DIFFERENCES IN HEALTHCARE EXPENDITURE, HEALTH-RELATED QUALITY OF LIFE, PERCEIVED QUALITY, MEDICATION ACCESS, AND PROVIDER RESPECT BETWEEN OPIOID AND NON-OPIOID USERS AMONG A NATIONAL SAMPLE OF COMMUNITY-BASED OLDER UNITED STATES ADULTS WITH PAIN, 2015

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As members of the Dissertation Committee, we certify that we have read the dissertation prepared by David Rhys Axon, titled An investigation of differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and respect shown by provider between opioid users and non-opioid users among a nationally representative sample of community-based older adults (≥50) with pain in the United States, 2015 and recommend that it be accepted as fulfilling the dissertation requirement for the Degree of Doctor of Philosophy.

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Abstract

Introduction: Increasing numbers of older adults, coupled with increasing use of opioids and opioid-related deaths, presents considerable healthcare challenges in the United States (US). This study compared the healthcare expenditure, health-related quality of life (HRQoL), perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Methods: This study employed a retrospective, cross-sectional database design using Medical Expenditure Panel Survey (MEPS) data from 2015. Eligible participants were those alive for the calendar year, aged 50 years or older, and reported having chronic pain in the past four weeks. The key independent variable was opioid use status (opioid users were defined as those who had a Multum Lexicon therapeutic class code of 60 or 191; the remainder was deemed non-opioid users). Hierarchical linear regression models were constructed to assess healthcare expenditures (inpatient, outpatient, office-based, emergency room, prescription medications, other, and total), HRQoL (short form 12 version 2 physical component summary [SF-12v2-PCS], short form 12 version 2 mental component summary [SF-12v2-MCS], and Kessler 6 [K6] scores), and perceived quality between opioid users and non-opioid users, adjusting for appropriate covariates. Hierarchical logistic regression models were constructed to assess access to medications (unable to receive prescription medications, delayed receiving prescription medications) and perceived respect shown by provider between opioid users and non-opioid users, adjusting for appropriate covariates. National estimates were obtained by adjusting for the complex survey design of MEPS. An alpha level of 0.05 was set a priori for all analyses. All analyses were conducted using SAS version 9.4. This study was deemed exempt from the human subject protection program.

Results: The study cohort consisted of 4,759 subjects - 1,525 opioid users and 3,234 non-opioid users. The weighted total number of non-institutionalized adults alive aged 50 or older with pain in the US in the year 2015 was 50,898,592 - 16,757,516 (32.9%) were opioid users and 34,141,076 (67.1%) were non-opioid users. Opioid use was associated with all personal characteristics ($p<0.05$), except gender and race. After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, opioid users had 61% greater outpatient expenditure ($\beta=0.477$, $p<0.0001$), 69% greater office-based expenditure ($\beta=0.524$, $p<0.0001$), 14% greater emergency room expenditure ($\beta=0.131$, $p=0.0045$), 63% greater prescription medication expenditure ($\beta=0.486$, $p<0.0001$), 29% greater other healthcare expenditure ($\beta=0.251$, $p=0.0002$), 105% greater total healthcare expenditure ($\beta=0.718$, $p<0.0001$), and 15% greater perceived healthcare quality scores ($\beta=0.154$, $p=0.0286$). After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.4 (95% CI = 1.0, 1.8) times more likely to be opioid users than non-opioid users. There was no significant difference between opioid users and non-opioid users for inpatient expenditures, SF-12v2-PCS scores, SF-12v2-MCS scores, K6 scores, or access to medications ($p>0.05$).

Conclusions: This study estimated that the number of older US adults (≥50 years) with pain in 2015 was approximately 51 million, and that the estimated prevalence of opioid use among older US adults (≥50 years) with pain in 2015 was approximately 17 million.

Opioid use was associated with all personal characteristics, except gender and race. Adjusted healthcare expenditures were greater among opioid users compared to non-opioid users for all categories of expenditure, except inpatient expenditures. Adjusted perceived healthcare quality measures and perceived respect shown by healthcare provider measures were greater among opioid users compared to non-opioid users. Adjusted health-related quality of life measures and access to prescription medication measures were not associated with opioid use status. Future research is warranted to investigate reasons why some of these findings exist, and to explore these variables in greater depth, over longer periods of time, and in additional populations.

Chapter 1: INTRODUCTION

Introduction to the chapter:

This chapter is organized into seven sections. First, background information about the characteristics of older adults, pain, and opioid use in the United States (US) is presented. Then, a statement of the problem explains why this study is important, followed by an overview of the theoretical model used in the analysis of this study. Next, the purpose of the study is described, along with the objectives of the study and the hypotheses tested. Finally, at the end of the chapter, a list of abbreviations used throughout the dissertation is provided.

1.1 Background

The number of adults aged 65 years and older in the US has increased substantially in recent years, from almost 35 million adults in 2000 (12.4% of the total population) to over 40 million in 2010 (13.0% of the total population), a 15.1% increase. Furthermore, the median age of the US population increased from 35.3 years in 2000 to 37.2 years in 2010 (Howden & Meyer, 2011). The increasing age of the population (population ageing) is due to a combination of declining fertility rates and rising life expectancy driven by economic and social development, advances in medical technology, and public health initiatives (United Nations Department of Economic and Social Affairs population division, 2015). Population ageing is likely to have considerable economic, political, and social implications, as society determines how best to care and pay for increasing numbers of older adults (United Nations Department of Economic and Social Affairs population division, 2015).

Recent estimates of annual healthcare expenditure rank the US among the top for healthcare spending globally. Annual health expenditure in the US was $9536 per capita in 2015 (16.8% of gross domestic product, GDP) according to the World Health Organization (WHO) (World Health Organization, 2018b), and $9892 per capita in 2016 according to the Organization for Economic Cooperation and Development (OECD) (Organization for Economic Cooperation and Development, 2017).

Data from the 2012 National Health Interview Survey (NHIS) indicated that US adults aged 65 or older had a higher prevalence of managing at least two chronic diseases (60.8%), compared to adults aged 45-64 (32.3%) and 18-44 (7.1%) (Ward, Schiller, & Goodman, 2014). Likewise, a 2008 study using 100% Medicare claims data of adults aged 65 years and older found that 67% of subjects had two or more chronic conditions, increasing to 85% of adults aged 85 years and older (Salive, 2013). Data from the 2013 and 2014 NHIS indicated that common chronic health conditions among adults aged 65 and older include hypertension (55.9%), arthritis (49.0%), heart disease (29.4%), cancer (23.4%), diabetes mellitus (20.8%), asthma (10.6%), chronic bronchitis or emphysema (8.1%), and stroke (7.9%) (Federal Interagency Forum on aging-Related Statistics, 2016). As a consequence of multiple morbidities, these patients also take more medications, which increase the number of combinations of medications and ultimately increases the risk of adverse drug reactions and drug-drug interactions (Frazier, 2005).

Polypharmacy (taking a number of medications above an arbitrary threshold or taking more medications than necessary) (Maher, Hanlon, & Hajjar, 2014; Tjia, Velten, Parsons, Valluri, & Briesacher, 2013) has been increasing among older adults (Charlesworth, Smit, Lee, Alramadhan, & Odden, 2015), and is present in approximately 50% of older adults (Maher, Hanlon, & Hajjar, 2014; Resnick et al., 2018). Several studies have found associations between polypharmacy and adverse outcomes (Frazier, 2005; Fried et al., 2014; Hajjar, Cafiero, & Hanlon, 2007; Maher, Hanlon, & Hajjar, 2014) while others have reported that this is not the case (Resnick et al., 2018). Older adults are therefore an important and interesting population to study.

Pain may be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (International Association for the Study of Pain, 1994). Pain may be classified as either acute (pain that comes on quickly, can be severe, but lasts a relatively short time) or chronic (ongoing or recurrent pain, lasting beyond the usual course of acute illness or injury or more than three to six months, and which adversely affects the individual's well being) (American Chronic Pain Association, 2018). An Institute of Medicine (IoM) report in 2011 estimated that 100 million US adults experience pain (Institute of Medicine (US) committee on advancing pain research, care and education, 2011), while a National Institute of Health (NIH) study reported that 126 million US adults had some pain in 2012 (Nahin, 2015).

Pain is therefore a major cause of disability, which results in frequent physician visits, the need to take medication, and subsequently poorer quality of life (Institute of Medicine (US) committee on advancing pain research, care and education, 2011). Pain also has significant economic consequences, for both patients and society; total costs in 2010 dollars range from $560 to $635 billion per year (Gaskin & Richard, 2012; Institute of Medicine (US) committee on advancing pain research, care and education, 2011), which is greater than the annual costs of major diseases such as heart disease, cancer, and diabetes (Gaskin & Richard, 2012).

Guidelines such as the WHO Pain Relief Ladder exist to facilitate the management of pain (World Health Organization, 1996). However, research also suggests that pain may be managed using a variety of pharmacological and non-pharmacological strategies (Ambrose & Golightly, 2015; Axon, Bhattacharjee, Warholak, & Slack, 2018; Axon, Hernandez, Lee, & Slack, 2018; Axon, Patel, Martin, & Slack, 2018; Barry et al., 2004; Barry, Gill, Kerns, & Reid, 2005; Bassols, Bosch, & Banos, 2002; Blyth, March, Cousins, 2003; Blyth, March, Nicholas, Cousins, 2005; Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Budh & Lundeberg, 2004; Chung & Wong, 2007; Crawford, Lee, & Freilich, 2014; Delgado et al., 2014; Dureja et al., 2004; Heutink, Post, Wollaars, & Van Asbeck, 2011; Jouini et al., 2014; Lee, Crawford, Teo, & Spevak, 2014; Mann, Lefort, & Vandenkerkhof, 2013; Mannerkorpi & Henriksson, 2007; Morlion, Kempke, Luyten, Coppens, & Van Wambeke, 2011; Moulin, Clark, Speechley, & Morley-Foster, 2002; Muller-Schwefe, 2011; Nawai, Leveille, Shmerling, van der Leeuw, & Bean, 2017; Perez, Margarit, Serrano, & Spanish group of CHANGE PAIN patient survey, 2013; Racine et al., 2014; Reid et al, 2008; Riley-Doucet, Fouladbakhsh, & Vallerand, 2004; Takai, Yamamoto-Mitani, Abe, & Suzuki, 2015; Tasdemir & Celik, 2016; Toblin, Mack, Perveen, & Paulozzi, 2011; Turunen, Mantyselka, Kumpusalo, & Ahonen, 2004; Vallerand, Fouladbakhsh, & Templin, 2004; Vallerand, Fouladbakhsh, & Templin, 2005; Warms, Turner, Marshall, & Cardenas, 2002; Widerstrom-Noga & Turk, 2003).

A sample of pharmacists with chronic pain used a mean of 12.6±4.6 pain management strategies, including pharmacological and non-pharmacological strategies (Axon, Bhattacharjee, Warholak, & Slack, 2018). The use of more pain management strategies and/or higher doses of medications is associated with a greater likelihood of adverse events, workdays lost, hospital admissions, emergency department visits, and interference with activities of daily living, leisure activities, relationships, and work, and less satisfaction with pain management strategies (Axon, Bhattacharjee, Warholak, & Slack, 2018). Chronic pain is also associated with decreased physical function (Patel, Guralnik, Dansie, & Turk, 2013), restrictions in mobility and daily activities, poor perceived health, and reduced quality of life (Gureje, Von Korff, Simon, & Gater, 1998; Smith et al., 2001).

Chronic pain is associated with dependence on opioids (Institute of Medicine (US) committee on advancing pain research, care and education, 2011). Multiple studies have reported that the use of opioid medications in the US has increased in recent years (Boudreau et al., 2009; Campbell et al., 2010; Daubresse et al., 2013; Dorn, Meek, &

Shah, 2011; Frenk, Porter & Paulozzi, 2015; Han, Kass, Wilsey, & Li, 2014; Kao, Minh, Huang, Mitra, & Smuck, 2014; Kenan, Mack, & Paulozzi, 2012; Olfson, Wang, Iza, Crystal, & Blanco, 2013; Parsells Kelly et al., 2008; Pletcher, Kertesz, Kohn, & Gonzales, 2008; Steinman, Komaiko, Fung, & Ritchie, 2015; Thielke et al., 2010). For example, an analysis of data from the 1999-2010 National Ambulatory and National Hospital Ambulatory Medical Care surveys found that the use of opioids more than doubled from 4.1% to 9.0% among adults aged 65 and older visiting clinics in the US (Steinman, Komaiko, Fung, & Ritchie, 2015). Among older adults, opioids may be preferred to other medications such as non-steroidal anti-inflammatory drugs (NSAIDs) to avoid gastro-intestinal side effects and renal toxicity (Ferrell et al., 2009). However, there are several side effects and complications of opioid therapy that disproportionately affect older adults, such as cardiovascular events, constipation, and bone fractures, thereby making opioids less suitable for use in older adults (Buckeridge et al., 2010; Solomon et al., 2010a; Solomon et al., 2010b).

The increase in opioid use has lead to a subsequent increase in opioid-related problems such as opioid addiction and deaths from opioid overdose (Bernacki, uspeh, Lavin, & Tao, 2012; Franklin et al., 2005; Han, Kass, Wilsey, & Li, 2014; Kenan, Mack, & Paulozzi, 2012). For example, opioid-related deaths increased by 345% from 9489 to 42245 between 2001 and 2016 in the US (Gomes, Tadrous, Mamdani, Paterson, & Juurlink, 2018).

Although considerable effort has been expended to investigate older adults, pain, and opioid use, to the best of my knowledge, no studies have explored differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between opioid users and non-opioid users in a nationally representative sample of older US adults (≥50 years) with pain. This information is important to know in order to provide the foundation for evidence-based policies to address the opioid epidemic in this ever-increasing population.

1.2 Statement of the problem

Increasing numbers of older adults relative to younger adults (population ageing) is a global phenomenon that presents challenges for all countries, including the US (United Nations Department of Economic and Social Affairs population division, 2015). There will continue to be increasing pressure on healthcare funds and resources as the proportion of older adults continues to increase. Pain was estimated to affect approximately 100-126 million US adults in 2011-2012 (Institute of Medicine (US) committee on advancing pain research, care and education, 2011; Nahin, 2015), with bothersome pain affecting 18.7 million (53%) US adults aged 65 and older in 2011 (Patel, Guralnik, Dansie, & Turk, 2013). Coupled with the rising number of older adults in the US, the number of older US adults with pain is also likely to increase. The opioid crisis, fueled by increases in opioid use and consequential negative outcomes makes the use of opioids among older US adults with pain an important and interesting population to investigate. Previous research has described the increasing numbers of older adults and investigated the prevalence of pain (Institute of Medicine (US) committee on advancing pain research, care and education, 2011; Nahin, 2015). However, to our knowledge, no studies have explored differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between opioid users and non-opioid users in a nationally representative sample of older US adults (≥50 years) with pain. There is a need to investigate this to fill this missing gap in the literature.

1.3 Theoretical Model:

The theoretical model used in this investigation was the Andersen Behavioral Model (ABM), initially developed by Ronald M. Andersen in 1968. The most recent version of the ABM, published in 1995, is outlined in Figure 1.1 and consists of five key components: (1) predisposing factors; (2) enabling factors; (3) need factors; (4) personal health practices factors; and (5) external environmental factors. Each of these factors is hypothesized to influence an individual's use of health services. Predisposing factors typically include an individual's demographic characteristics (e.g., age, gender, race, ethnicity). Enabling factors are those that assist an individual to access healthcare services (e.g., education, employment, health insurance status, marital status, poverty status). Need factors describe an individual's or healthcare professional's judgment that healthcare services are needed (e.g., chronic conditions, disabilities, pain, health status). Personal health practices (e.g., body mass index, exercise, smoking status) and external environmental factors (e.g., census region) are recent additions to the model, and can also influence an individual's healthcare utilization and expenditure (Andersen, 1968; Andersen 1995). The ABM was selected for this investigation because it can help organize the multiple factors (predisposing, enabling, need, personal health practices, and external environmental) that may influence healthcare utilization and expenditure of older US adults (≥50 years) with pain (the subjects of this study), and because it has been widely used in health service research studies, including those investigating healthcare utilization and expenditure. Further details about the ABM are provided in section 2.2 of this dissertation.

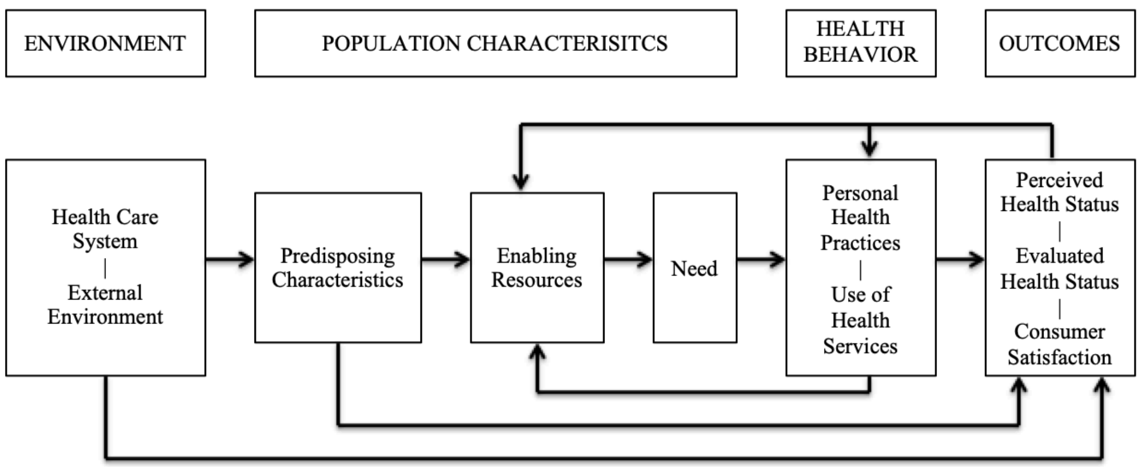

Figure 1.1 The Andersen Behavioral Model (Andersen, 1995).

1.4 Study purpose

The purpose of this study was to compare differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

This study aimed to answer the following question: “Are there significant differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications?”

1.5 Study objectives

This study had seven core objectives:

Objective 1: To estimate the prevalence of pain and to describe the proportion of opioid users versus non-opioid users among a sample of older US adults (≥50 years) with pain.

Objective 2: To determine if there are differences in the predisposing, enabling, need, personal health practices, and external environmental factors of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 3: To determine if there are differences in the healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 4: To determine if there are differences in the health-related quality of life (HRQoL) of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 5: To determine if there are differences in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 6: To determine if there are differences in the access to medications of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 7: To determine if there are differences in the perceived respect shown by provider of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

1.6 Study hypotheses

There were no testable hypotheses for objective 1.

The following null hypotheses were tested for objective 2:

Null hypothesis (H_0) 2.1: There is no difference in the age of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.1: There is a difference in the age of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.2: There is no difference in the gender of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.2: There is a difference in the gender of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.3: There is no difference in the race of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.3: There is a difference in the race of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.4: There is no difference in the ethnicity of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.4: There is a difference in the ethnicity of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.5: There is no difference in the education status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.5: There is a difference in the education status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.6: There is no difference in the employment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.6: There is a difference in the employment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.7: There is no difference in the health insurance status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.7: There is a difference in the health insurance status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.8: There is no difference in the marital status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.8: There is a difference in the marital status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.9: There is no difference in the poverty status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.9: There is a difference in the poverty status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.10: There is no difference in the number of chronic conditions of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.10: There is a difference in the number of chronic conditions of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.11: There is no difference in the instrumental activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.11: There is a difference in the instrumental activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.12: There is no difference in the activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.12: There is a difference in the activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.13: There is no difference in the functional limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.13: There is a difference in the functional limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.14: There is no difference in the work, housework, or school limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.14: There is a difference in the work, housework, or school limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.15: There is no difference in the pain intensity status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.15: There is a difference in the pain intensity status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.16: There is no difference in the physical health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.16: There is a difference in the physical health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.17: There is no difference in the mental health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.17: There is a difference in the mental health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.18: There is no difference in the body mass index of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.18: There is a difference in the body mass index of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.19: There is no difference in the exercise status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.19: There is a difference in the exercise status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.20: There is no difference in the smoking status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.20: There is a difference in the smoking status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.21: There is no difference in the census region of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.21: There is a difference in the census region of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

The following null hypotheses were tested for objective 3:

Null hypothesis (H_0) 3.1: There is no difference in the inpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.1: There is a difference in the inpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.2: There is no difference in the outpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.2: There is a difference in the outpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.3: There is no difference in the office-based expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.3: There is a difference in the office-based expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.4: There is no difference in the emergency room expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.4: There is a difference in the emergency room expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.5: There is no difference in the prescription medication expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.5: There is a difference in the prescription medication expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.6: There is no difference in the other healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.6: There is a difference in the other healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.7: There is no difference in the total healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.7: There is a difference in the total healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypotheses were tested for objective 4:

Null hypothesis (H_0) 4.1: There is no difference in the short form 12 item version 2 (SF-12v2®) physical component summary (PCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.1: There is a difference in the short form 12 item version 2 (SF-12v2®) physical component summary (PCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 4.2: There is no difference in the short form 12 item version 2 (SF-12v2®) mental component summary (MCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.2: There is a difference in the short form 12 item version 2 (SF-12v2®) mental component summary (MCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 4.3: There is no difference in the Kessler Index (K6) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.3: There is a difference in the Kessler Index (K6) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypothesis was tested for objective 5:

Null hypothesis (H_0) 5.1: There is no difference in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 5.1: There is a difference in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypotheses were tested for objective 6:

Null hypothesis (H_0) 6.1: There is no difference in the unable to receive prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 6.1: There is a difference in the unable to receive prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 6.2: There is no difference in the delayed receiving prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 6.2: There is a difference in the delayed receiving prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypothesis was tested for objective 7:

Null hypothesis (H_0) 7.1: There is no difference in the perceived respect shown by provider status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 7.1: There is a difference in the perceived respect shown by provider status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

1.7 Abbreviations

ABM	Andersen Behavioral Model
AHRQ	Agency for Healthcare Research and Quality
BMI	Body mass index
CAM	Complementary and alternative medicine
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
DMARDs	Disease-modifying anti-rheumatic drugs
E.g.	For example
ESRD	End stage renal disease
GDP	Gross domestic product
H_0	Null hypothesis
H_1	Alternative hypothesis

HBM	Health Belief Model
HHS	Health and Human Services
HRQoL	Health-related quality of life
IASP	International Association for the Study of Pain
I.e.	That is
IoM	Institute of Medicine
K6	Kessler Index
MCS	Mental component summary (of the SF-12v2®)
MEPS	Medical Expenditure Panel Survey
MEPS-HC	Medical Expenditure Panel Survey - household component
MEPS-IC	Medical Expenditure Panel Survey - insurance component
NHAMCS	National Ambulatory and National Hospital Ambulatory Medical Care Survey
NHANES	National Health and Nutrition Examination Survey
NHATS	National Health and Aging Trends Study
NHIS	National Health Interview Survey
NIH	National Institute of Health
NSAIDs	Non-steroidal anti-inflammatory drugs
OECD	Organization for Economic Cooperation and Development
OTC	Over the counter
PCS	Physical component summary (of the SF-12v2®)
PQA	Pharmacy Quality Alliance
PSU	primary sampling unit

SBD	Separately billing doctor
SCT	Social Cognitive Theory
SEM	Social Ecological Model
SF-12v2®	Short form 12 item version 2
TENS	Transcutaneous electronic nerve stimulation
TTM	Transtheoretical Model/Stages of Change
WHO	World Health Organization
UN	United Nations
US	United States
USC	Usual source of healthcare
Xm^2	Exposure multimodal

Chapter 2: LITERATURE REVIEW & THEORETICAL MODEL

Introduction to the chapter:

This chapter is organized into two parts: the first section provides a review of the literature relevant to this dissertation, and the second section provides a discussion of the theoretical model. The literature review section includes: an introduction to the issue, a description of previous research examining the issue with a discussion of the major findings and limitations of previous research, and an illustration of unresolved issues and unanswered questions that this dissertation could address. The theoretical model section includes: a description of the theoretical models most relevant to this dissertation, justification for selecting the model used in this dissertation, and potential limitations of this model.

