing to carry the medication with them, fear of addiction, the severity of pain itself, the side effects, forgetfulness, difficulties in social situations, the stigma of SCD patients taking advantage of the medication, psychological factors, fear of death, need to fulfill activities of daily living, partial or complete ineffectiveness, and a difficult patient-physician relationship.

1.56 Differences medication-taking behaviors were dependent on age, experience with medication, pain, responsibilities to others (e.g., children), side effects, time of day, weather, and any social events.

1.57 The momentary environment also affected medication-taking behavior. Depending on how much need the patient requires “to function”, in order to sit through church, or to go to social gatherings. Additionally, they would often take medication before or after settings, to prevent later difficulties taking medication during the event.

1.58 Some patients felt that they had to take medication in the company of family for the duration of the effects in order to avoid dangerous behaviors such as leaving the stovetop on.

1.59 Some patients felt they could sufficiently bear the pain without medication, and would often stop taking or take less medication when feeling sufficiently well.

1.60 SCD patients were divided on whether society affected the way they took medication. Some felt that the medication allowed them some power over their pain,

while others felt that the opioid medication could be used for impressing some friends and garnering popularity. Some felt isolated from society, sternly saying that society made absolutely no difference in their medication-taking behavior. For those that were neutral, SCD patients were still wary of what others might think of their medication taking medication and did not often take medication in front of strangers.

1.61 The patient-physician/provider relationship impacted how patients took medication; some felt negative reactions were common from pharmacists who felt the patients were addicts. Others felt some dissonance between their pharmacists and doctors' opinions.

1.62 Some SCD patients were wary of being in the presence of others when using medication. One study participant recalled children taking advantage of the drowsy state during the duration of the medicine. Others hid their medication-taking behavior to avoid the negative stigma of taking strong pain medicine. Several patients did not care what others thought and simply took their medication as usual.

1.63 Most participants felt that they had to be responsible to themselves and to others due to work and to avoid mistakes (such as when driving) or being a burden to others.

1.64 Most patients reported taking pain medicine during moderate pain instead of only severe pain, but many felt stronger pain when experiencing cold weather or environments. Some would take increased medication in anticipation of a cold environment (e.g., a fan or the cool water in a pool).

1.65 SCD patients would take their medicine after 4 to 24 hours of pain.

1.66 Most patients reported never missing medication when in moderate or severe pain, while many missed doses while experiencing mild pain.

1.67 SCD patients missed doses frequently or occasionally, depending on a variety of factors.

1.68 When missing doses, patients would wait to take their next dose (no change), take the medication whenever available and effectively shifting the medication "schedule", taking the medication more frequently, or might even miss medication on purpose in order to avoid dependency.

1.69 SCD patients had different perceptions about missed doses. Some felt missed doses would cause pain, that it would have no effect, or that missing few (1-2 doses) would have no effect on the pain level.

1.70 The impact of an environment impacted how patients felt about their SCD. Many SCD patients felt that hospital staff viewed them negatively as drug-abusers based on the medication or based on their home location. Indoor vs. outdoor, weather, and events altered their medication schedules. Familial environment often led to encouragement and increased medication taking.

1.71 SCD patients reported a wide variety of reasons for missing their medications. Among the most common reasons were travel, forgetfulness, and location.

1.72 Many SCD patients felt that short-acting medication was impossible to miss, and pain was a major reminder. Context of the environment made some patients likely to remember to take their medication, while some would purposely miss their

medication when not in pain.

1.73 SCD patients largely varied in opinions on taking medicine as prescribed. Opinions thought that medication was either not important at all or very important, but paid less importance to how they needed to take their medication. Others felt it was important, but felt equal or greater importance on "properly' taking their medication.

1.74 SCD patients felt that it was important to take the medications as prescribed in order to keep function as a "normal" individual, in order to relieve pain, in order to avoid addiction and dependence, in order to relieve health problems, and in belief that sickness can come from not taking the medication as prescribed.