2.1 Literature review:

The first part of this literature review will explore older adults, including how older adults can be defined, the characteristics of older adults, population ageing, and health outcomes of older adults.

Defining older adults:

Providing a definition for 'older adults' can be difficult, as everyone perceives the term 'old' differently depending on the purpose of the definition. In developed countries such as the United States (US), the arbitrary chronological age of 65 years is considered the definition of an older adult, as it often aligns with eligibility to receive pension benefits. However, this definition may not apply to all regions of the world or indeed to all individuals in the US. Furthermore, this calendar age is not necessarily synonymous with biological age (Stafford & Krell, 1997; World Health Organization, 2018a). In the US, an individual becomes eligible to receive Medicare (federal health insurance program) benefits when they reach the age of 65, or earlier if they have certain disabilities or end-stage renal disease (ESRD) (Centers for Medicare and Medicaid Services, 2018). The increase in the number of older adults in recent years has led some to classify older adults into three categories. However, there is a lack of consistency in how these categories are defined in terms of age ranges. For example, Forman, Berman, McCabe, Baim, & Wei (1992) used the categories 'young old' (60-69 years), 'middle old' (70-79 years), and 'very old' (80 years and older). Chang et al. (2016) used 'young-old' (65-74 years), 'old-old' (75-84 years), and 'oldest-old' (85-94 years). A transgenerational organization (2018) used 'young-old' (65-74 years), 'old' (74-84 years), and 'oldest-old' (85 years and older). In order to avoid confusion due to varied naming conventions, the actual age will be used in this literature review wherever possible (i.e., the term adults aged 85 years and older will be used rather than using terms such as 'old-old').

Demographic characteristics of older adults:

The characteristics of older adults such as gender, ethnicity, and race should be considered when providing health and social care. Across the globe, women typically lived an average of 4.5 years longer than men between 2010 and 2015, and thus accounted for a higher proportion of adults aged 60 years and older (54%) and 80 years and older (61%) in 2015. However, average male survival is projected to increase in future years, thus diminishing this age disparity. The number of adults aged 60 years and older increased most in urban areas (68% increase) compared to rural areas (25% increase) between 2000 and 2015 (United Nations Department of Economic and Social Affairs population division, 2015).

Among the US general population, the sex ratio was 96.7 males per 100 females in 2010. Although the birth rate of males is higher than that of females, higher mortality rates among males and greater longevity among women leads to a higher proportion of women than men among the older adult population in the US. In 2010, the majority of the US general population reported their race as white (72.4%) and their ethnicity as not Hispanic/Latino (83.7%). Data on race and ethnicity are not delineated by age category in the 2010 census report, however the trend from 2000 to 2010 indicated a reduction in the proportion of individuals who were white (75.1% to 72.4%) and non-Hispanic/non-Latino (87.5% to 83.7%), and a consequent increase in the proportion that were non-white (24.9% to 27.6%) and Hispanic/Latino (12.5% to 16.3%) (Howden & Meyer, 2011).

Population ageing:

The most recent report from the United Nations (UN) World Population Prospects (published in 2015) commented that in most countries the number of adults aged 60 years and older had increased substantially and was likely to continue growing. The number of adults aged 60 years and older in the population is increasing in almost every country, and is thus a global trend. The global number of adults aged 60 years and older is forecasted to increase from 901 million to 2.1 billion between 2015 and 2050. Similarly, the global number of adults aged 80 years and older is forecasted to increase from 125 million to 434 million between 2015 and 2050. It is estimated that one-fifth of the global population will be 60 years or older by 2050, compared to one-eighth of the population in 2015. In addition, there will be more adults aged 60 years or older (2.1 billion) by 2050 than those aged 24 years or younger (2.0 billion) (United Nations Department of Economic and Social Affairs population division, 2015).

In the US, census data indicates that the number of adults aged 65 or older is increasing. In the 2000 census, there were nearly 35 million older adults, representing 12.4% of the total population. By 2010, there were over 40 million adults aged 65 or older, representing 13.0% of the total population. This represents a net increase of over five million adults aged 65 or older in this ten-year period, a 15.1% increase. The growth rate of adults aged 65 or older in the US is considerably larger than the less than 18 years age group (2.6%) and the 18-44 year age group (0.6%), but not as large as the 45-64 year age group (31.5%) (Howden & Meyer, 2011).

The median age of the US population increased from 35.3 years in 2000 to 37.2 years in 2010. At the state level, there were seven states with a median age over 40 years in 2010, including Maine (42.7 years), Vermont (41.5 years), West Virginia (41.3 years), New Hampshire (41.1 years), Florida (40.7 years), Pennsylvania (40.1 years), and Connecticut (40.0 years). The states with the highest numbers of older adults were Florida (17.3%) and West Virginia (16.0%) (Howden & Meyer, 2011). This may present particular challenges to these states that have a greater number of older adults for whom to care. Older adults are therefore an important population to study.

Reasons for population ageing:

Population ageing, or the increasing median age of the population, is due to a combination of declining fertility rates and rising life expectancy (increased longevity), and is driven by economic and social development (United Nations Department of Economic and Social Affairs population division, 2015). The growth rate of the older adult population today is due to the fertility levels and birth rates 60 years ago, when the current older adult generation was born (the 'baby-boomer' generation). Among other things, improved education, employment, and healthcare, contribute to reductions in birthrates. Meanwhile, declining mortality rates from communicable and non-communicable diseases, accidents, and homicides, further contribute to increasing numbers of older adults. Recent advancements in medical technologies and public health initiatives have resulted in more people living longer, healthier lives. A decreasing fertility rate and increases in longevity cause shifts in the population age structure, resulting in a shrinking share of children and younger adults and a corresponding increase in the number of older adults. International migration can also account for changes in population age structures; however, the effects of migration are typically small in most areas (Transgenerational design matters, 2018; United Nations Department of Economic and Social Affairs population division, 2015).

Implications of population ageing:

Population ageing is likely to have considerable economic, political, and social implications. Economically, an increasing number of older adults and a decreasing number of working age adults may result in the need to increase retirement ages to increase the workforce and reduce the burden on the pensions system. Caring for increasing numbers of older adults is anticipated to exert additional pressure on the utilization and expenditure of healthcare services, social care, and health technologies (United Nations Department of Economic and Social Affairs population division, 2015).

It is important to consider the distinction between quantity of life and quality of life. Although many older adults are living longer (quantity of life), it is unclear from the existing evidence whether adults are healthy or at least partially disabled during these additional years (quality of life). If healthy, additional pressure on the health service can be managed, however, if individuals are living with more disabilities during these additional years of life, there may be a substantial burden on the healthcare service and society (United Nations Department of Economic and Social Affairs population division, 2015).

Thus, governments and healthcare systems will need to adapt to meet the needs of this changing population worldwide. However, these changes do not need to cause substantial increases in healthcare budgets if technological solutions and economic growth can be used effectively. Given that population growth and population ageing are expected to continue to increase, governments and policy makers should be able to proactively design policies and take action to prepare for the changes needed. Action should also be taken to address the most common health conditions that adults aged 60 years and older typically have, which currently includes depressive disorders, hearing loss, back and neck pain, Alzheimer's disease and dementia, osteoarthritis, falls, chronic obstructive pulmonary disease, and diabetes mellitus (United Nations Department of Economic and Social Affairs population division, 2015).

Health Outcomes of Older Adults:

Data from the 2012 National Health Interview Survey (NHIS) indicated that US adults aged 65 or older had a higher prevalence of managing at least two chronic diseases (60.8%), compared to adults aged 45-64 (32.3%) and adults aged 18-44 (7.1%) (Ward, Schiller, & Goodman, 2014). Data from the 2013 and 2014 NHIS in the US indicated that common chronic health conditions among adults aged 65 and older include hypertension (55.9%), arthritis (49.0%), heart disease (29.4%), cancer (23.4%), diabetes mellitus (20.8%), asthma (10.6%), chronic bronchitis or emphysema (8.1%), and stroke (7.9%) (Federal Interagency Forum on aging-Related Statistics, 2016). A 2008 study using 100% Medicare claims data of adults aged 65 years and older found that 67% of subjects had two or more chronic conditions increasing to 85% of adults aged 85 years and older (Salive, 2013). As a consequence of multiple morbidities, these patients also take more medications, which increase the number of combinations of medications and ultimately increases the risk of adverse drug reactions and drug-drug interactions (Frazier, 2005). Older adults with multiple comorbidities therefore have particular pharmaceutical needs that should be considered, such as polypharmacy.

Polypharmacy in US older adults:

Polypharmacy may be defined inconsistently as taking a number of medications above an arbitrary threshold (e.g., greater than five medications), or alternatively as taking more medications than necessary (Maher, Hanlon, & Hajjar, 2014; Tjia, Velten, Parsons, Valluri, & Briesacher, 2013). A recent review highlights how polypharmacy is common in older adults, with approximately 50% of older adults taking at least one unnecessary medication and having polypharmacy (Maher, Hanlon, & Hajjar, 2014; Resnick et al., 2018). An analysis of data from the National Health and Nutrition Examination Survey (NHANES) found that between 1988 and 2010, the median number of medications used by older adults increased from two to four. Meanwhile, the percent of older adults using at least five medications increased from 12.8% to 39% (Charlesworth, Smit, Lee, Alramadhan, & Odden, 2015). Resnick et al. (2018) found that 51% of their sample of 242 individuals from assisted living settings in the US had polypharmacy (five or more medications). Their study also found that the socio-demographic characteristics of these individuals were not correlated with polypharmacy (Resnick et al., 2018). Research has found strong associations between polypharmacy and negative clinical outcomes (Maher, Hanlon, & Hajjar, 2014). However, others have reported that this is not the case. For example, Resnick et al. (2018) found that polypharmacy was not associated with a variety of outcomes including emergency room visits, falls, and hospitalizations.

Previous studies have found that the number of medications used by older adults is associated with adverse outcomes (Frazier, 2005; Hajjar, Cafiero, & Hanlon, 2007). A systematic review of health outcomes associated with polypharmacy in community-dwelling older adults published in 2014 found that there was an association between polypharmacy and outcomes in 12 of 14 highly-rated studies for adjustment of chronic conditions (Fried et al., 2014).

The next section of this literature review describes the US healthcare system, indicators of health and health system performance, and healthcare expenditure.

The US healthcare system:

There are four main types of healthcare service models, including the Beveridge model, the Bismark model, the National Health Insurance Model, and the Out-of-Pocket model (Reid, 2010). In the Beveridge model, a country raises funds for the healthcare system through taxation, and provides care through government-owned facilities or reimburses providers directly so a patient doesn't receive the bill. In the Bismarck model, patients obtain health insurance to cover healthcare costs. However, in contrast to the US, insurers must cover all patients and do not make a profit. The National Health Insurance model combines elements of the Beveridge and Bismark models. Patients pay into a government-run health insurance system, which in turn funds private-sector healthcare providers. Again, this system does not make a profit. The Out-of Pocket model involves patients paying their healthcare fees themselves, without the government or insurance (Reid, 2010). The US has aspects of each of these four systems. For example, Medicare patients receive services paid for by the government, many employees receive health insurance paid for by health insurance companies, while others pay for their care themselves (Reid, 2010). In the US, adults aged 65 and older, as well as those with certain disabilities or ESRD, are eligible to receive Medicare healthcare benefits (Centers for Medicare and Medicaid Services, 2018).

Indicators of health:

Life expectancy is a key indicator of overall health. The US has values close to the average of Organization for Economic Cooperation and Development (OECD) countries (36 developed countries with high-income economies and high human development indices) for several indicators of health status including life expectancy at birth for men (US 77.3 years; OECD average 77.9 years) and women (US 81.2 years; OECD average 83.1 years), life expectancy at age 65 (US 19.3 years; OECD average 19.5 years), ischemic mortality (US 113 per 100000; OECD average 112 per 100000), and dementia prevalence (US 11.6 per 100000; OECD average 14.8 per 100000) (Organization for Economic Cooperation and Development, 2017).

Typical risk factors for health include smoking, alcohol, obesity, and air pollution. Compared to other OECD countries, the US has similar levels of alcohol consumption (US 8.8 liters per year; OECD average 9.0 liters per year) and air pollution exposure (8.4mg per cubic meter per year; OECD average 15.1mg per cubic meter per year), a lower percent of the population who smoke daily (US 11.4%; OECD average 18.4%), but a greater proportion of people with a body mass index (BMI) greater than 30 (US 38.2%; OECD average 19.4%) (Organization for Economic Cooperation and Development, 2017).

Indicators of health system performance:

Access to care is a key measure of health system performance. The US is one of the few advanced nations not to provide universal healthcare to all of its citizens. Data from 2015 indicate that 90.9% of the population has health insurance, which is below the average of 97.9% for all OECD countries. The share of out of pocket expenses as a percentage of final household consumption in the US was comparable to the OECD average (2.5% versus 3.0%). However, the number of consultations skipped due to cost was considerably higher in the US compared to the OECD average (22.3 per 100 population versus 10.5 per 100 population) (Organization for Economic Cooperation and Development, 2017).

Healthcare resources are also important measures of how well a healthcare system is working. Healthcare resources include healthcare expenditure (described previously), the number of healthcare workers, and the number of hospital beds available. The US ranked close to average for the number of physicians (US 2.6 per 1000 population; OECD average 3.4 per 1000 population) and nurses (US 11.3 per 1000 population; OECD average 9.0 per 1000 population), but below average for number of hospital beds (US 2.8 per 1000 population; OECD average 4.7 per 1000 population) (Organization for Economic Cooperation and Development, 2017).

Healthcare expenditure:

According to 2015 data reported by the World Health Organization (WHO), annual health expenditure in the US was $9536 per capita, and constituted 16.8% of gross domestic product (GDP). Thus, the US ranks among the top for healthcare spending globally in both per capita terms and as a proportion of GDP. Government health expenditure constituted 22.6% of government expenditure, again ranking towards the top worldwide (World Health Organization, 2018b). Data from 2016 reported by the OECD found that the US spends $9892 per capita annually, making it the highest spending of all 35 OECD nations and far above the OECD average of $4003 per capita (Organization for Economic Cooperation and Development, 2017).

The next section of this literature review will focus on pain, including how pain is defined, the prevalence of pain, consequences of pain, and pain management, followed by a review of opioid use in the US.

Definition of pain:

Many definitions exist to describe pain, which often involve the classification of pain according to a particular characteristic of interest. The International Association for the Study of Pain (IASP) defines pain as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*" (International Association for the Study of Pain, 1994). More specifically from a time course perspective, the American Chronic Pain Association defines chronic pain as "*ongoing or recurrent pain, lasting beyond the usual course of acute illness or injury or more than three to six months, and which adversely affects the individual's well* *being*" (American Chronic Pain Association, 2018). This contrasts with acute pain, which may be defined as "*pain that comes on quickly, can be severe, but lasts a relatively short tim*e" (American Chronic Pain Association, 2018). Pain can change over time; for example, persistent acute pain can become chronic pain (Voscopoulos & Lema, 2010).

Epidemiology of pain in the US

Pain is prevalent in the US although precise estimates are difficult to calculate due to the subjectivity of pain, fluctuations in pain intensity, and variations in definitions. An Institute of Medicine (IoM) report in 2011 estimated that 100 million US adults experience pain (Institute of Medicine (US) committee on advancing pain research, care and education, 2011), while a National Institute of Health (NIH) study reported that 126 million US adults had some pain in 2012. Of these 126 million, 25 million had chronic pain, and a further 23 million had severe pain (Nahin, 2015).

Data from the 2011 National Health and Aging Trends Study (NHATS) found the prevalence of bothersome pain in the past month among US adults aged 65 and older was 52.9%, affecting 18.7 million US adults aged 65 or older. This study also found pain prevalence was higher among women and older adults with obesity, musculoskeletal conditions, and depressive symptoms ($p<0.001$). Furthermore, this study revealed that most (75%) US adults aged 65 or older with pain had pain at multiple anatomical sites (Patel, Guralnik, Dansie, & Turk, 2013).

Data from the 2016 National Health Interview Survey (NHIS) found that an estimated 50,009,000 (20.4%) US adults aged 18 years or older had chronic pain. This study also found variation in pain prevalence among different subgroups, one of which was older adults. An estimated 13,574,000 adults age 65 years or older had chronic pain (Dahlhamer et al., 2018).

Consequences of Pain:

Pain is therefore a major cause of disability, which results in frequent physician visits, the need to take medication, and subsequently poorer quality of life (Institute of Medicine (US) committee on advancing pain research, care and education, 2011). Pain has typically been regarded as a symptom of other medical conditions, however pain is increasingly being recognized as a disease state in its own right (The European Federation of IASP Chapters, 2001). This has led to the need for a cultural transformation in the way patients, practitioners, and society view, diagnose, and treat pain in order to improve outcomes (Institute of Medicine (US) committee on advancing pain research, care and education, 2011). Appropriate pain relief is considered a basic human right (Cousins, Brennan, & Carr, 2004) and patients should expect to receive adequate pain management, yet it is apparent that pain is uncontrolled for many patients, (Institute of Medicine (US) committee on advancing pain research, care and education, 2011; Jouini et al., 2014).

Pain also has significant economic consequences, for both patients and society; total costs in 2010 dollars range from $560 to $635 billion per year (Gaskin & Richard, 2012; Institute of Medicine (US) committee on advancing pain research, care and education, 2011), which is greater than the annual costs of major diseases such as heart disease, cancer, and diabetes (Gaskin & Richard, 2012).

Previous research using 2008-2011 Medical Expenditure Panel Survey (MEPS) data found that 'a little bit' of chronic pain was associated with a $2,498 and $1,008 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively. Moderate chronic pain was associated with a $3,707 and $2,218 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively. Severe chronic pain was associated with a $5,804 and $4,315 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively (Stockbridge, Suzuki, & Pagan, 2015).

Previous research has identified chronic pain was associated with restrictions in mobility and daily activities, poor perceived health, and reduced quality of life (Gureje, Von Korff, Simon, & Gater, 1998; Smith et al., 2001). Bothersome pain has been associated with decreased physical function (Patel, Guralnik, Dansie, & Turk, 2013). More recently, through multivariable adjusted analyses, Axon, Bhattacharjee, Warholak, and Slack (2018) identified that the use of more pain management strategies and/or higher doses of medications was associated with a greater likelihood of adverse events, workdays lost, hospital admissions, emergency department visits, and interference with activities of daily living, leisure activities, relationships, and work, and less satisfaction with pain management strategies.

Management of pain:

The WHO Pain Relief Ladder was originally developed for use in cancer patients, but is now used for patients with any type of pain. The general principle involves treating mild pain with non-opioid drugs, and adding additional medications or replacing existing medications with alternative ones as pain becomes more severe (World Health Organization, 1996). However, the WHO pain ladder focuses only on pharmacological pain management, and does not account for non-pharmacological strategies.

Research suggests pain may be managed using a variety of strategies. A recent systematic review by Axon, Patel, Martin, and Slack (2018) identified the types of self-management strategies used by community-dwelling adults with pain. This review included 18 studies and identified 22 pharmacological strategies, of which 16 were prescription products and six were over-the counter (OTC), as well as 22 non-pharmacological strategies (Axon, Patel, Martin, & Slack, 2018).

Prescription pain medications included: non-steroidal anti-inflammatory drugs (NSAIDs), opioids, anticonvulsants, antidepressants, acetaminophen, topical, muscle relaxants, acetylsalicylic acid, disease-modifying anti-rheumatic drugs (DMARDs) and steroids, injections, anxiolytics, beta-blockers and calcium-channel blockers, triptans, simple, combined, and adjuvant analgesics, and others. Non-prescription medications included NSAIDs, acetaminophen, and acetylsalicylic acid (Axon, Patel, Martin, & Slack, 2018).

Non-pharmacological strategies included consulted medical practitioner, chiropractor, surgery, activity modification and restriction, acupuncture, alter body position, assistive devices, exercise, hot or cold modalities, massage, physical therapy, transcutaneous electronic nerve stimulation (TENS), prayer and meditation, relaxation, therapy, complementary and alternative medicine (CAM), dietary and herbal supplements, dietary modifications, among others (Axon, Patel, Martin, & Slack, 2018).

In their report about the development of the exposure multimodal (Xm^2) tool, Axon, Bhattacharjee, Warholak, & Slack (2018) identified that pharmacists with chronic pain in a Southwestern state reported using a mean of 12.6±4.6 pain management strategies. Altogether, participants in their survey identified 99 different pain management strategies, which included 13 classes of prescription medications, OTC medications, and many non-pharmacological strategies (Axon, Bhattacharjee, Warholak, & Slack, 2018).

Examples of pain management strategies are shown in Table 2.1 organized according to the conceptual framework described by Axon, Patel, Martin, & Slack (2018). This framework includes prescription and OTC medications, as well as medical interventions, physical strategies, psychological strategies, and self-initiated strategies (Axon, Patel, Martin, & Slack, 2018).

Table 2.1. Examples of pain management interventions organized by category according to the conceptual framework described by Axon, Patel, Martin, & Slack (2018).

Pharmacological	**Medical**	**Physical**	**Psychological**	**Self-initiated**
Acetaminophen	Chiropractor	Activity modification/ restriction	Attention imagery	Alcohol
Acetylsalicylic acid	Consult medical practitioner	Acupressure/ Acupuncture/ magnetizing	Autogenic training	Aromatherapy
Analgesics	Dental program	Alter body position/posture	Behavioral activation	Art therapy
Anticonvulsants	Medication management program	Assistive device	Biofeedback	Body awareness therapy
Antidepressants	Surgery	Cranial electrical stimulation	Cognitive-behavior therapy	Cannabis/ marijuana
Antispasticity agents		Dance therapy	Cognitive coping/ restructuring	Color therapy
Anxiolytics		Electromyograph bio-feedback (direct/ indirect)	Commitment therapy/ commitment to action and overcoming obstacles	Clothing choice
Benzodiazepines		Exercise	Counseling/ psychotherapy	Complementary & alternative medicine (CAM)
Beta-blockers		Gardening	Emotional support	Diaries/ journaling
Calcium channel blockers		Hot/ cold modalities	Faith/ prayer/ religion	Dietary/ nutritional management
Disease-modifying anti-rheumatic drugs (DMARDs)		Kinesio taping	Guided imagery	Education/ knowledge
Injections		Massage	Hypnosis	Goal setting/ action plans
Muscle relaxants		Monochromatic near-infrared energy	Laughter	Guided breathing

Non-steroidal anti-inflammatory drugs (NSAIDs)		Physical therapy/ physiotherapy	Meditation/ mindfulness	Herbal & dietary supplements
Opioids		Play therapy	Mental healing	Identifying beliefs/ principles/ responsibilities/ values
Sedatives		Reiki/ touch therapy	Mental training	Lifestyle changes
Steroids		Spinal cord stimulator	Relaxation	Multimodal integrative therapies
Topical		Transcutaneous electrical nerve stimulation (TENS)	Rest/ sleep	Music therapy
Triptans		Ultrasound	Self-care/ self help/ self-management program	No treatment
				Occupational therapy
				Perseverance
				Placebo
				Problem solving
				Relapse prevention
				Self-regulatory skills
				Time management
				Wait list control

Data for Table 2.1 were obtained from multiple studies (Ambrose & Golightly, 2015; Axon, Bhattacharjee, Warholak, & Slack, 2018; Axon, Hernandez, Lee, & Slack, 2018; Axon, Patel, Martin, & Slack, 2018; Barry et al., 2004; Barry, Gill, Kerns, & Reid, 2005; Bassols, Bosch, & Banos, 2002; Blyth, March, Cousins, 2003; Blyth, March, Nicholas, Cousins, 2005; Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Budh & Lundeberg, 2004; Chung & Wong, 2007; Crawford, Lee, & Freilich, 2014; Delgado et al., 2014; Dureja et al., 2004; Heutink, Post, Wollaars, & Van Asbeck, 2011; Jouini et al., 2014; Lee, Crawford, Teo, & Spevak, 2014; Mann, Lefort, & Vandenkerkhof, 2013; Mannerkorpi & Henriksson, 2007; Morlion, Kempke, Luyten, Coppens, & Van Wambeke, 2011; Moulin, Clark, Speechley, & Morley-Foster, 2002; Muller-Schwefe, 2011; Nawai, Leveille, Shmerling, van der Leeuw, & Bean, 2017; Perez, Margarit, Serrano, & Spanish group of CHANGE PAIN patient survey, 2013; Racine et al., 2014; Reid et al, 2008; Riley-Doucet, Fouladbakhsh, & Vallerand, 2004; Takai, Yamamoto-Mitani, Abe, & Suzuki, 2015; Tasdemir & Celik, 2016; Toblin, Mack, Perveen, & Paulozzi, 2011; Turunen, Mantyselka, Kumpusalo, & Ahonen, 2004; Vallerand, Fouladbakhsh, & Templin, 2004; Vallerand, Fouladbakhsh, & Templin, 2005; Warms, Turner, Marshall, & Cardenas, 2002; Widerstrom-Noga & Turk, 2003).

Opioid Use in the US:

In recent years there has been a debate among clinicians on the appropriate use of opioids in older adults (Reid et al., 2011). From one perspective, opioids may be preferred to other medications such as NSAIDs to avoid gastro-intestinal side effects and renal toxicity (Ferrell et al., 2009). Conversely, there are several side effects and complications of opioid therapy that disproportionately affect older adults, such as cardiovascular events, constipation, and bone fractures, thereby making opioid less suitable for use in older adults (Buckeridge et al., 2010; Solomon et al., 2010a; Solomon et al., 2010b).

Chronic pain is associated with dependence on opioids (Institute of Medicine (US) committee on advancing pain research, care and education, 2011). Multiple studies have reported that the use of opioid medications in the US has increased in recent years (Boudreau et al., 2009; Campbell et al., 2010; Daubresse et al., 2013; Dorn, Meek, & Shah, 2011; Frenk, Porter & Paulozzi, 2015; Han, Kass, Wilsey, & Li, 2014; Kao, Minh, Huang, Mitra, & Smuck, 2014; Kenan, Mack, & Paulozzi, 2012; Olfson, Wang, Iza, Crystal, & Blanco, 2013; Parsells Kelly et al., 2008; Pletcher, Kertesz, Kohn, & Gonzales, 2008; Steinman, Komaiko, Fung, & Ritchie, 2015; Thielke et al., 2010).

An analysis of data from the 1999-2012 NHANES found a significant increase in opioid use in the past 30 days among US adults age 20 and older, increasing from 5.0% in 1999-2002 to 6.9% in 2003-2006. However, the use of opioids among this sample remained consistent among three subsequent measurement periods; at approximately 6.9% during 2003-2006, 6.7% during 2007-2010, and 6.9% during 2011-2012 (Frenk, Porter & Paulozzi, 2015). This analysis also found that, between 2007 and 2012, use of opioids was higher among adults aged 40-59 (8.1%) and 60 and older (7.9%) compared to younger adults age 20-39 years (4.7%) (Frenk, Porter & Paulozzi, 2015). Use of opioids was also higher among women compared to men (7.2% versus 6.3% respectively) (Frenk, Porter & Paulozzi, 2015).

Meanwhile, an analysis of data from the 1999-2010 National Ambulatory and National Hospital Ambulatory Medical Care Surveys (NHAMCS) found that the use of opioids more than doubled from 4.1% to 9.0% among adults aged 65 and older visiting clinics in the US (Steinman, Komaiko, Fung, & Ritchie, 2015).

This had lead to a subsequent increase in opioid-related problems such as opioid addiction and dependence, and deaths from overdose of opioids (Bernacki, Yuspeh, Lavin, & Tao, 2012; Franklin et al., 2005; Han, Kass, Wilsey, & Li, 2014; Kenan, Mack, & Paulozzi, 2012). Opioid-related deaths (where an opioid contributed substantially to the cause of death) increased from 9489 to 42245, a 345% increase, between 2001 and 2016 in the US (Gomes, Tadrous, Mamdani, Paterson, & Juurlink, 2018). The number of opioid deaths in the US increased in most age groups between 2014 and 2015 and was most prevalent among younger adults and middle aged adults, but remained constant for those age 65 and older (Rudd, Seth, David, & Scholl, 2016).

This phenomenon has been termed the ‘opioid crisis’ or ‘opioid epidemic’, and in response the US Department of Health and Human Services (HHS) has declared a public health emergency and developed a strategy to overcome it (Price, 2017; US Department of Health and Human Services, 2017; US Department of Health and Human Services, 2018).

Summary of Literature Review and Future Research Directions:

In summary, increasing numbers of older adults relative to younger adults (population ageing) is a global phenomenon that presents challenges for all countries, including the US (United Nations Department of Economic and Social Affairs population division, 2015). There will continue to be increasing pressure on healthcare funds and resources as the proportion of older adults continues to increase.

Pain was estimated to affect approximately 100-126 million US adults in 2011-2012 (Institute of Medicine (US) committee on advancing pain research, care and education, 2011; Nahin, 2015), with bothersome pain affecting 18.7 million (53%) US adults aged 65 and older in 2011 (Patel, Guralnik, Dansie, & Turk, 2013). Coupled with the rising number of older adults in the US, the number of older US adults with pain is also likely to increase. The opioid crisis, fueled by increases in opioid use and consequential negative outcomes makes the use of opioids among older US adults with pain an important and interesting population to investigate.

Previous research has described the increasing numbers of older adults and investigated the prevalence of chronic pain (Institute of Medicine (US) committee on advancing pain research, care and education, 2011; Nahin, 2015). However, to our knowledge, no studies have explored differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between opioid users and non-opioid users in a nationally representative sample of older US adults (≥50 years) with pain. There is a need to investigate this to fill this missing gap in the literature.

2.2 Theoretical Model:

When conducting research where complex or hierarchical relationships may exist between factors, a conceptual model should be used to help guide the use of multivariate techniques and to assist in the interpretation of results (Victora, Huttly, Fuchs, & Olinto, 1997). Studies developed with a theoretical foundation or combination of theoretical model are typically more successful than those developed without a theoretical model (Ammerman, Lindquist, Lohr, & Hersey, 2002; Glanz & Bishop, 2010; Legler et al., 2002; Noar, Benac, & Harris, 2007).

2.2.1 Description of models most relevant to the issue:

Commonly used theoretical models in health services research include the Health Belief Model, the Transtheoretical Model and Stages of Change, Social Cognitive Theory, and the Social Ecological Model (Glanz & Bishop, 2010).

The Health Belief Model (HBM) was one of the first theories of health behavior and is still commonly used today (Hochbaum, 1958). The HBM is based on the notion that an individual's readiness to take action about their health is influenced by their beliefs and perceptions of their risk for a particular health condition. The HBM includes an individual's perception of: their susceptibility, disease severity, health or other benefits, and barriers to action; as well as cues to action and self-efficacy (Champion & Skinner, 2008; Glanz, 1997; Glanz & Bishop, 2010; Rosenstock, 1974; Rosenstock, Strecher, & Becker, 1988).

The Transtheoretical Model/Stages of Change (TTM) is also commonly used and includes five stages of change (pre-contemplation, contemplation, preparation, action, and maintenance). Each stage represents a different level of readiness for an individual to make or maintain a change in their health behaviors. Individuals may recycle and repeat some stages over time, depending on their circumstances (Glanz & Bishop, 2010; Prochaska, Redding, & Evers, 2008).

Social Cognitive Theory (SCT) describes the dynamic interaction of behavior, environmental influences, and personal factors to explain human behavior. The premise is that individuals learn through their own experiences as well as by observing the actions and outcomes of others. SCT includes observational learning, reinforcement, self-control, and self-efficacy as important components of effective healthcare interventions (Bandura, 1986; Glanz & Bishop, 2010; McAlister, Perry, & Parcel, 2008; Will, Farris, Sanders, Stockmyer, & Finkelstein, 2004).

The Social Ecological Model (SEM) describes several levels of influence on an individuals' health (individual, interpersonal, organizational, community, and public policy), and suggests that behaviors both shape, and are shaped by, the social environment (Bandura, 1986; Glanz & Bishop, 2010; McLeroy, Bibeau, Steckler, & Glanz, 1998; Sallis, Owen, & Fisher, 2008).

Although each of these aforementioned models has their own merits and are widely used, they focus on an individuals' behavior, beliefs, or external influences and do not adequately address other factors associated with medication use and health outcomes. These models are therefore not comprehensive enough for the needs of this study. Alternative models that may be applied for health services research include Complexity theory and the Health Outcomes Conceptual Framework, both described below:

Complexity theory is a more sophisticated model that accounts for non-linear systems as compared to more simplistic models commonly used in health services research, which usually involve a reductionist approach that prevents the correct interpretation of what is being studied (Kernick, 2006). Complex models view systems as a network of elements, where a change in one element leads to changes in other elements. Complexity theory focuses on the interaction between system elements that lead to a complex behavioral pattern (Kernick, 2006). When a change occurs in a complex system, the size of the change rarely relates to the size of the trigger, and the components of the system reconfigure themselves close to their original state. Therefore, expending considerable effort to change one part of the system may not produce long-term change as the system will adjust and return to its original state (Kernick, 2006). Examples where complexity theory has been applied to health services research include assessing: practitioner consultations (Miller, Crabtree, McDaniel, & Strange, 1998), changes in primary care practices (Moss, 2002), and leadership, education, and governance (Kernick, 2004). Quantitative methods based on non-linear systems include non-linear variability analysis (Seely & Macklem, 2004), pattern recognition techniques (Ohno-Machado & Holt, 2004), and population dynamics (Guastello, 2002). Although complexity theory appears to be a good descriptor of the healthcare system (i.e., it is complex and has many dynamic components that interact to affect an outcome) it is not clear if the methodologies needed for this study can adequately account for a complex system. In addition, given that complex systems tend to return to their original state when a change is made, it may be difficult to detect the effects of an intervention. Furthermore, complexity theory does not directly inform the variables that should be included in any statistical models. Therefore, complexity theory is not the most appropriate model for this investigation, but the concept of multiple factors interacting to influence a medication use and health outcomes will be considered when analyzing data in this study. The Health Outcomes Conceptual Framework was first described in a 2008 report entitled: "A framework for health outcomes analysis: Diabetes and depression case studies", published by The Canadian Institute for Health Information and Statistics Canada (Canadian Institute for Health Information, 2008). These organizations created the Health Outcomes Conceptual Framework analysis to guide data development and analysis across Canada, however, the framework can also be used at local and international levels to examine health outcomes. The Health Outcomes Conceptual Framework contains four components, including the characteristics of patients and the characteristics of the healthcare system, which both feed into the care path. These three components are considered within the context of the environment in which the intervention occurs (Canadian Institute for Health Information, 2008).

Despite the merits of these aforementioned models, they do not adequately assist in framing the research question, guiding the analysis, or informing the interpretation of results for the purposes of this study. Therefore, it is necessary it identify an alternative framework, such as the Andersen Behavioral Model.

Ronald M. Andersen first developed the Andersen Behavioral Model (ABM) in 1968 (Andersen, 1968). The ABM has been adapted and revised several times since its inception; Andersen discussed the various iterations and described how the latest version was still applicable to health care in a seminal article published in 1995 (Andersen, 1995). The ABM is outlined in Figure 2.1 and consists of five key components: (1) predisposing factors; (2) enabling factors; (3) need factors; (4) personal health practices factors; and (5) external environmental factors. Each of these factors is hypothesized to influence an individual's use of health services. Predisposing factors typically include an individual's demographic characteristics (e.g., age, gender, race, ethnicity). Enabling factors are those that assist an individual to access healthcare services (e.g., insurance status, education status, and poverty status). Need factors describe an individual's or healthcare professional's judgment that healthcare services are needed (e.g., chronic diseases, disabilities, pain, health status). Personal health practices (e.g., BMI, smoking status, exercise) and external environmental factors (e.g., census region, metropolitan area) are recent additions to the model, and can also influence an individual's use of healthcare services and healthcare expenditures (Andersen, 1968; Andersen, 1995).

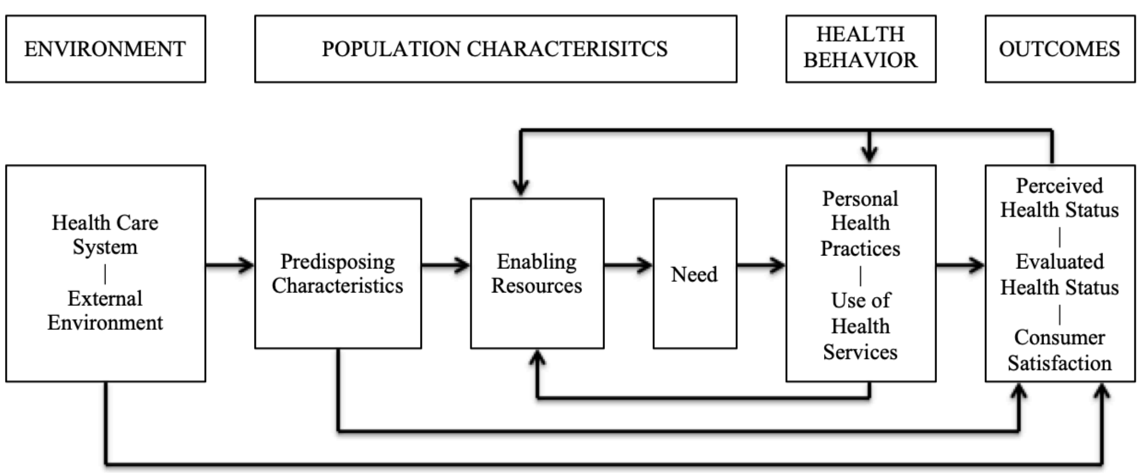

Figure 2.1 The Andersen Behavioral Model (Andersen, 1995).

2.2.2 Justification for selecting the Anderson Behavioral Model:

The ABM was selected for this investigation because it represents the notion that multiple factors, including predisposing, enabling, need, personal health, and external environmental characteristics, are all important considerations that can affect healthcare service use and expenditure. The ABM helps classify and organize the variables that may be associated with healthcare services expenditures and use. This model is appropriate for the research question, available data, and study design because healthcare expenditures and healthcare services used by older adults with pain in the US (the subjects of this study) may be influenced by a variety of factors that are captured in the several components of the model. Any adjustment in one or more of these factors may lead to changes in healthcare expenditures and healthcare service use. Likewise, knowledge of which factors typically influence healthcare expenditures and healthcare service use can help inform policy makers and healthcare professionals about the most important factors to modify in order to best use the limited resources available to improve health outcomes for these individuals. Furthermore, the ABM has been widely used in health service research studies, including those investigating healthcare expenditures and use of healthcare services.

2.2.3 Limitations associated with using the Anderson Behavioral Model in this investigation:

The ABM offers many merits for the purposes of this study, but there are a few potential limitations of this model pertinent to this study. For example, previous work has demonstrated that variables are classified inconsistently between categories of the ABM (Babitsch, 2012). Therefore, there may be disagreement about the classification of certain variables available in the dataset, or the dataset may not contain variables for all components of the model. Overall, however, the merits of using the ABM (i.e., that it provides an appropriate, innovative and sophisticated model) outweigh the potential limitations for the purposes of this investigation.

Chapter 3: METHODS

Introduction to the chapter:

This chapter is organized into ten sections. First, the study purpose, objectives, and hypotheses are provided. Next, a description of the data source, eligibility criteria, study design, human subject protections, and sample size is provided. Then, a detailed data dictionary and description of the independent and dependent variables is provided, along with the proposed data analysis procedures. Finally, limitations anticipated with the methodological approach are discussed.

3.1 Statement of purpose, objectives and hypothesis

3.1.1 Study purpose

The purpose of this study was to compare differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

This study aimed to answer the following question: "Are there significant differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications?"

3.1.2 Study objectives

This study had seven core objectives:

Objective 1: To estimate the prevalence of pain and to describe the proportion of opioid users versus non-opioid users among a sample of older US adults (≥50 years) with pain.

Objective 2: To determine if there are differences in the predisposing, enabling, need, personal health practices, and external environmental factors of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 3: To determine if there are differences in the healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 4: To determine if there are differences in the health-related quality of life (HRQoL) of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 5: To determine if there are differences in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 6: To determine if there are differences in the access to medications of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

Objective 7: To determine if there are differences in the perceived respect shown by provider of older US adults (≥50 years) with pain who use opioid medications versus those who do not use opioid medications.

3.1.3 Study hypotheses

There were no testable hypotheses for objective 1.

The following null hypotheses were tested for objective 2:

Null hypothesis (H_0) 2.1: There is no difference in the age of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.1: There is a difference in the age of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.2: There is no difference in the gender of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.2: There is a difference in the gender of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.3: There is no difference in the race of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.3: There is a difference in the race of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.4: There is no difference in the ethnicity of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.4: There is a difference in the ethnicity of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.5: There is no difference in the education status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.5: There is a difference in the education status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.6: There is no difference in the employment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.6: There is a difference in the employment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.7: There is no difference in the health insurance status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.7: There is a difference in the health insurance status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.8: There is no difference in the marital status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.8: There is a difference in the marital status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.9: There is no difference in the poverty status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.9: There is a difference in the poverty status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.10: There is no difference in the number of chronic conditions of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.10: There is a difference in the number of chronic conditions of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.11: There is no difference in the instrumental activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.11: There is a difference in the instrumental activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.12: There is no difference in the activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.12: There is a difference in the activities of daily living limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Null hypothesis (H_0) 2.13:</u> There is no difference in the functional limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Alternative hypothesis (H_1) 2.13:</u> There is a difference in the functional limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Null hypothesis (H_0) 2.14:</u> There is no difference in the work, housework, or school limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Alternative hypothesis (H_1) 2.14:</u> There is a difference in the work, housework, or school limitation status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Null hypothesis (H_0) 2.15:</u> There is no difference in the pain intensity status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

<u>Alternative hypothesis (H_1) 2.15:</u> There is a difference in the pain intensity status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.16: There is no difference in the physical health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.16: There is a difference in the physical health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.17: There is no difference in the mental health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.17: There is a difference in the mental health status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.18: There is no difference in the body mass index of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.18: There is a difference in the body mass index of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.19: There is no difference in the exercise status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.19: There is a difference in the exercise status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.20: There is no difference in the smoking status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.20: There is a difference in the smoking status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Null hypothesis (H_0) 2.21: There is no difference in the census region of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

Alternative hypothesis (H_1) 2.21: There is a difference in the census region of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.

The following null hypotheses were tested for objective 3:

Null hypothesis (H_0) 3.1: There is no difference in the inpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.1: There is a difference in the inpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.2: There is no difference in the outpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.2: There is a difference in the outpatient expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.3: There is no difference in the office-based expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.3: There is a difference in the office-based expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.4: There is no difference in the emergency room expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.4: There is a difference in the emergency room expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.5: There is no difference in the prescription medication expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.5: There is a difference in the prescription medication expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.6: There is no difference in the other healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.6: There is a difference in the other healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 3.7: There is no difference in the total healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 3.7: There is a difference in the total healthcare expenditure of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypotheses were tested for objective 4:

Null hypothesis (H_0) 4.1: There is no difference in the short form 12 item version 2 (SF-12v2®) physical component summary (PCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.1: There is a difference in the short form 12 item version 2 (SF-12v2®) physical component summary (PCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 4.2: There is no difference in the short form 12 item version 2 (SF-12v2®) mental component summary (MCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.2: There is a difference in the short form 12 item version 2 (SF-12v2®) mental component summary (MCS) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 4.3: There is no difference in the Kessler Index (K6) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 4.3: There is a difference in the Kessler Index (K6) score of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypothesis was tested for objective 5:

Null hypothesis (H_0) 5.1: There is no difference in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 5.1: There is a difference in the perceived healthcare quality of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypotheses were tested for objective 6:

Null hypothesis (H_0) 6.1: There is no difference in the unable to receive prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 6.1: There is a difference in the unable to receive prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Null hypothesis (H_0) 6.2: There is no difference in the delayed receiving prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 6.2: There is a difference in the delayed receiving prescription medication treatment status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

The following null hypothesis was tested for objective 7:

Null hypothesis (H_0) 7.1: There is no difference in the perceived respect shown by provider status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

Alternative hypothesis (H_1) 7.1: There is a difference in the perceived respect shown by provider status of older US adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.

3.2 Data source

This study used Medical Expenditure Panel Survey (MEPS) data from the years 2015 to create an analytical cohort. MEPS is conducted by the Agency for Healthcare Research and Quality (AHRQ) and uses the sampling framework of the National Health Interview Survey (NHIS) to obtain a nationally representative sample of US citizens. MEPS oversamples minority groups and disabled people to achieve nationally representative estimates. MEPS collects data on healthcare expenditures, healthcare service use, insurance coverage, medical and mental health conditions, and treatments such as prescription drugs. There are two major components to MEPS: The household component (MEPS-HC) and the insurance component (MEPS-IC) (Medical Expenditure Panel Survey, 2009).

MEPS-HC collects data from a nationally representative sample of US households who participated in the NHIS the previous year (Medical Expenditure Panel Survey, 2009). MEPS-HC data are collected for all household members on many variables, including demographic characteristics, health conditions, healthcare service use, and healthcare expenditures among others (Medical Expenditure Panel Survey, 2009). MEPS has a panel design and involves multiple interview rounds over two full calendar years (Medical Expenditure Panel Survey, 2009).

The MEPS 2015 full-year consolidated data file (MEPS HC-181) was used to identify the study cohort (individuals who were alive for the full year, age ≥50 years, and had pain), subject characteristics, healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider. The 2015 prescribed medicines file (MEPS HC-178A) was used to identify opioid users and non-opioid users. These files are publically available on the MEPS website (Agency for Healthcare Research and Quality, 2019).

Data for expenditures in the MEPS dataset refers to the sum of direct payments for healthcare provided during the year, including payments by private insurance, Medicaid, Medicare, out-of-pocket, and other sources. Indirect payments and over-the-counter medicines are not captured in MEPS (Agency for Healthcare Research and Quality, 2017a).