1.75 SCD patients find it important to take medication as prescribed when having any level of pain.

1.76 SCD patients felt that the important of taking opioid medication was more, less, or rivaled the important of taking other medication for other conditions.

1.77 When experiencing worse pain than usual would go immediately to the hospital, taking less than prescribed medication, using home remedies (such as heat, how baths), and trying massages. Some patients felt that the pain was not bettered by medication when in severe pain.

1.78 In order to get rid of pain before going to a hospital, patients would increase the dose in frequency, amount, and/or shortened interval. This was often done in conjunction with home remedies. However, some patients would not change their

medication-taking behavior.

1.79 After feeling some amount of pain relief after using pain medication, patients would often revert to their "regular schedule," some would take more medication for some while, while others would decrease medication use in order to avoid addiction or dependency.

1.80 After feeling better when not having pain, SCD patients would often use only long-acting medication, and some younger SCD patients would use opioid in anticipation of pain.

1.81 Factors influencing how patients took their medication included effectiveness, information about medication-taking behavior (doctor, online, on the bottle), severity of pain, emotional state, social events, forgetfulness, social factors, other pains, and events.

1.82 Experience with medication changed how patients took their medication.

1.83 Some SCD patients took immediate release medication for only breakthrough pain, while using long-acting medication for pain prevention instead for active pain alleviation.

1.84 When running out of medication, some SCD patients would use OTC medications; call their prescriber, take medication as needed, or going to the ER.

1.85 Some patients would crush their medication for a faster effect.

1.86 When having no pain but choosing to take pain medicine, SCD patients were often experiencing fear of pain coming back or recovering from the end of a crisis.

1.87 Some patients would save medication in anticipation of future need for pain medication. Other patients would take medication on a regular schedule in fear of recurring pain.

1.88 When dealing with activities, patients would take medication as usual, take more after an event, or take some before an event.

1.89 Most patients would take medication before social or religious events in order to "get through" the event, as a precaution to avoid pain, and to avoid possible resulting stigma from others seeing them take medication.

1.90 SCD patients were fairly divergent regarding taking medication in front of others. Most did not mind taking medication in front of others or family, especially if they were secure about their role and the role of prescribed opioids in their lives. Some patients simply preferred being alone while under the effects of medication, while others did not like the presence of others in case of attracting a negative stigma.

1.91 For family, social, and religious events or rituals, many SCD patients would take the minimum amount of pain medicine, forget to take medicine, take the medicine before the event, or postpone the event if possible

1.92 Some SCD patients altered their medicine-taking behavior based on the location of pain. Some would take less, by changing the quantity, time interval, or changing the frequency of doses. Some patients would also not change their medicine-taking behavior.

1.93 When not at home, patients varied in the extent they could take their medication

(very much to hardly ever) depending on when they felt they were in an appropriate situation. Those comfortable with their medicine were more likely to feel that they were frequently able to take their medication away from home.

1.94 During events, SCD patients felt that outdoor activities affected their medication more than indoor events. Physical activities were likely to increase the need of pain medicine; so many patients also avoided physically-heavy events.

1.95 When having pain during an event, many SCD patients either change the quantity, time interval, frequency, take inappropriate OTC medications, take medication in anticipation, postpone medication, leave the event, or use medication as typical.

1.96 When medication is not accessible, some patients try to get to their medication to avoid further pain or miss their medicaiton.

1.97 When having pain before a social event, SCD patients either made no adjustments or stayed home during the event.

1.98 Most patients would not take medication for stress, but they would take medication if experiencing both pain and stress. Patients found that alternative therapies such as breathing, praying, or listening to calming music.

1.99 SCD patients found a great deal of stressors, including: financial stress, possible loss of employment, familial strain, sickle cell pain, mental stress, social stress, and physical stress.

1.100 When having pain and stress, patients would self-adjust their medication by changing the quantity, time interval, and frequency of their medication. Other patients

would make no change to their dosage.

1.101 Many patients felt strongly that they should not take advantage of their medication due to the side effects.

1.102 Most patients felt that taking more pain medicine in terms of time intervals would have a negative effect on their hearts, kidneys, and organs.