One component of MEPS is the paper-and-pencil self-administered questionnaire (SAQ). The SAQ was administered in panel 19, round 4 and panel 20, round 2. An individual was eligible to complete the SAQ if they were: alive, not institutionalized, did not move out of the US or to a military facility, responded to the round 2 or 4 interview, and was 18 years of age or older. The SAQ collected information on health status and healthcare quality of adults, and can be administered in English or Spanish (Agency for Healthcare Research and Quality, 2017a). SAQ items were used for assessing self-reported health-related quality of life (HRQoL) and healthcare quality.

Another component of MEPS is the access to care (AC) section. Like the SAQ, the AC section was administered in panel 19, round 4 and panel 20, round 2. The AC section collected information on family members' usual source of healthcare (USC), characteristics of USC provider, access to and satisfaction with USC provider, and access to medical, dental, and prescription medication treatment (Agency for Healthcare

Research and Quality, 2017a). AC items were used for assessing self-reported access to medications and perceived respect shown by provider.

3.3 Eligibility criteria

Inclusion criteria: Subjects from the MEPS dataset were included in this study if they were US adults alive for the full year, aged 50 years or older, and reported having pain in the past four weeks. For the expenditure analyses, subjects were only included if they had positive total healthcare expenditure. For the HRQoL, perceived healthcare quality, access to medications, and perceived respect shown by provider analyses, subjects were only included if they had complete data for the dependent variables of interest.

Exclusion criteria: Subjects were excluded from this study if they were not alive for the full year, less than 50 years of age, or did not report having pain in the past four weeks. For the expenditure analyses, subjects were excluded if they had an expenditure of zero for total healthcare expenditure. For the HRQoL, perceived healthcare quality, access to medications, and perceived respect shown by provider analyses, subjects were excluded if they had incomplete data for the dependent variables of interest.

3.4 Study design

An *in silico* (via computer simulation) retrospective, cross-sectional database study design was used to investigate differences in healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider between older US adults with pain who used opioid medications and those who did not.

3.5 Human subjects

The University of Arizona Institutional Review Board (IRB) approved this study and deemed it to be exempt from human subject protection requirements.

3.6 Sample size

A feasibility study using 2015 MEPS data indicated that 4,759 subjects met the study inclusion criteria. Of these, 1,525 were considered opioid users and 3,234 were considered non-opioid users.

3.7 Data dictionary

The data dictionary includes the variables required to develop the cohort according to the study eligibility criteria, as well as the key independent variable, other independent variables that serve as covariates organized by the theoretical model (Andersen Behavioral Model), and dependent variables (healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider). Furthermore, the variables required to correctly perform analytical procedures are described. A description of each variable, the MEPS files from where the data can be obtained, and the 2015 MEPS variable names are provided in Table 3.1, and are described in detail below.

<u>Cohort development (according to eligibility criteria):</u>

<u>ID:</u> The variable "DUPERSID" is a combination of the unique person identification number and the dwelling unit. DUPERSID can be used to link records in other files, such as the prescribed medicines file (Agency for Healthcare Research and Quality, 2017a).

<u>Alive:</u> The variables "PSTATS31", "PSTATS42", and "PSTATS53" indicated the person disposition status, from which the eligibility of each subject for each round of the MEPS interview was determined. This variable was used to determine subjects who were alive for the study period (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

<u>Age:</u> The variable "AGE15X" indicated the age of subjects as of December 31, 2015, and is top-coded at age 85 to protect the identity of older subjects (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, it was necessary to construct two age variables. The first age variable distinguished subjects aged 50 or older, and thus eligible for study inclusion. The second age variable characterized subjects as aged 50-64 years or ≥65 years.

<u>Pain:</u> The variable "ADPAIN42" indicated the pain status of subjects. As part of the 2015 self-administered questionnaire (SQA) component of MEPS, subjects were asked to complete the Short-Form 12 version 2 (SF-12v2) to obtain a measure of subjects' health status. One of the SF-12v2 questions was: During past 4 weeks, pain interfered with normal work outside the home and housework". Response categories for the pain item included: (1) not at all; (2) a little bit; (3) moderately; (4) quite a bit; and (5) extremely (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, it was necessary to construct two pain variables. The first pain variable distinguished subjects with pain, which included subjects who responded a little bit, moderately, quite a bit, or extremely, and were thus eligible for study inclusion. The second pain variable characterized those with pain as having: little/moderate pain or quite a bit/extreme pain.

Key independent variable:

Opioid use status: The variable "TC1S1_1" was used to identify the Multum Lexicon therapeutic class codes for opioid medications. Within this variable, a code of 60 indicated narcotic analgesics, and a code of 191 indicated narcotic analgesic combinations (Agency for Healthcare Research and Quality, 2017c; Agency for Healthcare Research and Quality, 2017d). For the purposes of this study, individuals who used at least one narcotic analgesic or narcotic analgesic combination in the study period were considered opioid users, while the remainder was considered non-opioid users.

Independent variables (according to theoretical model):

Age: A description of the age variable was provided previously.

Gender: The variable "SEX" indicated the gender of subjects as male or female (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the gender of subjects was characterized as male or female.

Race: The variable "RACEV1X" indicated the race of subjects. The construction of the race variable has been revised in recent years. Since 2013, only one race question is asked in the MEPS interview, which contains a comprehensive list of options for 2015 including: White only, Black only, American Indian/Alaska Native only, Asian/Native Hawaiian/Pacific Islander only, and multiple races. Other variables (not of interest for this study) delve deeper into specific race characteristics (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the race of subjects was characterized as white or other.

Ethnicity: The variable "HISPANX" indicated the ethnicity of subjects, specifically whether they considered themselves Hispanic or non-Hispanic. As with the race variable, the 2015 data allows for subjects to report greater detail about their Hispanic status, but this was not required for this study (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the ethnicity of subjects was characterized as Hispanic or non-Hispanic.

Education: The variable “EDRECODE” indicated the educational attainment of subjects when they first entered MEPS, typically round 1. Due to changes in the education questions in 2015 and previous years, data for the other education variables may be incomplete, and thus the recoded education variable should be used to ensure all subjects have a value for the education variable. Possible categories for the recoded education variable included: (1) less than or equal to grade eight; (2) grades nine through 12, no high school diploma, or no general education development; (3) general education development or high school graduate; (4) beyond high school, college without a four-year degree, or an associates degree; (5) four-year college degree or bachelor’s degree; and (6) Master’s, Doctorate, or professional degree (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the educational attainment of subjects was characterized as less than high school, up to high school, or higher than high school.

Employment: The variables “EMPST31”, “EMPST42”, and “EMPST53” indicated the employment status of subjects at the time of interview. Response options for employment status included: (1) currently employed; (2) has a job to return to; (3) employed during the reference period; and (4) not employed with no job to return to (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the employment status of subjects was characterized as employed or unemployed.

Health insurance: The variable "INSCOV15" indicated the health insurance status of subjects for 2015. Response categories for health insurance status included: (1) any private insurance coverage any time during 2015; (2) public only insurance coverage during 2015; and (3) uninsured for all of 2015 (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the health insurance status of subjects was characterized as private, public, or uninsured.

Marital: The variable "MARRY15X" indicated the marital status of subjects as of December 31, 2015. Response options for marital status included: (1) married; (2) widowed; (3) divorced; (4) separated; and (5) never married. Round-level versions of the marital status variable include additional variables to identify changes to marital status during the round, including: (1) married in round; (2) widowed in round; (3) divorced in round; and (4) separated in round (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the marital status of subjects was characterized as married or other.

Poverty: The variable "POVCAT15" indicated the poverty status of subjects. Definitions of poverty were based on 2015 statistics developed by the Current Population Survey (CPS). Family income was categorized into one of five poverty categories, including: (1) poor/negative, defined as less than 100% of the poverty line; (2) near poor, defined as 100% to less than 125% of the poverty line; (3) low income, defined as 125% to less than 200% of the poverty line; (4) middle income, defined as 200% to less than

400% of the poverty line; and (5) high income, defined as 400% or greater of the poverty line (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the poverty status of subjects was characterized as poor/near poor/low income or middle/high income (split at the 200% poverty line).

Chronic conditions: MEPS asks a series of questions about 15 medical conditions, which included: hypertension, coronary heart disease, angina, myocardial infarction, other unspecified heart disease, stroke, emphysema, chronic bronchitis, high cholesterol, cancer, diabetes joint pain, arthritis, asthma, and Attention Deficit Hyperactivity Disorder/Attention Deficit Disorder. MEPS includes these particular conditions because of their relatively high prevalence in the population, and because clinical care standards exist for them.

The variable “HIBPDX” indicated if the subject had ever been diagnosed with high blood pressure (other than pregnancy). The variable “CHDDX” indicated if the subject had ever been diagnosed with coronary heart disease. The variable “ANGIDX” indicated if the subject had ever been diagnosed with angina or angina pectoris. The variable “MIDX” indicated if the subject had ever been diagnosed with heart attack, or myocardial infarction. The variable “OHRTDX” indicated if the subject had ever been diagnosed with any other heart disease or condition. The variable “STRKDX” indicated if the subject had ever been diagnosed with stroke or transient ischemic attack. The variable “EMPHDX” indicated if the subject had ever been diagnosed with emphysema.

The variables "CHBRON31" and "CHBRON53" indicated if the subject had chronic bronchitis in the last 12 months. The variable "CHOLDX" indicated if the subject had ever been diagnosed with high cholesterol. The variable "CANCERDX" indicated if the subject had ever been diagnosed with any type of cancer or malignancy. The variable "DIABDX" indicated if the subject had ever been diagnosed with diabetes (excluding gestational diabetes). The variables "JTPAIN31" and "JTPAIN53" indicated if the subject had experienced pain, swelling, or stiffness around a joint in the last 12 months. The variable "ARTHDX" indicated if the subject had ever been diagnosed with arthritis. The variable "ASTHDX" indicated if the subject had ever been diagnosed with asthma. The final condition was ever diagnosed with Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder, however, this question was only asked to subjects between the ages of 5 and 17, and thus not applicable to this study, whose subjects had an age ≥50 years to meet the eligibility criteria (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the total number of aforementioned chronic conditions was summed, and subjects were characterized as having none, one, two, three, four, or at least five chronic conditions.

Instrumental activities of daily living limitation: The variables "IADLHP31" and "IADLHP53" indicated the instrumental activities of daily living (IADL) status of subjects. Subjects were asked if they required help or supervision with IADLs such as using the telephone, paying bills, taking medications, preparing light meals, doing laundry, or going shopping. Responses to IADL help or supervision were coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare

Research and Quality, 2017b). For the purposes of this study, IADL limitations of subjects were characterized as yes or no.

Activities of daily living limitation: The variables “ADLHLP31” and “ADLHLP53” indicated the activities of daily living (ADL) status of subjects. Responses to ADL help or supervision were coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, ADL limitations of subjects were characterized as yes or no.

Functional limitation: The variables “WLKLIM31” and “WLKLIM53” indicated the functional limitation status of subjects. Subjects were asked if they have difficulty lifting ten pounds, walking up ten steps, walking three blocks, walking a mile, standing for 20 minutes, bending or stooping, reaching overhead, or using fingers to grasp. Responses to functional limitations were coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, functional limitations of subjects were characterized as yes or no.

House, school, or work limitation: The variables “ACTLIM31” and “ACTLIM53” indicated the work, housework, and school limitation status of subjects. Responses to work, housework, and school limitations were coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and

Quality, 2017b). For the purposes of this study, work, housework, and school limitations of subjects were characterized as yes or no.

Pain: A description of the pain variable was provided previously.

Perceived physical health status: The variables "RTHLTH31", "RTHLTH42", and "RTHLTH53" indicated the perceived physical health status of subjects. Response options for perceived physical health status included: (1) excellent; (2) very good; (3) good; (4) fair; and (5) poor (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the perceived physical health status of subjects was characterized as excellent/very good, good, or fair/poor.

Perceived mental health status: The variables "MNHLTH31", "MNHLTH42", and "MNHLTH53" indicated the perceived mental health status of subjects. Response options for perceived mental health status included: (1) excellent; (2) very good; (3) good; (4) fair; and (5) poor (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the perceived mental health status of subjects was characterized as excellent/very good, good, or fair/poor.

Body mass index: The variable "BMINDX53" indicated the body mass index (BMI) of subjects. BMI was calculated using the reported height and weight of the subject, and reported as a raw number. From this, BMI categories can be calculated as follows: (1) underweight – BMI less than 18.5; (2) normal weight – BMI between 18.5 and 24.9 inclusive; (3) overweight – BMI between 25.0 and 29.9 inclusive; and (4) obese – BMI greater than or equal to 30.0 (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the BMI of subjects was characterized as underweight/normal or overweight/obese.

Exercise: The variable "PHYEXE53" indicated the physical exercise status of subjects. Subjects were asked if they currently spend half an hour or more in moderate to vigorous physical activity at least five times a week, which was coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the physical exercise status of subjects was characterized as yes or no.

Smoking: The variable "ADSMOK42" indicated the smoking status of subjects. As part of the 2015 self-administered questionnaire (SQA) component of MEPS, subjects were asked if they currently smoke, which was coded as yes or no (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, the smoking status of subjects was characterized as yes or no.

Census region: The variable "REGION15" indicated the census region for the reporting unit. There are four possible categories for census region: (1) Northeast

(Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont); (2) Midwest (Indiana, Illinois, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin); (3) South (Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia); and (4) West (Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, census region was characterized using the existing categories (Northeast, Midwest, South, and West).

Dependent variables (healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider):

Inpatient expenditure: The variable "IPTEXP15" indicated the total expenditure for hospital inpatient visits (including zero-night stays) for subjects in 2015. In instances where a patient visited the emergency room and was then admitted to hospital, the emergency room expenditure would be included in the inpatient expenditure. An alternative variable is able to account for the length of hospital stay, but that calculation is beyond the needs of this study. To avoid double counting, such expenditures are not also included in the emergency room expenditures. Inpatient expenditure associated with a healthy newborn baby is included with the inpatient expenditure of the mother. The total expenditure variable includes the sum of facility expenses and separately billing doctor

(SBD) expenses (payments to physicians for services provided that were billed separately) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Outpatient expenditure: The variable "OPTEXP15" indicated the total hospital outpatient department expenditure for subjects in 2015. The total number of hospital outpatient department visits includes hospital outpatient department visits to physicians and hospital outpatient department visits to non-physician provider visits. The total expenditure variable includes the sum of facility expenses and separately billing doctor (SBD) expenses (payments to physicians for services provided that were billed separately) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Office-based expenditure: The variable "OBVEXP15" indicated the total office-based expenditure for subjects in 2015. The total number of office-based visits includes physician visits and non-physician provider visits (including chiropractor, midwife, nurse, nurse practitioner, optometrist, podiatrist, physician's assistant, physical therapist, occupational therapist, psychologist, social worker, technician, receptionist/clerk/secretary, among others) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Emergency room expenditure: The variable "ERTEXP15" indicated the total expenditure for emergency room (ER) visits for subjects in 2015. In instances where a patient visited the ER and was then admitted to hospital, the ER expenditure would be included in the inpatient expenditure. To avoid double counting, such expenditures are not also included in the ER expenditures, thus there may be some ER visits with no associated expenditures. The total expenditure variable includes the sum of facility expenses and separately billing doctor (SBD) expenses (payments to physicians for services provided that were billed separately) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Prescription medication expenditure: The variable " "RXEXP15" indicated the total expenditure for prescribed medicines (including initial and refill medicines) for subjects in 2015. The total expenditure variable includes the sum of the amount paid out-of-pocket and by third-party payers (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Other expenditure: Other healthcare expenditure involved the combination of other, dental, vision, and home health variables. The variable "OTHEXP15" indicated the total expenditure for other medical equipment and services, including ambulance services, orthopedic items, hearing devices, prostheses, bathroom aids, medical equipment, disposable supplies, alterations/modifications, and other miscellaneous items or services that were obtained, purchased, or rented. Diabetic supplies including insulin are not included in this variable (they are included in the prescribed medicines variable). The variable "DVTEXP15" indicated the total expenditure for dental care for subjects in 2015, which includes expenditure for general dentist, dental hygienist, dental technician, dental surgeon, orthodontist, endodontist, and periodontist visits. The variable "VISEXP15" indicated the total expenditure for vision aids for subjects in 2015, which included expenditure for glasses and/or contact lenses purchased. The variables "HHAEXP15" and "HHNEXP15" were summed to indicate the total expenditure for home healthcare for subjects in 2015. The total number of home health care visits includes care from paid or unpaid caregivers, such as those from agencies, hospitals or nursing homes, self-employed persons, and unpaid informal caregivers not living with the sample person. Home healthcare expenditure includes only agency sponsored and paid independent providers, not informal caregiver expenses (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Total expenditure: The variable "TOTEXP15" indicated the total expenditure for all healthcare services for subjects in 2015 (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Health-related quality of life: The SAQ contained three HRQoL measures: (1) the short-form 12 version 2 (SF-12v2®) (Ware, Kolinski, & Keller, 1996), the Kessler Index (K6) of non-specific psychological distress (Kessler et al., 2002), and the Patient Health Questionnaire (PHQ-2) (Kroenke, Spitzer, & Williams, 2003). In this study, the SF12-v2 physical component summary (PCS) and mental component summary (MCS), and the Kessler Index (K-6) summary scores were used to assess self-reported HRQoL.

The SF-12v2 consists of 12 items: (1) General health today (ADGENH42); (2)

During a typical day, limitations in moderate activities (ADDAYA42); (3) During a typical day, limitations in climbing several flights of stairs (ADCLIM42); (4) During the past four weeks, as result of physical health, accomplished less than would like (ADPALS42); (5) During the past four weeks, as result of physical health, limited in kind of work or other activities (ADPWLM42); (6) During the past four weeks, as result of mental problems, accomplished less than you would like (ADMALS42); (7) During the past four weeks, as result of mental problems, did work or other activities less carefully than usual (ADMWLM42); (8) During the past four weeks, pain interfered with normal work outside the home and housework (ADPAIN42); (9) During the past four weeks, felt calm and peaceful (ADCAPE42); (10) During the past four weeks, had a lot of energy (ADNRGY42); (11) During the past four weeks, felt downhearted and depressed (ADDOWN42); and (12) During the past four weeks, physical health or emotional problems interfered with social activities (ADSOCA42).

An algorithm developed by Optum™ includes each of these items to create two summary scores for analysis: (1) the PCS; and (2) the MCS. However, the first five items and the pain item are weighted more heavily in the PCS, while the remaining items are weighted more heavily in the MCS. A proprietary method was used to impute missing data for PCS and MCS scores. The variable "PCS42" indicated the physical component summary (PCS) score while the variable "MCS42" indicated the mental component summary (MCS) score of the SF-12v2 for subjects in 2015 (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

The K-6 consists of six items that assess an individual's non-specific (rather than disorder-specific) psychological distress during the past 30 days. The items ask, "During the past 30 days, have you felt": (1) nervous (ADNERV42); (2) hopeless (ADHOPE42); restless or fidgety (ADREST42); so sad that nothing could cheer the person up (ADSAD42); (5) that everything was an effort (ADEFRT42); and (6) worthless (ADWRTH42). Responses are scored: 0 = none of the time; 1 = a little of the time; 2 = some of the time; 3 = most of the time; 4 = all of the time. The variable "K6SUM42" indicated the K-6 summary score for subjects in 2015, where a higher value indicated a greater tendency for that individual towards mental disability (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Perceived healthcare quality: The healthcare quality measures included in the SAQ are obtained from the health plan version of Consumer Assessment of Healthcare Providers and Systems (CAHPS®). CAHPS® is an AHRQ-sponsored family of survey instruments designed to measure quality of care from the consumer's perspective over the past 12 months (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b), and enables comparisons of quality between different health plans (Agency for Healthcare Research and Quality, 2017e). In total, MEPS contains 17 CAHPS® questions, which includes three independent questions each with associated follow-up questions. In this study, only the final CAHPS® item was used to assess self-reported healthcare quality. The variable "ADHECR42" was used to determine the rating of healthcare from all doctors and other health providers, from zero (worst health care possible) to 10 (best health care possible). Subjects only responded to this question if they earlier indicated that the number of times they went to the doctor's office or clinic to get care was greater than zero (ADAPPT42) (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Access to medications: The variable "PMUNAB42" indicated whether or not an individual was unable to receive prescription medication treatment, while the variable "PMDLAY42" indicated whether or not an individual was delayed in receiving prescription medication treatment (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b). For the purposes of this study, each self-reported access to prescription medication variable was characterized as yes or no.

Perceived respect shown by provider: One of the five satisfaction variables asked in the AC section was "Does the USC provider ask about and show respect for medical, traditional, and alternative treatments that the person is happy with?" This question was indicated by the variable "RESPCT42", which had response options of: (1) never; (2) sometimes; (3) usually; and (4) always. For the purposes of this study, self-reported perceived respect shown by provider was characterized as never/sometimes or usually/always.

Analytical variables:

Weight: The variable "PERWT15F" was used as a weight variable to generate estimates of the civilian non-institutionalized population (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Cluster: The variable "VARPSU" was used to identify the primary sampling units (PSU) required by the variance estimation program (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Strata: The variable "VARSTR" was used to identify the sampling strata required by the variance estimation program (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b).

Table 3.1. Data dictionary for variables under investigation in this study

Variable description	MEPS file	MEPS variable
Cohort development (according to eligibility criteria):		
ID	Full year consolidated data	DUPERSID
Alive	Full year consolidated data	PSTATS31/42/53
Age1	Full year consolidated data	AGE15X
Pain1	Full year consolidated data	ADPAIN42
Key independent variable		
Opioid use status	Prescribed medicines	TC1S1_1
Independent variables (according to theoretical model):		
Predisposing factors:		
Age2	Full year consolidated data	AGE15X
Gender	Full year consolidated data	SEX
Race	Full year consolidated data	RACEV1X
Ethnicity	Full year consolidated data	HISPANX
Enabling factors:		
Education	Full year consolidated data	EDRECODE
Employment	Full year consolidated data	EMPST31/42/53
Health insurance	Full year consolidated data	INSCOV15
Marital status	Full year consolidated data	MARRY15X
Poverty status	Full year consolidated data	POVCAT15
Need factors:		
Chronic conditions	Medical conditions	HIBPDX CHDDX ANGDX MIDX OHRTDX STRKDX EMPHDX CHBRON31/53 CHOLDX CANCERDX DIABDX JTPAIN31/53 ARTHDX ASTHDX
Instrumental activities of daily living limitation	Full year consolidated data	IADLHP31/53
Activities of daily living limitation	Full year consolidated data	ADLHLP31/53
Functional limitation	Full year consolidated data	WLKLIM31/53
Work, housework, or school limitation	Full year consolidated data	ACTLIM31/53
Pain2	Full year consolidated data	ADPAIN42
Perceived physical health status	Full year consolidated data	RTHLTH31/42/53

	Perceived mental health status	Full year consolidated data	MNHLTH31/42/53
Personal health practices factors:			
	Body mass index	Full year consolidated data	BMINDX53
	Exercise	Full year consolidated data	PHYEXE53
	Smoking status	Full year consolidated data	ADSMOK42
External environmental factors:			
	Census region	Full year consolidated data	REGION15
Dependent variables (expenditure):			
	Inpatient expenditures	Full year consolidated data	IPTEXP15
	Outpatient expenditures	Full year consolidated data	OPTEXP15
	Office-based expenditures	Full year consolidated data	OBVEXP15
	Emergency room expenditures	Full year consolidated data	ERTEXP15
	Home health expenditures	Full year consolidated data	HHAEXP15 HHNEXP15
	Prescription medication expenditures	Full year consolidated data	RXEXP15
	Other expenditures	Full year consolidated data	OTHEXP15 DVTEXP15 VISEXP15
	Total expenditures	Full year consolidated data	TOTEXP15
Dependent variables (health-related quality of life):			
	SF-12v2 physical component summary	Full year consolidated data	PCS42
	SF-12v2 mental component summary	Full year consolidated data	MCS42
	Kessler index	Full year consolidated data	K6SUM42
Dependent variables (perceived healthcare quality):			
	Perceived healthcare quality	Full year consolidated data	ADHECR42
Dependent variables (access to medications):			
	Unable to receive medication	Full year consolidated data	PMUNAB42
	Delayed receiving medication	Full year consolidated data	PMDLAY42
Dependent variables (respect):			
	Perceived respect shown by provider	Full year consolidated data	RESPCT42
Analytical variables:			
	Weight	Full year consolidated data	PERWT15F
	Cluster	Full year consolidated data	VARPSU
	Strata	Full year consolidated data	VARSTR

Data for Table 3.1 were taken from MEPS 2015 full year consolidated data file documentation and codebook (Agency for Healthcare Research and Quality, 2017a; Agency for Healthcare Research and Quality, 2017b), MEPS 2015 prescribed medicines file documentation and codebook (Agency for Healthcare Research and Quality, 2017c; Agency for Healthcare Research and Quality, 2017d).

3.8 Independent and dependent variables

3.8.1 Independent variables

The key independent variable in the regression models was opioid use status (opioid user or non-opioid user). Opioid users were defined as those who used an opioid or combination opioid medication during the study period. Conversely, non-opioid users were defined as those who did not use an opioid or combination opioid medication during the study period.

Other independent variables were organized according to the Andersen Behavioral Model (Andersen, 1995). Predisposing factors included: age (50-64 years, ≥65 years); gender (male, female); race (white, other); and ethnicity (Hispanic, non-Hispanic).

Enabling factors included: education status (less than high school, up to high school, higher than high school); employment status (employed, other); health insurance status (private, public, uninsured); marital status (married, other); and poverty status (poor/near poor/low income, middle/high income).

Need factors included: chronic conditions (none, one, two, three, four, five or more); instrumental activities of daily living (IADL) limitation (yes, no); activities of daily living (ADL) limitation (yes, no); work, housework, or school limitation (yes, no); pain (little/moderate, quite a bit/extreme); perceived physical health status (excellent/very good, good, fair/poor); and perceived mental health status (excellent/very good, good, fair/poor).

Personal health practices factors included: body mass index (underweight/normal, overweight/obese); exercise (yes, no); and smoking status (current smoker, other).

External environmental factors included: census region (mid-west, northeast, west, south).

3.8.2 Dependent variables

The dependent variables in the regression models were healthcare expenditure, self-reported health-related quality of life, self-reported perceived healthcare quality, self-reported access to medications, and self-reported perceived respect shown by provider. There were seven healthcare expenditure variables, which included: inpatient; outpatient; office-based; emergency room; prescription medication; other; and total expenditure. There were three health-related quality of life variables, which included: the SF-12v2-PCS; SF-12v2-MCS; and the K-6 summary score. There was one perceived healthcare quality variable, which used a 0-10 rating scale. There were two access to medications variables, which included unable to receive medication and delayed receiving medication, with responses for both categorized as yes or no. Finally, there was one variable for perceived respect shown by provider, which was classified as never/sometimes or usually/always.

3.9 Data analysis

The necessary data files (full-year consolidate data, medical conditions, and prescribed medicines files) for the study year 2015 were downloaded from the MEPS website (Agency for Healthcare Research and Quality, 2019) and imported into SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). The study cohort was developed in accordance with the eligibility criteria, and the two study groups were created using the opioid use variable.

First, the predisposing, enabling, need, personal health practices, and external environmental factors of older US adults with pain who used opioids versus those who did not use opioids were assessed. Univariate associations of each of these variables with opioid use status (opioid user versus non-opioid user) were assessed using the PROC SURVEYFREQ procedure for categorical variables and the PROC SURVEYMEANS procedure for continuous variables.

The PROC SURVEYFREQ, SURVEYMEANS, SURVEYREG, and SURVEYLOGISTIC procedures are similar to the PROC FREQ, MEANS, REG, and LOGISTIC procedures used to obtain frequencies, means, and run linear or logistic regressions in SAS, but are also able to account for the complex survey design of MEPS when calculating standard errors (Gorrell, 2014).

The WEIGHT, CLUSTER, and STRATA statements were used with the SURVEYFREQ and SURVEYMEANS procedures to specify the variables that contain the sampling weights, clusters, and strata in a complex survey sample design, respectively. The DOMAIN statement was used to read the entire person-level file and thus maintain the survey design structure when conducting subgroup analyses (i.e., opioid users versus non-opioid users).

Chi-square tests (for categorical variables) and t-tests (for continuous variables) were used to determine statistically significant differences between opioid use status groups (i.e., opioid users versus non-opioid users). Variables that did not have a significant association with opioid use status were not further considered in this investigation.

A series of unadjusted and adjusted linear regression models were constructed with log-transformed data using the PROC SURVEYREG procedure to estimate healthcare expenditure (inpatient, outpatient, office-based, emergency room, prescription medication, other, and total expenditure) attributable to opioid users (versus non-opioid users) using a hierarchical regression approach.

A series of unadjusted and adjusted linear regression models were constructed using the PROC SURVEYREG procedure to estimate health-related quality of life (SF-12v2-PCS, SF-12v2-MCS, and K-6 summary score) and perceived healthcare quality attributable to opioid users (versus non-opioid users) using a hierarchical regression approach.

The univariable linear regression model was:

Model: $y = \alpha + \beta x + e$

Where: y = dependent variable

α = intercept

β = slope of the line

x = independent variable

e = residual error

The multivariable linear regression model was:

Model: $y = \alpha + \beta_1.x_1 + \beta_2.x_2 + \ldots + \beta_k.x_k + e$

Where: y = dependent variable

α = intercept

β_1 = slope of the line corresponding to the 1st independent variable

β_2 = slope of the line corresponding to the 2nd independent variable

β_k = slope of the line corresponding to the kth independent variable

x_1 = 1st independent variable

x_2 = 2nd independent variable

x_k = kth independent variable

e = residual error

The assumptions of linear regression models were assessed as follows: (1) linearity; (2) normality; (3) homoscedasticity; (4) independent observations; and (5) no multicollinearity.

Linearity: When considering linearity, there were three types of linearity that may occur with the data: 1) linear model; 2) intrinsically linear; and 3) intrinsically non-linear. Ideally, the model would be linear in the parameters. Intrinsically non-linear data in the parameters was log-transformed into a linear model, whereas intrinsically nonlinear data in the parameters required a nonlinear regression program to convert it to a linear model.

Normality: A histogram was used to assess normality. Ideally the data would have a Gaussian (normal) distribution. Data that appeared to be not normal may have affected the statistical significance of the model, although this is usually only a problem for small samples. Data that appeared not to have a normal distribution required either y or x (or both) to be transformed.

Homoscedasticity: The White test was used to assess heteroscedasticity (SAS command: *spec*). A *p* value for White's test of less that 0.05 indicated there was not constant variance in the residuals. In this case, either a transformation was performed to stabilize the variance or the weighted least squares procedure was employed.

Independent observations: The sample selection determined whether or not the data were independent of each other. Ideally data should be independent, but if they were not, a model was used that accounted for the correlation between the data.

<u>Multicolinearity:</u> Variance inflation factors (VIF) were used to assess multicolinearity between the independent variables; lower VIF's are desirable.

If the assumptions of the linear model were not met, data for the dependent variable were logarithmically transformed, and the regressions were conducted again with transformed data. In instances where it was unclear if logarithmic transformation produced a more normal distribution, the log-transformed data were used.

A series of unadjusted and adjusted logistic regression models were constructed using the PROC SURVEYLOGISTIC procedure to estimate access to medications (unable to receive medication and delayed receiving medication, yes/no), and perceived respect shown by provider (never/sometimes and usually/always) attributable to opioid users (versus non-opioid users) using a hierarchical regression approach.

The univariable logistic regression model was:

Model: $y = \pi(x) = e^{\alpha + \beta_k . x_k} / 1+e^{\alpha + \beta_k . x_k} + \varepsilon$

Where: y = dependent variable

$\pi(x)$ = probability of outcome

α = intercept

β_k = slope of the line corresponding to the k^{th} independent variable

x_k = k^{th} independent variable

ε = residual error

The multivariable logistic regression model was:

Model: $y = \pi(x) = e^{\alpha + \beta_1 . x_1 + \beta_2 . x_2 + \ldots + \beta_k . x_k} / 1 + e^{\alpha + \beta_1 . x_1 + \beta_2 . x_2 + \ldots + \beta_k . x_k} + \varepsilon$

Where: y = dependent variable

$\pi(x)$ = probability of outcome

α = intercept

β_1 = slope of the line corresponding to the 1^{st} independent variable

β_2 = slope of the line corresponding to the 2^{nd} independent variable

β_k = slope of the line corresponding to the k^{th} independent variable

x_1 = 1^{st} independent variable

x_2 = 2^{nd} independent variable

x_k = k^{th} independent variable

ε = residual error

There were no assumptions to assess for logistic regression models.

The first model was an unadjusted model that assessed only the association of the key independent variable (opioid use status; opioid users versus non-opioid users) on the dependent variable. Successive models were multivariable in nature, adjusting for an additional group of factors (predisposing, enabling, need, personal health practices, and external environmental) until a fully adjusted model that incorporated all potential variables of interest was constructed and assessed. Adjusted models included variables that were significantly associated with opioid use status in the univariate analyses ($p<0.05$). This process is outlined for a generic dependent variable in Table 3.2, and in detail for every model constructed in this study to assess healthcare expenditure in Table 3.3, health-related quality of life in Table 3.4, perceived healthcare quality in Table 3.5, access to medications in Table 3.6, and perceived respect shown by provider in Table 3.7.

Table 3.2. Generic series of unadjusted and adjusted models constructed for a generic dependent variable using a hierarchical regression approach

Model #	Independent variable(s)
1	Opioid status
2	Opioid status + predisposing
3	Opioid status + predisposing + enabling
4	Opioid status + predisposing + enabling + need
5	Opioid status + predisposing + enabling + need + personal
6	Opioid status + predisposing + enabling + need + personal + environmental

Table 3.3. Complete series of unadjusted and adjusted models constructed using a hierarchical regression approach to assess healthcare expenditures

Model #	Dependent variable	Independent variable(s)
1	Inpatient expenditure	Opioid status
2		Opioid status + predisposing
3		Opioid status + predisposing + enabling
4		Opioid status + predisposing + enabling + need
5		Opioid status + predisposing + enabling + need + personal
6		Opioid status + predisposing + enabling + need + personal + environmental
7	Outpatient expenditure	Opioid status
8		Opioid status + predisposing
9		Opioid status + predisposing + enabling
10		Opioid status + predisposing + enabling + need
11		Opioid status + predisposing + enabling + need + personal
12		Opioid status + predisposing + enabling + need + personal + environmental
13	Office-based expenditure	Opioid status
14		Opioid status + predisposing
15		Opioid status + predisposing + enabling
16		Opioid status + predisposing + enabling + need
17		Opioid status + predisposing + enabling + need + personal
18		Opioid status + predisposing + enabling + need + personal + environmental
19	Emergency room expenditure	Opioid status
20		Opioid status + predisposing
21		Opioid status + predisposing + enabling
22		Opioid status + predisposing + enabling + need
23		Opioid status + predisposing + enabling + need + personal
24		Opioid status + predisposing + enabling + need + personal + environmental
25	Prescription medication expenditure	Opioid status
26		Opioid status + predisposing
27		Opioid status + predisposing + enabling
28		Opioid status + predisposing + enabling + need
29		Opioid status + predisposing + enabling + need + personal
30		Opioid status + predisposing + enabling + need + personal + environmental
31	Other expenditure	Opioid status
32		Opioid status + predisposing
33		Opioid status + predisposing + enabling
34		Opioid status + predisposing + enabling + need

35		Opioid status + predisposing + enabling + need + personal
36		Opioid status + predisposing + enabling + need + personal + environmental
37	Total expenditure	Opioid status
38		Opioid status + predisposing
39		Opioid status + predisposing + enabling
40		Opioid status + predisposing + enabling + need
41		Opioid status + predisposing + enabling + need + personal
42		Opioid status + predisposing + enabling + need + personal + environmental

Table 3.4. Complete series of unadjusted and adjusted models constructed using a hierarchical regression approach to assess health-related quality of life

Model #	Dependent variable	Independent variable(s)
1	SF-12v2 physical component summary	Opioid status
2		Opioid status + predisposing
3		Opioid status + predisposing + enabling
4		Opioid status + predisposing + enabling + need
5		Opioid status + predisposing + enabling + need + personal
6		Opioid status + predisposing + enabling + need + personal + environmental
7	SF-12v2 mental component summary	Opioid status
8		Opioid status + predisposing
9		Opioid status + predisposing + enabling
10		Opioid status + predisposing + enabling + need
11		Opioid status + predisposing + enabling + need + personal
12		Opioid status + predisposing + enabling + need + personal + environmental
13	Kessler Index summary	Opioid status
14		Opioid status + predisposing
15		Opioid status + predisposing + enabling
16		Opioid status + predisposing + enabling + need
17		Opioid status + predisposing + enabling + need + personal
18		Opioid status + predisposing + enabling + need + personal + environmental

Table 3.5. Complete series of unadjusted and adjusted models constructed using a hierarchical regression approach to assess perceived healthcare quality

Model #	Dependent variable	Independent variable(s)
1	Perceived healthcare quality	Opioid status
2		Opioid status + predisposing
3		Opioid status + predisposing + enabling
4		Opioid status + predisposing + enabling + need
5		Opioid status + predisposing + enabling + need + personal
6		Opioid status + predisposing + enabling + need + personal + environmental

Table 3.6. Complete series of unadjusted and adjusted models constructed using a hierarchical regression approach to assess access to medications

Model #	Dependent variable	Independent variable(s)
1	Unable to receive medication	Opioid status
2		Opioid status + predisposing
3		Opioid status + predisposing + enabling
4		Opioid status + predisposing + enabling + need
5		Opioid status + predisposing + enabling + need + personal
6		Opioid status + predisposing + enabling + need + personal + environmental
7	Delayed receiving medication	Opioid status
8		Opioid status + predisposing
9		Opioid status + predisposing + enabling
10		Opioid status + predisposing + enabling + need
11		Opioid status + predisposing + enabling + need + personal
12		Opioid status + predisposing + enabling + need + personal + environmental

Table 3.7. Complete series of unadjusted and adjusted models constructed using a hierarchical regression approach to assess perceived respect shown by provider

Model #	Dependent variable	Independent variable(s)
1	Perceived respect shown by provider	Opioid status
2		Opioid status + predisposing
3		Opioid status + predisposing + enabling
4		Opioid status + predisposing + enabling + need
5		Opioid status + predisposing + enabling + need + personal
6		Opioid status + predisposing + enabling + need + personal + environmental

National estimates were obtained by adjusting for the complex survey design of MEPS. An alpha level of 0.05 was set *a priori* for all analyses. All analyses were conducted using SAS version 9.4 (SAS institute Inc., Cary, NC, USA).

3.10 Limitations with anticipated methodological approach

There were several limitations associated with this study. MEPS uses self-reported data that may be subject to recall bias, although MEPS interviews are conducted at regular intervals (every four to five months during the study period) in an attempt to minimize recall bias (Machlin, Cohen, Elixhauser, Beauregard, & Steiner, 2009). No indication is provided at the medication level, thus it was not possible to confirm that opioid medications were being used for pain (rather than another condition). Healthcare expenditure data are for all healthcare expenditure, rather than pain-related expenditure. However, this approach allowed for a holistic overview of patient healthcare expenditure. Finally, due to the nature of using secondary data in a retrospective database study, it is not possible to ascertain a cause and effect relationship, although statistical associations can be identified.

Despite these limitations, strengths of the study include use of a nationally representative sample of community-dwelling older adults with pain, allowing for generalizations to be made to the population of older US adults (≥50 years) with pain, and the inclusion of many individual-level variables to assess healthcare expenditure, health-related quality of life, perceived healthcare quality, access to medications, and perceived respect shown by provider among older US adults (≥50 years) with pain.

Chapter 4: RESULTS

Introduction to the chapter:

This chapter is organized into four sections. First, the selection of study participants is presented. Second, the demographics of study participants are described. Next, the results for each hypothesis are provided, and finally, the findings by each hypothesis are summarized.

4.1 Selection of study participants

The selection of study participants is outlined in Figure 1. There were a total of 35,427 subjects in the 2015 MEPS dataset. The study eligibility criteria (alive for the full calendar year, aged 50 years or older, and had pain in the past four weeks) were applied to these potential study subjects, where 30,668 subjects were excluded, resulting in a study cohort of 4,759 subjects. Of these, 1,525 were considered opioid users, while the remaining 3,234 were considered non-opioid users. All study subjects had positive total healthcare expenditures thus no further exclusions from the study were necessary.

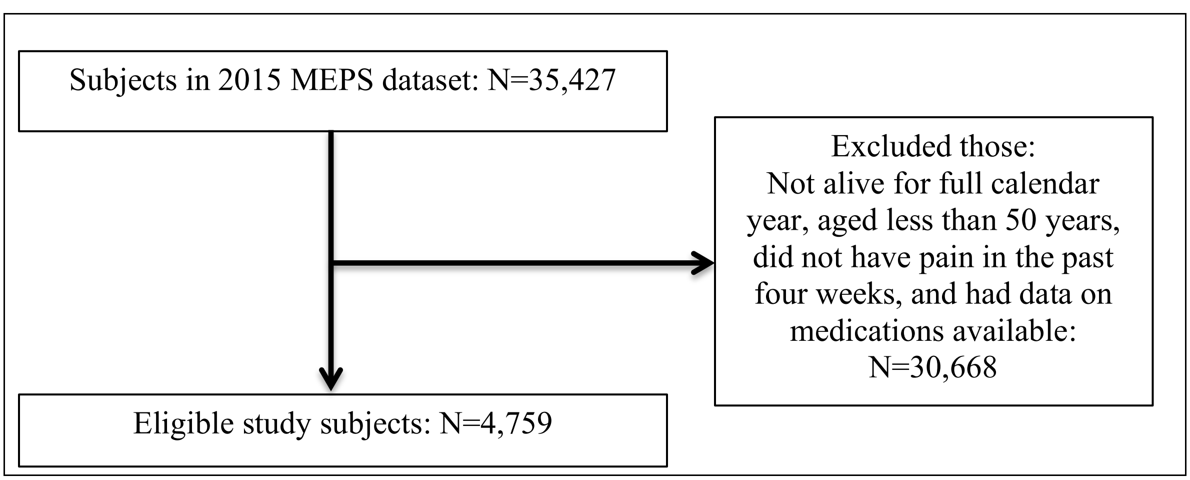

Figure 4.1. Cohort flowchart diagram

4.2 Demographics of study participants

The weighted total number of non-institutionalized adults alive aged 50 or older with pain in the US in the year 2015 was 50,898,592. Of these, a weighted 16,757,516 (32.9%) were considered opioid users, and 34,141,076 (67.1%) were considered non-opioid users.

The majority of subjects in this study were at least 65 years of age (50.2), female (56.3%), white (83.3%) and non-Hispanic (90.7%). There were more opioid users in the younger age category (age 50-64 years) than non-opioid users (53.4% versus 48.1%, p=0.0122). Meanwhile, there were fewer Hispanic individuals in the opioid group than the non-opioid group (7.8% versus 10.1%, p=0.0101). There were no significant differences between opioid users and non-opioid users in terms of gender and race (p>0.05).

Overall, most had completed high school (84.4%), and over half had an education status of higher than high school (52.4%). The majority was unemployed (63.0%), had private health insurance (62.2%), and was married (58.6%). Most were categorized as having a middle or high income (68.0%), with some variation between the opioid (62.8%) and non-opioid (70.6%) groups.

Overall, a considerable number of individuals had at least five chronic conditions (41.2%), although there were more opioid users with at least five chronic conditions than non-opioid users (49.8% versus 37.0%).

The majority had no instrumental activities of daily living (IADL) limitations (86.1%) or activities of daily living limitations (91.3%). Overall, a small majority did have a functional limitation (51.7%); the majority of opioid users did have a functional limitation (66.5%) while the majority of non-opioid users did not (55.6%). Conversely, the majority did not have a work, housework, or schoolwork limitation (63.0%), yet the majority of opioid users did have a work, housework, or schoolwork limitation (52.8%) while the majority of non-opioid users did not (70.8%).

In terms of pain, overall approximately two-thirds (69.6) reported that they had little or moderate pain, while approximately one-third (30.4%) reported they had quite a bit or extreme pain. There was considerable variation between the two groups, with significantly more opioid users reporting quite a bit or extreme pain compared to non-opioid users (49.5% versus 21.0%, $p<0.0001$).

From a perceived health perspective, overall the majority rated their physical and mental health positively; 71.9% rated their physical health as excellent, very good, or good, while 85.7% rated their mental health as excellent, very good, or good. However, opioid users perceived their physical health to be poorer compared to non-opioid users (39.9% of opioid users indicated their physical health was fair or poor compared to 22.4% of non-opioid users, $p<0.0001$). A similar trend was observed for perceived mental health, although the proportions were lower compared to physical health (18.4%

of opioid users indicated their mental health was fair or poor compared to 12.2 % of non-opioid users, $p<0.0001$).

Overall, the majority of individuals were considered overweight or obese (74.9%), and did not report participating in regular exercise (59.8%). Most were no current smokers (86.0%), although there was a greater proportion of current smokers in the opioid group compared to the non-opioid group (18.4% versus 11.9%, $p<0.0001$).

Overall, the largest region of the country that individuals were from was the South (39.0%), followed by the Midwest (23.6%), West (21.4%), and Northeast (16.0%). See Table 4.1 for further information.