1.103 Most of the older SCD participants felt that they took more pain medicine when they were younger and more carefree about their pain medicine.

1.104 Most of the older SCD participants also felt that, when younger, they did not wait until they experienced severe pain to take their opioid medication.

1.105 SCD patients who took more medication at younger age possibly took more medication due to more freedom and less responsibilities.

1.106 A few patients also experienced their instructions changing over the years, often to a shorter time interval.

1.107 When experiencing pain, many SCD patients felt that they should "catch" their pain before it worsened, and might take more medication in terms of frequency, time interval, and quantity.

1.108 Participants varied in their opinion of an abnormal waiting time: 1-4 hours was typically see as too little of a waiting time under typical pain.

1.109 A few patients felt that when having pain, then should keep their short-acting medication on a schedule to keep pain at a minimum throughout the day.

1.110 Most SCD patients experienced preference for waiting, taking medicine ahead of

time, or as pain escalated. Others would have no preference for how to take pain medication as long as the medication worked.

1.111 Several patients denied self-adjustment of medication timing, dosage, or type of medication.

1.112 After missing a dose, the general reaction among SCD patients included more obvious pain, increased focus, having no or a lot of energy, feeling sick, or feeling a generally unwell feeling.

1.113 Emotionally, patients missing a dose felt the same, felt "bad", or were apathetic about missing a dose.

1.114 Most patients strictly took their medication with water, while a few patients took medication with alcohol, another juice, dissolved their medicine, or crushed the medicine.

1.115 Many patients felt that their ER stays were crowded, uncomfortable, cold, or caused more aching than self-treatment of crisis at home.

1.116 The prescribed amount of medication varied greatly among patients based on the short- or long-acting medicine.

1.117 Most participants felt that their medication was sufficiently effective, while several patients felt that their medication was either too strong or too weak to deal with their medicine.

1.118 Many patients did not like their behavior under the influence of medication. Many did not like taking the medication due to possible long-term consequences of long-

term medication use, lack of effectiveness, lack of control while under the influence of the medication, possibility of misuse, and the disadvantages of having to take medication.

1.119 When pain is not relieved, many SCD patients resorted to bedrest, fluids, increasing medicine quantity/interval/dosage, or calling an ambulance.

1.120 Medication was not always available for patients, although several patients cited the unpredictable nature of sickle cell disease and inability to prepare for it when traveling, out of the house or with different people.

1.121 A majority of patients would not combine medications.

1.122 Several patients would need/want medication but would not take it due to need for driving or fine motor skills or coordination

1.123 When deviating from taking medicaiton when pain arose was typically intentional among patients.

1.124 SCD patients would, at least some of the time, decreased the interval between two doses of long-acting intervals. However, several patients also forgot to take their medication.

1.125 Most participants who missed doses did so at night.

1.126 When taking short-acting, SCD patients increased the quantity, increased the frequency, taking medication regularly regardless of pain intensity, taking other prescribed or OTc medications concomitantly, or increasing the duration of therapy.

1.127 Most SCD patients felt that they took their medication differently or less than

other SCD patients, although several noted that they probably deviated from the "right" methods of taking their medication.

1.128 Methods of aberrancy included stopping medication use, missing doses, taking less than prescribed, taking ER medication instead of typical prescribed medicine, or not taking long-acting medication even when feeling well.

1.129 Reasons for aberrancy is to take the prescribed medicine for reasons other than pain: stress, improve sleep or appetite, headaches, anxiety, nervousness, depression, and boredom. Many patients also took their medication out of habit.

1.130 Some patients shared stories of overuse/addiction/aberrant behavior.

1.131 A few SCD patients denied harm that could stem from opioids, and would ask for or take more opioids despite recognition of harmful effects.

1.132 A few patients also did not adhere to physician advice by insisting, accepting, or asking for more opioids, despite going against medical advice or despite recognition of fatal effects.

1.133 Some participants express inability to adhere to prescribed pain medication regiment because insurance refuse to approve the type and amount of medication necessary for treatment.

Appendix M

VITA

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