Table 4.1. Descriptive statistics of older United States adults (age ≥50 years) with pain in the past four weeks, stratified by opioid users and non-opioid users (Medical Expenditure Panel Survey, 2015)

Variables	Total (Weighted N=50,898,592) Weighted % (95% CI)	Opioid user (Weighted N=16,757,516) Weighted % (95% CI)	Non-opioid user (Weighted N=34,141,076) Weighted % (95% CI)	p
Predisposing factors:				
Age (years)				0.0122 *
50-64	49.8 (47.7-51.9)	53.4 (50.0-56.7)	48.1 (45.4-50.7)	
≥65	50.2 (48.1-52.3)	46.6 (43.3-50.0)	51.9 (49.3-54.6)	
Gender				0.3186
Male	43.7 (42.6-44.9)	42.6 (40.2-45.0)	44.3 (42.6-46.0)	
Female	56.3 (55.1-57.4)	57.4 (55.0-59.8)	55.7 (54.0-57.4)	
Race				0.1345
White	83.3 (81.4-85.2)	84.5 (82.0-86.9)	82.7 (80.7-84.7)	
Other	16.7 (14.8-18.6)	15.5 (13.1-18.0)	17.3 (15.3-19.3)	
Ethnicity				0.0101 *
Hispanic	9.3 (7.8-10.9)	7.8 (6.3-9.4)	10.1 (8.2-11.9)	
Non-Hispanic	90.7 (89.1-92.2)	92.2 (90.6-93.7)	89.9 (88.1-91.8)	
Enabling factors:				
Education				0.0034 **
Less than high school	15.6 (14.2-16.9)	16.5 (14.4-18.6)	15.1 (13.7-16.6)	
Up to high school	32.0 (30.2-33.9)	35.1 (32.0-38.1)	30.6 (28.6-32.6)	
Higher than high school	52.4 (50.2-54.6)	48.5 (44.8-52.1)	54.3 (51.9-56.7)	
Employment				0.0005 ***
Employed	37.0 (35.0-39.0)	33.2 (30.4-35.9)	38.9 (36.4-41.3)	
Unemployed	63.0 (61.0-65.0)	66.8 (64.1-69.6)	61.1 (58.7-63.6)	
Health insurance				0.0007 ***
Private	62.2 (60.1-64.3)	58.0 (54.5-61.4)	64.3 (62.1-66.6)	
Public	34.4 (32.5-36.4)	39.0 (35.7-42.3)	32.2 (30.1-34.3)	
Uninsured	3.3 (2.6-4.0)	3.1 (1.9-4.2)	3.4 (2.6-4.3)	
Marital status				0.0056 **
Married	58.6 (56.4-60.8)	55.1 (51.6-58.5)	60.4 (57.9-62.8)	
Other	41.4 (39.2-43.6)	44.9 (41.5-48.4)	39.6 (37.2-42.1)	
Poverty status				<0.0001 ***
Poor/near poor/low	32.0 (30.0-33.9)	37.2 (33.9-40.6)	29.4 (27.2-31.5)	

income				
Middle/high income	68.0 (66.1-70.0)	62.8 (59.4-66.1)	70.6 (68.5-72.8)	
Need factors:				
Chronic conditions				<0.0001 ***
0	1.7 (1.3-2.2)	0.9 (0.3-1.5)	2.1 (1.5-2.8)	
1	6.0 (5.2-6.8)	3.5 (2.3-4.6)	7.2 (6.2-8.3)	
2	13.1 (11.9-14.3)	10.9 (8.8-13.1)	14.2 (12.7-15.6)	
3	18.7 (17.4-20.1)	16.6 (14.3-18.8)	19.8 (18.2-21.4)	
4	19.2 (17.9-20.6)	18.3 (15.9-20.8)	19.7 (18.0-21.4)	
≥5	41.2 (39.2-43.2)	49.8 (46.4-53.2)	37.0 (34.8-39.2)	
Instrumental activities of daily living limitation				<0.0001 ***
Yes	13.9 (12.6-15.2)	19.6 (17.1-22.1)	11.1 (9.7-12.4)	
No	86.1 (84.8-87.4)	80.4 (77.9-82.9)	88.9 (87.6-90.3)	
Activities of daily living limitation				<0.0001 ***
Yes	8.7 (7.6-9.7)	13.7 (11.5-15.9)	6.2 (5.1-7.3)	
No	91.3 (90.3-92.4)	86.3 (84.1-88.5)	93.8 (92.7-94.9)	
Functional limitation				<0.0001 ***
Yes	51.7 (49.7-53.6)	66.5 (63.3-69.7)	44.4 (42.1-46.7)	
No	48.3 (46.4-50.3)	33.5 (30.3-36.7)	55.6 (53.3-57.9)	
Work, housework, or school limitation				<0.0001 ***
Yes	37.0 (35.0-39.0)	52.8 (49.6-56.0)	29.2 (27.1-31.3)	
No	63.0 (61.0-65.0)	47.2 (44.0-50.4)	70.8 (68.7-72.9)	
Pain				<0.0001 ***
Little/moderate	69.6 (67.9-71.4)	50.5 (47.6-53.5)	79.0 (77.3-80.7)	
Quite a bit/extreme	30.4 (28.6-32.1)	49.5 (46.5-52.4)	21.0 (19.3-22.7)	
Perceived physical health status				<0.0001 ***
Excellent/very good	35.8 (33.6-37.9)	24.5 (21.8-27.2)	41.3 (38.8-43.8)	
Good	36.1 (34.4-37.8)	35.6 (32.9-38.3)	36.3 (34.2-38.4)	
Fair/poor	28.2 (26.5-29.9)	39.9 (37.2-42.6)	22.4 (20.6-24.3)	
Perceived mental health status				<0.0001 ***
Excellent/very good	52.2 (50.2-54.3)	46.2 (42.8-49.6)	55.2 (52.7-57.7)	

Good	33.5 (31.8-35.3)	35.4 (32.6-38.3)	32.6 (30.3-34.9)	
Fair/poor	14.2 (13.1-15.4)	18.4 (16.2-20.6)	12.2 (10.8-13.6)	
Personal health practices factors:				
Body mass index				0.0238 *
Underweight/ normal	25.1 (23.6-26.5)	22.8 (20.5-25.1)	26.2 (24.3-28.0)	
Overweight/ obese	74.9 (73.5-76.4)	77.2 (74.9-79.5)	73.8 (72.0-75.7)	
Exercise				0.0090 **
Yes	40.2 (37.9-42.4)	36.5 (33.0-40.1)	41.9 (39.3-44.6)	
No	59.8 (57.6-62.1)	63.5 (59.9-67.0)	58.1 (55.4-60.7)	
Smoking status				<0.0001 ***
Yes	14.0 (12.7-15.4)	18.4 (15.8-20.9)	11.9 (10.3-13.5)	
No	86.0 (84.6-87.3)	81.6 (79.1-84.2)	88.1 (86.5-89.7)	
External environmental factors:				
Census region				0.0212 *
Northeast	16.0 (13.9-18.2)	12.9 (9.9-16.0)	17.6 (15.2-19.9)	
Midwest	23.6 (21.3-25.8)	24.6 (21.1-28.2)	23.1 (20.6-25.5)	
South	39.0 (36.2-41.8)	39.1 (35.2-43.1)	38.9 (35.9-42.0)	
West	21.4 (18.9-23.9)	23.3 (19.5-27.1)	20.5 (18.0-22.9)	

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: % = percentage; CI = confidence interval; Sig = significant.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.

The annual mean healthcare expenditure was higher among opioid users for inpatient ($24,360 versus $20,708, p=0.0010), outpatient ($3,723 versus $2,165, p<0.0001), office-based ($3,941 versus $2,438, p<0.0001), prescription medications ($5,020 versus $2,758, p=0.0001), other healthcare expenditure ($2,500 versus $1,643, p<0.0001), and total healthcare expenditure ($20,035 versus $9,125, <0.0001). There was no significant difference between opioid users and non-opioid users for annual mean emergency room expenditures ($1,971 versus $1,470, p=0.1970). See Table 4.2 for further information.

Table 4.2. Descriptive statistics for healthcare expenditure of older United States adults (age ≥50 years) with pain in the past four weeks, stratified by opioid users and non-opioid users (Medical Expenditure Panel Survey, 2015)

Healthcare expenditures	Opioid-user Mean (SE)	Non-opioid user Mean (SE)	Sig
Inpatient	24,360.00 (822.35)	20,708.00 (846.39)	0.0010 **
Outpatient	3,723.09 (319.63)	2,165.10 (251.54)	<0.0001 ***
Office-based	3,941.10 (193.64)	2,438.02 (119.02)	<0.0001 ***
Emergency room	1,971.32 (345.48)	1,470.14 (205.44)	0.1970
Prescription medications	5,020.26 (560.03)	2,758.30 (112.15)	0.0001 ***
Other	2,500.26 (187.97)	1,642.90 (116.41)	<0.0001 ***
Total	20,035.00 (1,012.12)	9,124.63 (337.21)	<0.0001 ***

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Inpatient N=755; Outpatient N=1600; Office-based N=4532; Emergency room N=1130; Prescription medications N=4758; Other N=2874; Total N=4759.
Abbreviations: SE = standard error; Sig = significant.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** $p<0.001$; ** $0.001\leq p<0.01$; * $0.01\leq p0.05$.

4.3 Results by hypothesis

4.3.1 Healthcare expenditure

<u>Hierarchical linear regression results, **unadjusted models**:</u>

In unadjusted linear regression models, opioid users had 61% greater outpatient expenditure ($\beta=0.477$, $p<0.0001$), 89% greater office-based expenditure ($\beta=0.634$, $p<0.0001$), 125% greater prescription medication expenditure ($\beta=0.812$, $p<0.0001$), 42% greater other healthcare expenditure ($\beta=0.352$, $p<0.0001$), and 157% greater total healthcare expenditure ($\beta=0.942$, $p<0.0001$). Inpatient and emergency room expenditures were not significant ($p>0.05$). See Table 4.3 for further information.

Table 4.3. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **unadjusted for any covariates**, using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare Expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	9.283	0.086	<0.0001 ***	
Opioid users	0.187	0.119	0.1179	20.6
Non-opioid user				
Outpatient				
Intercept	6.475	0.068	<0.0001 ***	
Opioid users	0.477	0.098	<0.0001 ***	61.1
Non-opioid user				
Office-based				
Intercept	6.960	0.033	<0.0001 ***	
Opioid users	0.634	0.057	<0.0001 ***	88.5
Non-opioid user				
Emergency room				
Intercept	6.470	0.081	<0.0001 ***	
Opioid users	0.163	0.105	0.1220	17.7
Non-opioid user				
Prescription medications				
Intercept	6.583	0.043	<0.0001 ***	
Opioid users	0.812	0.066	<0.0001 ***	125.2
Non-opioid user				
Other				
Intercept	6.346	0.037	<0.0001 ***	
Opioid users	0.352	0.063	<0.0001 ***	42.2
Non-opioid user				
Total				
Intercept	8.258	0.032	<0.0001 ***	
Opioid users	0.942	0.052	<0.0001 ***	156.5
Non-opioid user				

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.

Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Hierarchical linear regression results, **models adjusted for predisposing factors**:

After adjustment for predisposing factors, opioid users had 57% greater outpatient expenditure (β=0.450, $p<0.0001$), 89% greater office-based expenditure (β=0.634, $p<0.0001$), 127% greater prescription medication expenditure (β=0.819, $p<0.0001$), 45% greater other healthcare expenditure (β=0.369, $p<0.0001$), and 158% greater total healthcare expenditure (β=0.949, $p<0.0001$). Inpatient and emergency room expenditures were not significant ($p>0.05$). See Table 4.4 for further information.

Table 4.4. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing factors,** using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	9.253	0.203	<0.0001 ***	
Opioid users	0.189	0.112	0.0941	20.8
Non-opioid user				
Outpatient				
Intercept	6.134	0.194	<0.0001 ***	
Opioid users	0.450	0.096	<0.0001 ***	56.8
Non-opioid user				
Office-based				
Intercept	6.663	0.083	<0.0001 ***	
Opioid users	0.634	0.057	<0.0001 ***	88.5
Non-opioid user				
Emergency room				
Intercept	6.282	0.169	<0.0001 ***	
Opioid users	0.127	0.103	0.2161	13.5
Non-opioid user				
Prescription medications				
Intercept	6.444	0.131	<0.0001 ***	
Opioid users	0.819	0.067	<0.0001 ***	126.8
Non-opioid user				
Other				
Intercept	6.370	0.135	<0.0001 ***	
Opioid users	0.369	0.063	<0.0001 ***	44.6
Non-opioid user				
Total				
Intercept	8.053	0.096	<0.0001 ***	
Opioid users	0.949	0.052	<0.0001 ***	158.3
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.

Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Hierarchical linear regression results, **models adjusted for predisposing and enabling factors**:

After adjustment for predisposing and enabling factors, opioid users had 69% greater outpatient expenditure (β=0.527, $p<0.0001$), 94% greater office-based expenditure (β=0.662, $p<0.0001$), 107% greater prescription medication expenditure (β=0.729, $p<0.0001$), 43% greater other healthcare expenditure (β=0.357, $p<0.0001$), and 153% greater total healthcare expenditure (β=0.927, $p<0.0001$). Inpatient and emergency room expenditures were not significant ($p>0.05$). See Table 4.5 for further information.

Table 4.5. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing and enabling factors,** using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	9.546	0.270	<0.0001 ***	
Opioid users	0.200	0.114	0.0813	22.1
Non-opioid user				
Outpatient				
Intercept	6.580	0.243	<0.0001 ***	
Opioid users	0.527	0.092	<0.0001 ***	69.4
Non-opioid user				
Office-based				
Intercept	6.543	0.092	<0.0001 ***	
Opioid users	0.662	0.055	<0.0001 ***	93.9
Non-opioid user				
Emergency room				
Intercept	6.624	0.237	<0.0001 ***	
Opioid users	0.174	0.097	0.075	19.0
Non-opioid user				
Prescription medications				
Intercept	5.534	0.139	<0.0001 ***	
Opioid users	0.729	0.064	<0.0001 ***	107.3
Non-opioid user				
Other				
Intercept	6.068	0.179	<0.0001 ***	
Opioid users	0.357	0.063	<0.0001 ***	42.9
Non-opioid user				
Total				
Intercept	7.605	0.115	<0.0001 ***	
Opioid users	0.927	0.050	<0.0001 ***	152.7
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.

*** $p<0.001$; ** $0.001 \leq p<0.01$; * $0.01 \leq p0.05$.
Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Hierarchical linear regression results, **models adjusted for predisposing, enabling, and need factors**:

After adjustment for predisposing, enabling, and need factors, opioid users had 58% greater outpatient expenditure ($\beta=0.458$, $p<0.0001$), 67% greater office-based expenditure ($\beta=0.514$, $p<0.0001$), 12% greater emergency room expenditure ($\beta=0.112$, $p=0.0059$), 57% greater prescription medication expenditure ($\beta=0.450$, $p<0.0001$), 27% greater other healthcare expenditure ($\beta=0.241$, $p=0.0003$), and 99% greater total healthcare expenditure ($\beta=0.689$, $p<0.0001$). Inpatient expenditures were not significant ($p>0.05$). See Table 4.6 for further information.

Table 4.6. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, and need factors,** using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	8.471	0.529	<0.0001 ***	
Opioid users	0.081	0.105	0.4409	8.4
Non-opioid user				
Outpatient				
Intercept	5.456	0.287	<0.0001 ***	
Opioid users	0.458	0.043	<0.0001 ***	58.1
Non-opioid user				
Office-based	0.165			
Intercept	5.160	0.260	<0.0001 ***	
Opioid users	0.514	0.053	<0.0001 ***	67.2
Non-opioid user				
Emergency room				
Intercept	5.849	0.248	<0.0001 ***	
Opioid users	0.112	0.040	0.0059 **	11.9
Non-opioid user				
Prescription medications				
Intercept	3.811	0.309	<0.0001 ***	
Opioid users	0.450	0.062	<0.0001 ***	56.8
Non-opioid user				
Other				
Intercept	6.837	0.333	<0.0001 ***	
Opioid users	0.241	0.065	0.0003 ***	27.3
Non-opioid user				
Total				
Intercept	6.309	0.250	<0.0001 ***	
Opioid users	0.689	0.047	<0.0001 ***	99.2
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status.

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but

only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, and personal health practices factors**:

After adjustment for predisposing, enabling, need, and personal health practices factors, opioid users had 59% greater outpatient expenditure (β=0.466, p<0.0001), 68% greater office-based expenditure (β=0.520, p<0.0001), 12% greater emergency room expenditure (β=0.112, p=0.0052), 60% greater prescription medication expenditure (β=0.470, p<0.0001), 28% greater other healthcare expenditure (β=0.248, p=0.0002), and 103% greater total healthcare expenditure (β=0.708, p<0.0001). Inpatient expenditures were not significant (p>0.05). See Table 4.7 for further information.

Table 4.7. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, and personal factors,** using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	8.317	0.690	<0.0001 ***	
Opioid users	0.086	0.105	0.4159	9.0
Non-opioid user				
Outpatient				
Intercept	5.389	0.339	<0.0001 ***	
Opioid users	0.466	0.045	<0.0001 ***	59.4
Non-opioid user				
Office-based				
Intercept	4.990	0.267	<0.0001 ***	
Opioid users	0.520	0.053	<0.0001 ***	68.2
Non-opioid user				
Emergency room				
Intercept	5.969	0.238	<0.0001 ***	
Opioid users	0.112	0.039	0.0052 **	11.9
Non-opioid user				
Prescription medications				
Intercept	3.686	0.334	<0.0001 ***	
Opioid users	0.470	0.063	<0.0001 ***	60.0
Non-opioid user				
Other				
Intercept	6.895	0.360	<0.0001 ***	
Opioid users	0.248	0.065	0.0002 ***	28.1
Non-opioid user				
Total				
Intercept	6.137	0.257	<0.0001 ***	
Opioid users	0.708	0.048	<0.0001 ***	103.0
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status.

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, personal health practices, and external environmental factors**:

After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, opioid users had 61% greater outpatient expenditure (β=0.477, p<0.0001), 69% greater office-based expenditure (β=0.524, p<0.0001), 14% greater emergency room expenditure (β=0.131, p=0.0045), 63% greater prescription medication expenditure (β=0.486, p<0.0001), 29% greater other healthcare expenditure (β=0.251, p=0.0002), and 105% greater total healthcare expenditure (β=0.718, p<0.0001). Inpatient expenditures were not significant (p>0.05). See Table 4.8 and Figure 4.2 for further information.

Table 4.8. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, personal, and environmental factors,** using logged positive healthcare expenditures (Medical Expenditure Panel Survey, 2015)

Healthcare expenditure	Beta	Standard Error	Significance	Percent Change
Inpatient				
Intercept	8.351	0.694	<0.0001 ***	
Opioid users	0.077	0.110	0.4826	8.0
Non-opioid user				
Outpatient				
Intercept	5.252	0.361	<0.0001 ***	
Opioid users	0.477	0.044	<0.0001 ***	61.1
Non-opioid user				
Office-based				
Intercept	5.063	0.267	<0.0001 ***	
Opioid users	0.524	0.053	<0.0001 ***	68.9
Non-opioid user				
Emergency room				
Intercept	5.914	0.254	<0.0001 ***	
Opioid users	0.131	0.045	0.0045 ***	14.0
Non-opioid user				
Prescription medications				
Intercept	3.503	0.342	<0.0001 ***	
Opioid users	0.486	0.063	<0.0001 ***	62.6
Non-opioid user				
Other				
Intercept	6.931	0.358	<0.0001 ***	
Opioid users	0.251	0.066	0.0002 ***	28.5
Non-opioid user				
Total				
Intercept	6.083	0.263	<0.0001 ***	
Opioid users	0.718	0.047	<0.0001 ***	105.0
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health

practices factors included body mass index, exercise, and smoking status. External environmental factors included census region.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015, but only includes those who had positive healthcare expenditures for each healthcare expenditure category.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** $p<0.001$; ** $0.001 \leq p<0.01$; * 0.01≤p0.05.
Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

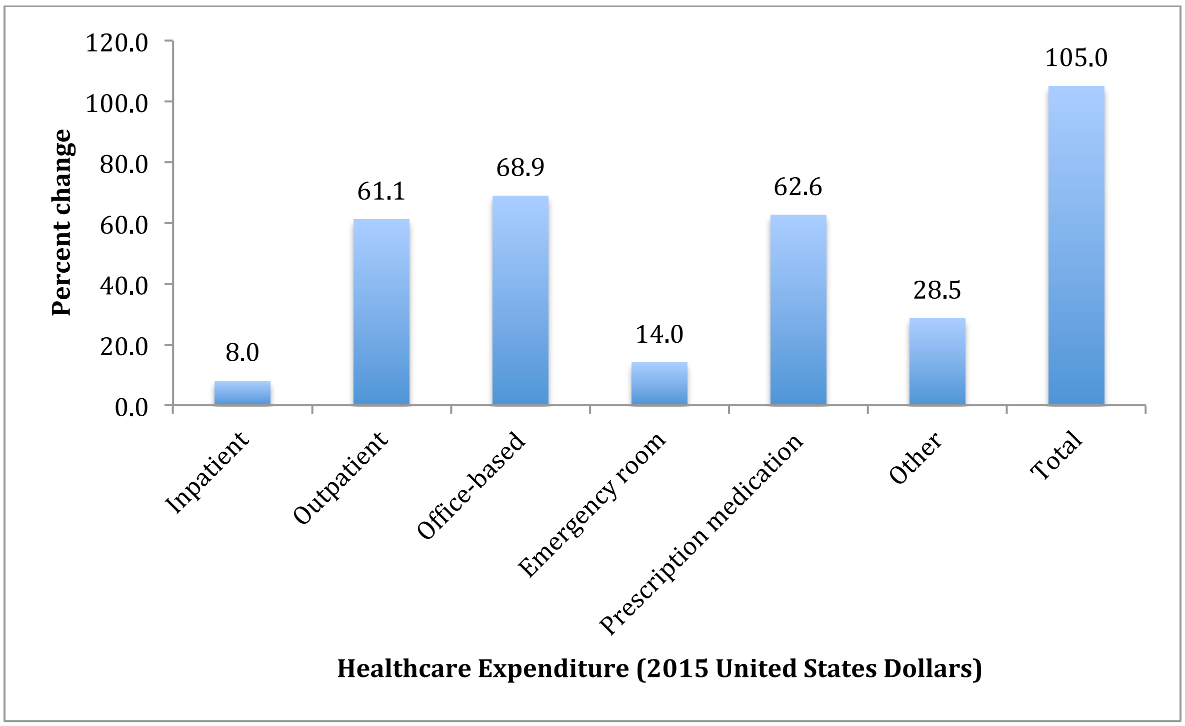

Figure 4.2. Annual percent change in healthcare expenditure for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, adjusted for predisposing, enabling, need, personal, and environmental factors (Medical Expenditure Panel Survey, 2015)

Percent change represents the difference in expenditure between opioid users and non-opioid users, calculated using semi-logarithmic equation (e^{β}-1) (Halvorsen, 1980).

Assessment of model assumptions:

The fully adjusted models for healthcare expenditure met all assumptions for linear regression, including: (1) linearity; (2) normality; (3) homoscedasticity; (4) independent observations; and (5) no multicollinearity.

R-squared values for the fully adjusted models were: inpatient r^2=0.133; outpatient r^2=0.093; office-based r^2=0.174; emergency room r^2=0.096; prescription medications r^2=0.256; other r^2=0.124; and total expenditure r^2=0.292.

4.3.2 Health-related quality of life

Hierarchical linear regression results, **unadjusted models**:

In unadjusted linear regression models, opioid users had 593% lower short form 12 version 2 physical component summary (SF-12v2-PCS) scores (β=-5.926, p<0.0001), 291% lower short form 12 version 2 mental component summary (SF-12v2-MCS) scores (β=-2.911, p<0.0001), and 161% greater K6 scores (β=1.605, p<0.0001). See Table 4.9 for further information.

Table 4.9. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **unadjusted for any covariates,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	40.391	0.239	<0.0001 ***	
Opioid users	-5.926	0.397	<0.0001 ***	-592.6
Non-opioid user				
SF-12v2-MCS				
Intercept	50.945	0.232	<0.0001 ***	
Opioid users	-2.911	0.473	<0.0001 ***	-291.1
Non-opioid user				
Kessler Index (K6)				
Intercept	3.814	0.103	<0.0001 ***	
Opioid users	1.605	0.187	<0.0001 ***	160.5
Non-opioid user				

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing factors**:

After adjustment for predisposing factors, opioid users had 615% lower SF-12v2-PCS scores (β=-6.151, p<0.0001), 285% lower SF-12v2-MCS scores (β=-2.853, p<0.0001), and 158% greater K6 scores (β=1.575, p<0.0001). See Table 4.10 for further information.

Table 4.10. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing factors,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	35.953	0.669	<0.0001 ***	
Opioid users	-6.151	0.381	<0.0001 ***	-615.1
Non-opioid user				
SF-12v2-MCS				
Intercept	47.962	0.720	<0.0001 ***	
Opioid users	-2.853	0.469	<0.0001 ***	-285.3
Non-opioid user				
Kessler Index (K6)				
Intercept	4.766	0.381	<0.0001 ***	
Opioid users	1.575	0.188	<0.0001 ***	157.5
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

<u>Hierarchical linear regression results, **models adjusted for predisposing and enabling factors**:</u>

After adjustment for predisposing and enabling factors, opioid users had 519% lower SF-12v2-PCS scores (β=-5.188, p<0.0001), 211% lower SF-12v2-MCS scores (β=-2.109, p<0.0001), and 121% greater K6 scores (β=1.206, p<0.0001). See Table 4.11 for further information.

Table 4.11. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing and enabling factors,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	43.972	0.823	<0.0001 ***	
Opioid users	-5.188	0.378	<0.0001 ***	-518.8
Non-opioid user				
SF-12v2-MCS				
Intercept	54.135	0.839	<0.0001 ***	
Opioid users	-2.109	0.444	<0.0001 ***	-210.9
Non-opioid user				
Kessler Index (K6)				
Intercept	1.617	0.430	0.0002 ***	
Opioid users	1.206	0.170	<0.0001 ***	120.6
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

<u>Hierarchical linear regression results, **models adjusted for predisposing, enabling, and need factors**:</u>

After adjustment for predisposing, enabling, and need factors, there was no significant difference between opioid users and non-opioid users for SF-12v2-PCS scores, SF-12v2-MCS scores, or K6 scores ($p>0.05$). See Table 4.12 for further information.

Table 4.12. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, and need factors,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	36.154	1.225	<0.0001 ***	
Opioid users	-0.095	0.297	0.7489	-9.5
Non-opioid user				
SF-12v2-MCS				
Intercept	40.245	1.974	<0.0001 ***	
Opioid users	-0.625	0.437	0.1543	-62.5
Non-opioid user				
Kessler Index (K6)				
Intercept	7.274	0.846	<0.0001 ***	
Opioid users	0.237	0.179	0.1876	23.7
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, and personal health practices factors**:

After adjustment for predisposing, enabling, need, and personal health practices factors, there was no significant difference between opioid users and non-opioid users for

SF-12v2-PCS scores, SF-12v2-MCS scores, or K6 scores ($p>0.05$). See Table 4.13 for further information.

Table 4.13. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, and personal factors,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	36.766	1.281	<0.0001 ***	
Opioid users	-0.187	0.295	0.5277	-18.7
Non-opioid user				
SF-12v2-MCS				
Intercept	37.421	2.036	<0.0001 ***	
Opioid users	-0.636	0.437	0.1471	-63.6
Non-opioid user				
Kessler Index (K6)				
Intercept	8.367	0.877	<0.0001 ***	
Opioid users	0.266	0.180	0.1412	26.6
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, personal health practices, and external environmental factors**:

After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, there was no significant difference between opioid users and non-opioid users for SF-12v2-PCS scores, SF-12v2-MCS scores, or K6 scores ($p>0.05$). See Table 4.14 for further information.

Table 4.14. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, personal, and environmental factors,** for health-related quality of life (Medical Expenditure Panel Survey, 2015)

Health-related quality of life	Beta	Standard Error	Significance	Percent Change
SF-12v2-PCS				
Intercept	36.925	1.340	<0.0001 ***	
Opioid users	-0.175	0.295	0.5535	-17.5
Non-opioid user				
SF-12v2-MCS				
Intercept	37.456	2.058	<0.0001 ***	
Opioid users	-0.637	0.438	0.1475	-63.7
Non-opioid user				
Kessler Index (K6)				
Intercept	8.536	0.871	<0.0001 ***	
Opioid users	0.263	0.178	0.1420	26.3
Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status. External environmental factors included census region.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Abbreviations: SF-12v2-PCS = short form 12 version 2 physical component summary; SF-12v2-MCS = short form 12 version 2 mental component summary.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in health-related quality of life between opioid users and non-opioid users.

Assessment of model assumptions:

The fully adjusted models for SF-12v2-PCS and SF-12v2-MCS met all assumptions for linear regression, including: (1) linearity; (2) normality; (3)

homoscedasticity; (4) independent observations; and (5) no multicollinearity. However, the fully adjusted model for K6 had did not meet the model assumptions well.

R-squared values for the fully adjusted models were: SF-12v2-PCS r^2=0.615; SF-12v2-MCS r^2=0.267; and K6 r^2=0.302.

4.3.3 Perceived healthcare quality

Hierarchical linear regression results, **unadjusted models**:

In unadjusted linear regression models, there was no significant difference between opioid users and non-opioid users for perceived healthcare quality scores ($p>0.05$). See Table 4.15 for further information.

Table 4.15. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **unadjusted for any covariates,** for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	8.377	0.039	<0.0001 ***	
	Opioid users	-0.084	0.080	0.2953	-8.4
	Non-opioid user				

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

<u>Hierarchical linear regression results, **models adjusted for predisposing factors**:</u>

After adjustment for predisposing factors, there was no significant difference between opioid users and non-opioid users for perceived healthcare quality scores (p>0.05). See Table 4.16 for further information.

Table 4.16. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing factors,** for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	8.421	0.118	<0.0001 ***	
	Opioid users	-0.065	0.077	0.4027	-6.5
	Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing and enabling factors**:

After adjustment for predisposing and enabling factors, there was no significant difference between opioid users and non-opioid users for perceived healthcare quality scores (p>0.05). See Table 4.17 for further information.

Table 4.17. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing and enabling factors**, for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	8.664	0.145	<0.0001 ***	
	Opioid users	-0.020	0.074	0.7930	-2.0
	Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing, enabling, and need factors**:

After adjustment for predisposing, enabling, and need factors, there was no significant difference between opioid users and non-opioid users for perceived healthcare quality scores (p>0.05). See Table 4.18 for further information.

Table 4.18. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, and need factors,** for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	7.611	0.395	<0.0001 ***	
	Opioid users	0.128	0.069	0.0659	12.8
	Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, and personal health practices factors**:

After adjustment for predisposing, enabling, need, and personal health practices factors, opioid users had 15% greater perceived healthcare quality scores (β=0.149, p=0.0369). See Table 4.19 for further information.

Table 4.19. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, and personal factors,** for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	7.304	0.467	<0.0001 ***	
	Opioid users	0.149	0.071	0.0369 *	14.9
	Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

<u>Hierarchical linear regression results, **models adjusted for predisposing, enabling, need, personal health practices, and external environmental factors**:</u>

After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, opioid users had 15% greater perceived healthcare quality scores (β=0.154, p=0.0286). See Table 4.20 for further information.

Table 4.20. Intercepts and parameter estimates for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, personal, and environmental factors,** for perceived healthcare quality (Medical Expenditure Panel Survey, 2015)

Perceived healthcare quality		Beta	Standard Error	Significance	Percent Change
	Intercept	7.238	0.455	<0.0001 ***	
	Opioid users	0.154	0.070	0.0286 *	15.4
	Non-opioid user				

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status. External environmental factors included census region.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on t-tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived healthcare quality between opioid users and non-opioid users.

Assessment of model assumptions:

The fully adjusted models for quality did not meet all assumptions for linear regression well. The r-squared value for the fully adjusted models was r^2=0.069

4.3.4 Access to prescription medications

Hierarchical logistic regression results, **unadjusted models**:

In unadjusted logistic regression models, older US adults (≥50 years) with pain in the past four weeks who were unable to receive prescription medications were 1.7 (95% confidence interval [CI] = 1.2, 2.3) times more likely to be opioid users than non-opioid users, while those who were delayed receiving prescription medications were 1.4 (95% CI = 1.1, 1.9) times more likely to be opioid users than non-opioid users. The models had a Wald statistic of 0.0017 and 0.0042 respectively, and a c-statistic of 0.568 and 0.567 respectively. See Table 4.21 for further information.

Table 4.21. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **unadjusted for any covariates,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications	Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications			
Opioid users	1.655	1.207-2.268	0.0017 ***
Non-opioid user			
Delayed receiving prescription medication			
Opioid users	1.447	1.123-1.863	0.0042 ***
Non-opioid user			

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing factors**:

After adjustment for predisposing factors, older US adults (≥50 years) with pain in the past four weeks who were unable to receive prescription medications were 1.6 (95% CI = 1.2, 2.2) times more likely to be opioid users than non-opioid users, while those who were delayed receiving prescription medications were 1.4 (95% CI = 1.1, 1.8) times more likely to be opioid users than non-opioid users. The models had a Wald statistic of 0.0123 and <0.0001 respectively, and a c-statistic of 0.606 and 0.629 respectively. See Table 4.22 for further information.

Table 4.22. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing factors,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications	Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications			
Opioid users	1.630	1.187-2.237	0.0025 **
Non-opioid user			
Delayed receiving prescription medication			
Opioid users	1.387	1.072-1.795	0.0129 *
Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** $p<0.001$; ** $0.001 \leq p<0.01$; * $0.01 \leq p0.05$.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing and enabling factors**:

After adjustment for predisposing and enabling factors, older US adults (≥50 years) with pain in the past four weeks who were unable to receive prescription medications were 1.5 (95% CI = 1.1, 2.1) times more likely to be opioid users than non-opioid users, while those who were delayed receiving prescription medications were 1.3 (95% CI = 1.0, 1.7) times more likely to be opioid users than non-opioid users. The models had a Wald statistic of 0.0009 and <0.0001 respectively, and a c-statistic of 0.645 and 0.667 respectively. See Table 4.23 for further information.

Table 4.23. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing and enabling factors,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications		Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications				
	Opioid users	1.496	1.077-2.079	0.0164 *
	Non-opioid user			
Delayed receiving prescription medication				
	Opioid users	1.293	0.985-1.697	0.0644
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** $p<0.001$; ** $0.001 \leq p<0.01$; * 0.01≤p0.05.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing, enabling, and need factors**:

After adjustment for predisposing, enabling, and need factors, there was no significant difference between opioid users and non-opioid users for unable to receive prescription medications status and delayed receiving prescription medications status ($p>0.05$). The models had a Wald statistic of <0.0001 and <0.0001 respectively, and a c-statistic of 0.695 and 0.715 respectively. See Table 4.24 for further information.

Table 4.24. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, and need factors,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications	Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications			
Opioid users	1.094	0.792-1.511	0.5865
Non-opioid user			
Delayed receiving prescription medication			
Opioid users	0.980	0.754-1.273	0.8784
Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** $p<0.001$; ** $0.001 \le p<0.01$; * 0.01≤p0.05.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

<u>Hierarchical logistic regression results, **models adjusted for predisposing, enabling, need, and personal health practices factors**:</u>

After adjustment for predisposing, enabling, need, and personal health practices factors, there was no significant difference between opioid users and non-opioid users for unable to receive prescription medications status and delayed receiving prescription medications status ($p>0.05$). The models had a Wald statistic of <0.0001 and <0.0001 respectively, and a c-statistic of 0.705 and 0.718 respectively. See Table 4.25 for further information.

Table 4.25. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, and personal factors,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications	Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications			
Opioid users	1.121	0.803-1.564	0.5024
Non-opioid user			
Delayed receiving prescription medication			
Opioid users	0.988	0.762-1.282	0.9292
Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing, enabling, need, personal health practices, and external environmental factors**:

After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, there was no significant difference between opioid users and non-opioid users for unable to receive prescription medications status and delayed receiving prescription medications status (p>0.05). The models had a Wald statistic of

<0.0001 and <0.0001 respectively, and a c-statistic of 0.706 and 0.718 respectively. See Table 4.26 for further information.

Table 4.26. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, personal, and environmental factors,** for access to prescription medications (Medical Expenditure Panel Survey, 2015)

Access to prescription medications	Odds ratio	95% Confidence Interval	Significance
Unable to receive prescription medications			
Opioid users	1.105	0.794-1.537	0.5544
Non-opioid user			
Delayed receiving prescription medication			
Opioid users	0.979	0.758-1.266	0.8735
Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status. External environmental factors included census region.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in access to prescription medications between opioid users and non-opioid users.

4.3.5 Perceived respect

<u>Hierarchical logistic regression results, **unadjusted models**:</u>

In unadjusted logistic regression models, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.1 (95% CI = 0.9, 1.5) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of 0.2832 and a c-statistic of 0.509. See Table 4.27 for further information.

Table 4.27. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **unadjusted for any covariates,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.145	0.894-1.466	0.2832
	Non-opioid user			

Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015. Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing factors**:

After adjustment for predisposing factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.1 (95% CI = 0.9, 1.5) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of <0.0001 and a c-statistic of 0.598. See Table 4.28 for further information.

Table 4.28. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing factors,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.148	0.894-1.475	0.2791
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing and enabling factors**:

After adjustment for predisposing and enabling factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.2 (95% CI = 1.0, 1.6) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of <0.0001 and a c-statistic of 0.609. See Table 4.29 for further information.

Table 4.29. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing and enabling factors,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.247	0.950-1.637	0.1121
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing, enabling, and need factors**:

After adjustment for predisposing, enabling, and need factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.3 (95% CI = 1.0, 1.8) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of <0.0001 and a c-statistic of 0.617. See Table 4.30 for further information.

Table 4.30. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, and need factors,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.327	0.998-1.764	0.0520
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** $p<0.001$; ** $0.001≤p<0.01$; * 0.01≤p0.05.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing, enabling, need, and personal health practices factors**:

After adjustment for predisposing, enabling, need, and personal health practices factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.3 (95% CI = 1.0, 1.8) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of <0.0001 and a c-statistic of 0.619. See Table 4.31 for further information.

Table 4.31. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, and personal factors,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.343	1.011-1.785	0.0417 *
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** p<0.001; ** 0.001≤p<0.01; * 0.01≤p0.05.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

Hierarchical logistic regression results, **models adjusted for predisposing, enabling, need, personal health practices, and external environmental factors**:

After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.4 (95% CI = 1.0, 1.8) times more likely to be opioid users than non-opioid users. The model had a Wald statistic of <0.0001 and a c-statistic of 0.619. See Table 4.32 for further information.

Table 4.32. Odds ratios for opioid users compared to non-opioid users in older United States adults (age ≥50 years) with pain in the past four weeks, **adjusted for predisposing, enabling, need, personal, and environmental factors,** for perceived respect (Medical Expenditure Panel Survey, 2015)

Perceived respect		Odds ratio	95% Confidence Interval	Significance
	Opioid users	1.371	1.035-1.816	0.0280 *
	Non-opioid user			

Predisposing factors included age, gender, race, and ethnicity. Enabling factors included education, employment, health insurance, marital status, and poverty status. Need factors included chronic conditions, instrumental activities of daily living limitation, activities of daily living limitation, functional limitation, work, housework, or school limitation, pain, perceived physical health status, and perceived mental health status. Personal health practices factors included body mass index, exercise, and smoking status. External environmental factors included census region.
Based on 4,759 (un-weighted) older United States adults (age ≥50 years) with self-reported pain in the past four weeks who were alive during the calendar year 2015.
Asterisks represent statistical significance between the opioid use groups [opioid user (un-weighted n=1,525) and non-opioid user (un-weighted n=3,234)] based on chi-square tests.
*** $p<0.001$; ** $0.001 \le p<0.01$; * $0.01 \le p0.05$.
Percent change represents the difference in perceived respect between opioid users and non-opioid users.

4.4 Summary of findings by hypothesis

There were no testable hypotheses for objective one. For objective two, the null hypothesis was that there is no difference in **<*variable*>** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, where **<*variable*>** indicates the dependent variable of interest. For objective two, the null hypothesis was rejected for almost all variables, except gender (p=0.3186) and race (p=0.1345).

For objectives three to seven, the null hypothesis was that there is no difference in **<*variable*>** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables, where ***<variable>*** indicates the dependent variable of interest. For objective three, the null hypothesis was rejected for almost all variables, except inpatient expenditure (p=0.4826). For objectives four and six, we failed to reject the null hypothesis for all variables (p>0.05). For objectives five and seven, the null hypothesis was rejected for all variables. See Table 4.33 for further information.

Table 4.33. Summary of findings by hypothesis

Hypothesis #	Null hypothesis (H_0): There is no difference in ***<variable>*** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications	p	Conclusion
2.1	Age	0.0122	Reject H_0
2.2	Gender	0.3186	Fail to reject H_0
2.3	Race	0.1345	Fail to reject H_0
2.4	Ethnicity	0.0101	Reject H_0
2.5	Education status	0.0034	Reject H_0
2.6	Employment status	0.0005	Reject H_0
2.7	Health insurance status	0.0007	Reject H_0
2.8	Marital status	0.0056	Reject H_0
2.9	Poverty status	<0.0001	Reject H_0
2.10	Number of chronic conditions	<0.0001	Reject H_0
2.11	Instrumental activities of daily living limitation status	<0.0001	Reject H_0
2.12	Activities of daily living limitation status	<0.0001	Reject H_0
2.13	Functional limitation status	<0.0001	Reject H_0
2.14	Work, housework, or school limitation status	<0.0001	Reject H_0
2.15	Pain intensity status	<0.0001	Reject H_0
2.16	Physical health status	<0.0001	Reject H_0
2.17	Mental health status	<0.0001	Reject H_0
2.18	Body mass index	0.0238	Reject H_0
2.19	Exercise status	0.0090	Reject H_0
2.20	Smoking status	<0.0001	Reject H_0
2.21	Census region	0.0212	Reject H_0
Hypothesis #	Null hypothesis (H_0): There is no difference in ***<variable>*** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables	p	Conclusion
3.1	Inpatient expenditure	0.4826	Fail to reject H_0
3.2	Outpatient expenditure	<0.0001	Reject H_0
3.3	Office-based expenditure	<0.0001	Reject H_0
3.4	Emergency room expenditure	0.0045	Reject H_0
3.5	Prescription medication expenditure	<0.0001	Reject H_0
3.6	Other healthcare expenditure	0.0002	Reject H_0
3.7	Total healthcare expenditure	<0.0001	Reject H_0
4.1	Short form 12 item version 2 (SF-12v2®) physical component summary (PCS) score	0.5535	Fail to reject H_0
4.2	Short form 12 item version 2 (SF-12v2®)	0.1475	Fail to reject H_0

	mental component summary (MCS) score		
4.3	Kessler Index (K6) score	0.1420	Fail to reject H_0
5.1	Perceived healthcare quality	0.0286	Reject H_0
6.1	Unable to receive prescription medication treatment status	0.5544	Fail to reject H_0
6.2	Delayed receiving prescription medication treatment status	0.8735	Fail to reject H_0
7.1	Perceived respect shown by provider status	0.0280	Reject H_0

To interpret Table 4.33 correctly for objective 2, the variable in column two should be read where the word ***<variable>*** exists in the following sentence: There is no difference in ***<variable>*** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications.
To interpret Table 4.33 correctly for objectives 3-7, the variable in column two should be read where the word ***<variable>*** exists in the following sentence: There is no difference in ***<variable>*** of older United States adults (≥50 years) with pain who use opioid medications and those who do not use opioid medications, after adjusting for potential confounding variables.
There was no testable hypothesis for objective 1.
The a priori alpha level for interpreting significance is 0.05.

Chapter 5: DISCUSSION

Introduction to the chapter:

This chapter is organized into seven sections. First, there is a discussion of how this study fits in with what is already known in the area, followed by a description of the most important findings. Then, a discussion of how the findings support the theoretical framework is provided, followed by limitations of the study. Next, study implications and future research implications are discussed, followed by a conclusion.

5.1 Key findings

This study had eight key findings:

Key finding 1: The estimated number of older United States (US) adults (≥50 years) with pain in 2015 was approximately 51 million.

Key finding 2: The estimated prevalence of opioid use among older US adults (≥50 years) with pain in 2015 was approximately 17 million.

Key finding 3: Opioid use was associated with all personal characteristics, except gender and race.

Key finding 4: Adjusted healthcare expenditures were greater among opioid users compared to non-opioid users for all categories of expenditure, except for inpatient expenditures.

Key finding 5: Adjusted health-related quality of life (HRQoL) measures were not associated with opioid use status.

Key finding 6: Adjusted perceived healthcare quality measures were greater among opioid users compared to non-opioid users.

Key finding 7: Adjusted access to prescription medication measures were not associated with opioid use status.

Key finding 8: Adjusted perceived respect shown by healthcare provider measures were greater among opioid users compared to non-opioid users.

5.2 Relating key findings to the literature

Key finding 1: In this study, the estimated number of older US adults (≥50 years) with pain in 2015 was approximately 51 million. Previous reports have indicated that pain is prevalent among US adults, for example, an Institute of Medicine (IoM) report in 2011 estimated that 100 million US adults experience pain (Institute of Medicine (US) committee on advancing pain research, care and education, 2011), while a National Institute of Health (NIH) study reported that 126 million US adults had some pain in 2012 (Nahin, 2015). Given that our study population was older adults (rather than all adults as reported in previous studies), it is difficult to determine how our findings compare with those of previous findings. However, this finding is useful as it provides an up-to-date estimate of the prevalence of pain among older adults in the US.

Key finding 2: This study also provided an updated estimate of the prevalence of opioid use among older US adults (≥50 years) with pain - approximately 17 million in 2015. This equates to approximately one third (32.9%) of older US adults (≥50 years) with pain – a staggering statistic. Multiple studies have reported that the use of opioid medications in the US has increased in recent years (Boudreau et al., 2009; Campbell et al., 2010; Daubresse et al., 2013; Dorn, Meek, & Shah, 2011; Frenk, Porter & Paulozzi, 2015; Han, Kass, Wilsey, & Li, 2014; Kao, Minh, Huang, Mitra, & Smuck, 2014; Kenan, Mack, & Paulozzi, 2012; Olfson, Wang, Iza, Crystal, & Blanco, 2013; Parsells Kelly et al., 2008; Pletcher, Kertesz, Kohn, & Gonzales, 2008; Steinman, Komaiko, Fung, & Ritchie, 2015; Thielke et al., 2010). For example, an analysis of data from the 1999-2012 National Health and Nutrition Examination Survey (NHANES) found a significant increase in opioid use in the past 30 days among US adults age 20 and older, increasing from 5.0% in 1999-2002 to 6.9% in 2003-2006. However, the use of opioids among that sample remained consistent among three subsequent measurement periods; at approximately 6.9% during 2003-2006, 6.7% during 2007-2010, and 6.9% during 2011-2012 (Frenk, Porter & Paulozzi, 2015). That analysis also found that, between 2007 and 2012, use of opioids was higher among adults aged 40-59 (8.1%) and 60 and older (7.9%) compared to younger adults age 20-39 years (4.7%) (Frenk, Porter & Paulozzi, 2015). Meanwhile, an analysis of data from the 1999-2010 National Ambulatory and National Hospital Ambulatory Medical Care Surveys (NHAMCS) found that the use of opioids more than doubled from 4.1% to 9.0% among adults aged 65 and older visiting clinics in the US (Steinman, Komaiko, Fung, & Ritchie, 2015). Recently, a study using Medical Expenditure Panel Survey (MEPS) data reported that the percentage of US adults with a painful health condition rose from 33% in 1997/1998 to 41% in 2013/14, equivalent to 178 million US adults (Nahin, Sayer, Stussman, & Feinberg, 2019). Another study using MEPS data reported that 49% of their sample with chronic back pain used opioids during 2011-2015, while 23% used opioids with non-steroidal anti-inflammatory drugs (NSAIDs) (Desai, Hong, & Huo, 2019).

This has lead to a subsequent increase in opioid-related problems such as opioid addiction and dependence, and deaths from overdose of opioids (Bernacki, Yuspeh, Lavin, & Tao, 2012; Franklin et al., 2005; Han, Kass, Wilsey, & Li, 2014; Kenan, Mack, & Paulozzi, 2012). Opioid-related deaths (where an opioid contributed substantially to the cause of death) increased from 9489 to 42245, a 345% increase, between 2001 and 2016 in the US (Gomes, Tadrous, Mamdani, Paterson, & Juurlink, 2018). The number of opioid deaths in the US increased in most age groups between 2014 and 2015 and was most prevalent among younger adults and middle aged adults, but remained constant for those age 65 and older (Rudd, Seth, David, & Scholl, 2016). This phenomenon has been termed the ‘opioid crisis’ or ‘opioid epidemic’, and in response the US Department of Health and Human Services (HHS) has declared a public health emergency and developed a strategy to overcome it (Price, 2017; US Department of Health and Human Services, 2017; US Department of Health and Human Services, 2018).

Most recently, Lyden and Binswanger (2017) describe how the opioid epidemic (and subsequent mortality statistics) was driven by the availability of prescription opioids; however, in recent years the problem has shifted to illegal opioids obtained without prescription. They argue that improved outcomes can be obtained using pharmacotherapy to treat opioid use disorder, and that appropriate terminology should be used to reduce the stigma associated with opioid use (Lyden & Binswanger, 2017).

There has been a debate among clinicians on the appropriate use of opioids in older adults (Reid et al., 2011). From one perspective, opioids may be preferred to other medications such as NSAIDs to avoid gastro-intestinal side effects and renal toxicity (Ferrell et al., 2009). Conversely, there are several side effects and complications of opioid therapy that disproportionately affect older adults, such as cardiovascular events, constipation, and bone fractures, thereby making opioid less suitable for use in older adults (Buckeridge et al., 2010; Solomon et al., 2010a; Solomon et al., 2010b). Access to these medications is also a challenge, which will be discussed later.

In 2016, the Centers for Disease Control and Prevention (CDC) published recommendations for prescribing opioids for chronic pain not related to cancer or palliative care. These recommendations included considering non-opioid alternatives wherever possible, initiating opioids only after reviewing the risks and benefits of opioid treatment in consultation with the patient, and using the lowest effective dose of opioids, among others (Centers for Disease Control and Prevention, 2016).

In addition, research also suggests that pain may be managed using a variety of strategies, not just opioids or prescription medications. A recent systematic review of 18 studies identified 22 pharmacological strategies, of which 16 were prescription products and six were over-the counter (OTC), as well as 22 non-pharmacological strategies, were used by community-dwelling adults with pain (Axon, Patel, Martin, & Slack, 2018). Prescription pain medications included: NSAIDs, opioids, anticonvulsants, antidepressants, acetaminophen, topical, muscle relaxants, acetylsalicylic acid, disease-modifying anti-rheumatic drugs (DMARDs) and steroids, injections, anxiolytics, beta-blockers and calcium-channel blockers, triptans, simple, combined, and adjuvant analgesics, and others. Non-prescription medications included NSAIDs, acetaminophen, and acetylsalicylic acid (Axon, Patel, Martin, & Slack, 2018). Non-pharmacological strategies included consulted medical practitioner, chiropractor, surgery, activity modification and restriction, acupuncture, alter body position, assistive devices, exercise, hot or cold modalities, massage, physical therapy, transcutaneous electronic nerve stimulation (TENS), prayer and meditation, relaxation, therapy, complementary and alternative medicine (CAM), dietary and herbal supplements, dietary modifications, among others (Axon, Patel, Martin, & Slack, 2018).

Furthermore, in their report about the development of the exposure multimodal (Xm^2) tool, Axon, Bhattacharjee, Warholak, & Slack (2018) identified that pharmacists with chronic pain in a Southwestern state reported using a mean of 12.6±4.6 pain management strategies. Altogether, participants in their survey identified 99 different pain management strategies, which included 13 classes of prescription medications, OTC medications, and many non-pharmacological strategies (Axon, Bhattacharjee, Warholak, & Slack, 2018).

Key finding 3: Univariable analyses indicated that opioid use was associated with almost all subject characteristics ($p<0.05$), with two notable exceptions: gender and race ($p>0.05$). Although gender and race were not statistically associated with opioid use in univariable models, they were included in multivariable models as they were considered to have a potentially clinically meaningful association with opioid use.

It was interesting that gender was not associated with opioid use, given that a previous study identified that opioid use was higher among women than men (7.2% versus 6.3% respectively, $p<0.05$) (Frenk, Porter & Paulozzi, 2015) and another found that opioid use was associated with female gender ($p<0.001$) (Ashworth, Green, Dunn, & Jordan, 2013). Likewise, others have reported that pain prevalence was higher among women than men (Eriksen, Sjogren, Bruera, Ekholm, and Rasmussen, 2006; Patel, Guralnik, Dansie, & Turk, 2013). Recently however, research using a sample of pharmacists has indicated that there are no differences in gender between opioid and non-opioid users (Mollon, Almutairi, & Slack, 2017), which support the findings of our study. Perhaps in an older adult population, men and women are doing similar activities and thus they become a more homogenous group as they age, reducing the effect of gender differences. The effect of gender on opioid use status is therefore unclear, with mixed results from multiple studies. This may be accounted for by the different samples studied, and may lend itself well as the topic of a future meta-analysis.

The lack of association between race and opioid use was also interesting, yet parallels the findings of previous studies (Mollon, Almutairi, & Slack, 2017). Others have reported that race was not associated with chronic pain among older adults (Patel, Guralnik, Dansie, & Turk, 2013). However, ethnicity was associated with opioid use, with a greater proportion of non-Hispanic individuals in the opioid group compared to the non-opioid group ($p=0.0034$). This is an interesting finding as other studies combine race and ethnicity into one variable for analysis (Patel, Guralnik, Dansie, & Turk, 2013). Our study with its more granular approach to analyzing race and ethnicity separately was able to identify differences between the two variables, which may explain some of the differences in association between race/ethnicity and opioid use or pain prevalence.

Hypothesizing that racial-ethnic disparities may exist among opioid prescriptions for non-medical use but not pain-related conditions, Singhal, Tien, & Hsia (2016) used NHAMCS data from 2007-2011 to investigate the odds of receiving a prescription for an opioid at discharge from the emergency room. They found that non-Hispanic Blacks were less likely compared to non-Hispanic Whites to receive an opioid prescription for back pain or abdominal pain, but not other conditions, which indicated racial-ethnic disparities (Singhal, Tien, & Hsia, 2016). It is therefore apparent that the association between race/ethnicity and opioid use is also unclear, which may warrant further investigation in other settings to better understand the true relationship, and to target appropriate interventions to reduce this disparity.

Age was associated with opioid use, with a greater proportion of 50-64 year olds among the opioid group compared to the non-opioid group (p=0.0122). This finding concurs with those of previous studies that have found differences between age categories for opioid use (Eriksen, Sjogren, Bruera, Ekholm, and Rasmussen, 2006), yet contrasts with those of other studies who found no difference in age between opioid users and non-opioid users (Ashworth, Green, Dunn, & Jordan, 2013; Mollon, Almutairi, & Slack, 2017). Patel, Guralnik, Dansie, & Turk (2013) also noted that there was no difference in pain prevalence across age groups in their study. Similar to the previous demographic characteristics, the association between age and opioid use therefore remains unclear.

Enabling factors were associated with opioid use, with a greater proportion of opioid users typically having lower educational attainment (p=0.0034), unemployment (p=0.0005), public health insurance (p=0.0007), not being married (p=0.0056), and greater poverty (p<0.0001). These findings are similar to those of other studies, for example, Eriksen, Sjogren, Bruera, Ekholm, & Rasmussen (2006) identified associations between opioid use and education status, and marital status (Eriksen, Sjogren, Bruera, Ekholm, & Rasmussen, 2006). Likewise, Ashworth, Green, Dunn, & Jordan (2013) found associations between opioid use and employment status, while Patel, Guralnik, Dansie, & Turk (2013) identified associations between decreasing pain prevalence and higher levels of education (p<0.001). Conversely, previous studies using samples of pharmacists with chronic pain have found that employment status was not associated with opioid use (p=0.194) (Mollon, Almutairi, & Slack, 2017). From a different perspective, in a study comparing high and low exposure scores to all pain management strategies among pharmacists with chronic pain, there was no association between exposure and employment status (p=0.30) or marital status (p=0.25) (Axon, Bhattacharjee, Warholak, & Slack, 2018).

Need factors were all strongly associated with opioid use (p<0.0001), with a greater proportion of opioid users having at least five chronic conditions, various limitations (instrumental activities of daily living, activities of daily living, functional, and work, housework, or school limitations), quite a bit or extreme pain, and poorer perceived physical and mental health compared to non-opioid users.

It was also not surprising that opioid users in our study were more likely to have a greater number of chronic conditions compared to non-opioid users. A 2008 study using 100% Medicare claims data of adults aged 65 years and older found that 67% of subjects had two or more chronic conditions increasing to 85% of adults aged 85 years and older (Salive, 2013). Data from the 2012 National Health Interview Survey (NHIS) also indicated that US adults aged 65 or older had a higher prevalence of managing at least two chronic diseases (60.8%), compared to adults aged 45-64 (32.3%) and adults aged 18-44 (7.1%) (Ward, Schiller, & Goodman, 2014). Data from the 2013 and 2014 NHIS in the US indicated that common chronic health conditions among adults aged 65 and older include hypertension (55.9%), arthritis (49.0%), heart disease (29.4%), cancer (23.4%), diabetes mellitus (20.8%), asthma (10.6%), chronic bronchitis or emphysema (8.1%), and stroke (7.9%) (Federal Interagency Forum on aging-Related Statistics, 2016). The prevalence of pain has also been found to increase with greater comorbidity (Patel, Guralnik, Dansie, & Turk, 2013).

Pain has been identified as a major cause of disability (Institute of Medicine (US) committee on advancing pain research, care and education, 2011), thus it was not surprising that individuals with pain reported limitations in their life. The study on exposure to pain management strategies by Axon, Bhattacharjee, Warholak, & Slack (2018) found that a greater proportion of pharmacists with chronic pain in the high exposure group reported that pain interfered with their daily activities more than those in the lower exposure group (p=0.03). Another study found an association between opioid use and usual pain intensity (Ashworth, Green, Dunn, & Jordan, 2013).

Interestingly, almost half (49.5%) of opioid users reported having quite a bit or extreme pain, which is considerably higher than the proportion in the non-opioid user group (21.0%) and may explain their higher use of opioids. Ashworth, Green, Dunn, & Jordan (2013) found an association between opioid use and usual pain intensity.

The overall proportion of individuals who perceived their physical and mental health positively (excellent, very good, or good) was high (71.9% and 85.7% respectively), although the proportions were lower for opioid users compared to non-opioid users. Eriksen, Sjogren, Bruera, Ekholm, & Rasmussen (2006) identified associations between opioid use and perceived health status, and pain in the past four weeks. However, in the previous exposure to pain management strategies study, there were no differences in the proportion of pharmacists with chronic pain who described their health as good/excellent or poor/fair between those in the high exposure group and those in the low exposure group (p=0.25) (Axon, Bhattacharjee, Warholak, & Slack, 2018). Poorer physical health may explain why some individuals were taking opioids, although this does not appear to explain all situations. The association between poorer perceived mental health status and opioid use may also relate to the association between opioid use and mental health conditions, as reported by Davis, Lin, Liu, & Sites (2017) who found that adults with mental health conditions receive 51% of the prescriptions written for opioids in the US each year (Davis, Lin, Liu, & Sites, 2017).

Personal health practices were associated with opioid use - a greater proportion of opioid users were overweight or obese (0.0238), did not do regular exercise ($p=0.0090$) and were smokers ($p<0.0001$) compared to non-opioid users. This concurs with previous studies that found pain prevalence was higher obese older adults (Patel, Guralnik, Dansie, & Turk, 2013), although others found that smoking status was not associated with pain prevalence higher in older adults (Patel, Guralnik, Dansie, & Turk, 2013). Although obesity and smoking are two major risk factors for health, put in context, the US has a lower percent of the population who smoke daily (US 11.4%; Organization for Economic Cooperation and Development [OECD] average 18.4%), but a greater proportion of people with a body mass index (BMI) greater than 30 (US 38.2%; OECD average 19.4%) (Organization for Economic Cooperation and Development, 2017).

Census region was also associated with opioid use, and highlighted differences in the proportion of opioid users in different regions of the country. The region with the highest proportion of opioid users was the South. Prescription data from 2008 indicated that there was considerable geographic variation in the prevalence of prescribed opioids, but also noted that areas with the highest rates of opioid prescribing were located in Appalachia and Southern and Western states (McDonald, Carlson, & Izrael, 2012). At the state level, one study from Kentucky reported that there was a significant decrease in the rates of prescribed opioids, but also noted that opioid prescription dispensing was significantly positively associated with emergency department visits and negatively associated with buprenorphine/naloxone prescribing rates (Luu et al., 2019).

Key finding 4: In fully adjusted models, opioid users had higher healthcare expenditures compared to non-opioid users for all categories of expenditure except inpatient expenditures, where there was no statistically significant difference between the two groups. Total healthcare expenditures were 105% higher in the opioid group compared to the non-opioid group, which highlights the considerable financial burden of opioids.

It was interesting that there was no statistically significant difference in inpatient healthcare expenditures between opioid users and non-opioid users. Reasons for this are unknown, but given that inpatient expenditures can be some of the most costly it is encouraging that they were not associated with opioid use.

Previous work has already identified the financial burden of pain for both patients and society, with total costs in 2010 dollars ranging from \$560 to \$635 billion per year (Gaskin & Richard, 2012; Institute of Medicine (US) committee on advancing pain research, care and education, 2011). This is greater than the annual costs of major diseases such as heart disease, cancer, and diabetes (Gaskin & Richard, 2012). Further work using 2008-2011 MEPS data found that ‘a little bit’ of chronic pain was associated with a \$2,498 and \$1,008 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively. Moderate chronic pain was associated with a \$3,707 and

$2,218 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively. Severe chronic pain was associated with a $5,804 and $4,315 increase in total adjusted expenditures compared to no pain and non-chronic pain respectively (Stockbridge, Suzuki, & Pagan, 2015). This study is able to add to this information by describing the economic burden of opioid users with pain, which overall is 105% greater than non-opioid users with pain. Given that annual health expenditure in the US was $9536 per capita in 2015, our study suggests that pain may constitute a considerable proportion of healthcare expenditure. Our study also indicates that among individuals with pain, opioid users have significantly higher expenditures compared to non-opioid users. However, our study design is only able to demonstrate an association, not causality, so further studies are needed to assess if switching from opioids to non-opioids causes a reduction in healthcare expenditure or not. Although controlled for in the model, it may be that those using opioids are generally more unwell, and therefore have higher healthcare expenditures, rather than attributing healthcare expenditures to opioid use per se.

Another study using MEPS data reported that among individuals with chronic back pain in 2011-2015, individuals using both opioids and NSAIDs had higher mean outpatient expenditures ($3,087 vs. $3,020 vs. $2,177), office-based expenditures ($3,083 vs. $2,652 vs. $1,984) and emergency room expenditures ($2,168 vs. $1,883 vs. $1,607) compared to those who only used opioids or NSAIDs, after adjusting for covariates (Desai, Hong, & Huo, 2019). The same study found that among individuals with chronic back pain in 2011-2015, opioid users reported significantly greater utilization of inpatient visits (0.29 vs. 0.09, p<0.0001), outpatient visits (1.39 vs. 0.80, p<0.0001), office-based visits (14.46 vs. 10.18, p<0.0001) and emergency room visits (0.60 vs. 0.38, p<0.0001) compared to NSAIDs users, but fewer outpatient (1.39 vs. 1.43, p<0.0001), office-based (14.46 vs. 14.98, p<0.0001) and emergency room visits (0.60 vs. 0.86, p<0.0001) compared to individuals using both opioids and NSAIDs (Desai, Hong, & Huo, 2019).

Key finding 5: After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, there was no significant difference between opioid users and non-opioid users for short form 12 item version 2 (SF-12v2) physical component summary (PCS) scores, SF-12v2 mental component summary (MCS) scores, or Kessler Index (K6) scores (p>0.05). The fully adjusted linear regression model for K6 scores did not meet the assumptions of the model well, thus the results for this outcome may be unreliable. However, the findings from both SF-12v2 scores are insightful – one might hypothesize that opioid users were associated with more physical and/or mental issues, but this proved not to be the case in this study. Previous studies have suggested that chronic pain is associated with poorer quality of life (Gureje, Von Korff, Simon, & Gater, 1998; Smith et al., 2001; Institute of Medicine (US) committee on advancing pain research, care and education, 2011), yet our study shows this does not translate into poorer patient-reported HRQoL among opioid users with pain.

Recently, a study using MEPS data reported that among individuals with chronic back pain in 2011-2015, opioid users had lower SF-12v2 MCS scores (44.42 vs. 46.67, p<0.001) and SF-12v2 PCS scores (35.34 vs. 40.11, p<0.001) compared to NSAID users (Desai, Hong, & Huo, 2019).

Key finding 6: After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, opioid users had 15% greater perceived healthcare quality scores (p=0.0286). The fully adjusted linear regression model for healthcare quality scores did not meet the assumptions of the model well, thus the results for this outcome may be unreliable. Nevertheless, healthcare quality is important to discuss as the US healthcare system is increasingly using quality measures to improve healthcare, although some argue that more work is required to realize the benefits from these measures (Burstin, 2016). In 2011, the Agency for Healthcare Research and Quality (AHRQ) proposed the National Quality Strategy that outlined six priorities to improve healthcare, including: making care safer, ensuring person and family-centered care, promoting effective communication and coordination of care, promoting the most effective prevention and treatment of the leading causes of mortality, starting with cardiovascular disease, working with communities to promote wide use of best practices to enable healthy living, and making quality care more affordable (US Department of Health and Human Services, 2011). Other organizations, such as the Pharmacy Quality Alliance (PQA), have developed quality measures to improve medication use that are used by Centers for Medicare and Medicaid Services (CMS) in pay-for-performance models (Pharmacy Quality Alliance, 2018). In particular, PQA has developed the Opioid core measure set that seeks to help address the opioid epidemic (Pharmacy Quality

Alliance, 2018). Therefore, there is considerable interest in assessing healthcare quality, which could be the focus of future work.

<u>Key finding 7:</u> After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, there was no statistically significant difference in the likelihood of opioid users among older US adults (≥50 years) with pain in the past four weeks who were unable to receive prescription medications or who were delayed receiving prescription medications compared to non-opioid users ($p>0.05$). This finding indicates that opioid use status does not affect access to medications, which is encouraging from an equality perspective. However, this study used data from 2015 and the opioid epidemic was not declared until 2017 (Price, 2017; US Department of Health and Human Services, 2017; US Department of Health and Human Services, 2018), so access to medications, in particular opioid medications, may since have become more difficult. Furthermore, this study was not able to quantify any problems affecting access to prescription medications, which may be interesting to know in the era of difficulty accessing medications due to drug shortages (2018-2019 Academy of Managed Care Pharmacy Professional Practice Committee, 2019; Jacob, 2019), and the need for prior authorizations from health insurance providers for certain medications (American Society of Health-System Pharmacists, 2019; Bowles, 2019).

From a broader perspective than just prescription medications, access to healthcare generally is a key measure of health system performance. The US is one of the few advanced nations not to provide universal healthcare to all of its citizens, with only

91% of the population having health insurance compared to an average of 98% for all OECD countries in 2015 (Organization for Economic Cooperation and Development, 2017). Healthcare resources (including expenditure, number of healthcare workers, and the number of hospital beds available) are also important measures of how well a healthcare system is working. The US ranked close to average for the number of physicians (US 2.6 per 1000 population; OECD average 3.4 per 1000 population) and nurses (US 11.3 per 1000 population; OECD average 9.0 per 1000 population), but below average for number of hospital beds (US 2.8 per 1000 population; OECD average 4.7 per 1000 population) (Organization for Economic Cooperation and Development, 2017). This information helps set access to medications in the broader context of access to healthcare in the US, and suggests there are additional areas for improvement alongside further investigations of access to medications.

Key finding 8: After adjustment for predisposing, enabling, need, personal health practices, and external environmental factors, older US adults (≥50 years) with pain in the past four weeks who perceived their provider showed them respect were 1.4 (95% CI = 1.0, 1.8) times more likely to be opioid users than non-opioid users. This is an interesting finding; one might presume that the stigma associated with opioid use would imply opioid users do not feel respected by their healthcare provider, yet this does not appear to be the case in this study. Reasons for this are unclear, but given that opioid prescriptions can only be written for a short period of time, opioid users may have more frequent visits to their healthcare provider and therefore perhaps have the opportunity to develop a good relationship that increases respect. This theory is partially supported by a recent study that found 70% of students from a variety of healthcare disciplines changed their perception of substance abuse disorder patients after participating on a patient panel experience, concluding that the patient panel experience was influential on healthcare students' views toward patients with opioid use disorder (Dumenco, 2019). In relation to our study findings however, a recent study found that overall satisfaction with healthcare provider was 96% among a sample of pain patients at a private pain management clinic in the US (Dragovich, 2015). Interestingly, Dragovich et al. (2015) also noted that there was no correlation between patient satisfaction with their healthcare provider and functional outcomes, suggesting that satisfaction is related more to a patient's perception of their healthcare provider's engagement with them rather than treatment outcomes.

5.3 How do the findings support or fail to support the theoretical framework?

The purpose of the theoretical framework (Andersen behavioral model, ABM) in this study was to help determine and categorize the variables that may be associated with each of the dependent variables, and to help guide the analytical approach. Using a hierarchical (linear or logistic) regression approach, groups of variables were added to statistical models according to the ABM. As additional variables were adjusted for, the models were able to control for more potential confounders, and typically became more robust. Therefore, the study findings support use of the ABM as an appropriate theoretical framework for this study.

5.4 Limitations

There were several limitations associated with this study. MEPS uses self-reported data that may be subject to recall bias, although MEPS interviews are conducted at regular intervals (every four to five months during the study period) in an attempt to minimize recall bias (Machlin, Cohen, Elixhauser, Beauregard, & Steiner, 2009). No indication is provided at the medication level, thus it was not possible to confirm that opioid medications were being used for pain (rather than another condition). Healthcare expenditure data are for all healthcare expenditure, rather than pain-related expenditure. However, this approach allowed for a holistic overview of patient healthcare expenditure. Due to the nature of using secondary data in a retrospective database study, it is not possible to ascertain a cause and effect relationship, although statistical associations can be identified. Only one year of data (2015) was used, although this provided a satisfactory sample size and was the most up to date data available at the time of the study. This study had a large sample size, thus even small differences between groups could be statistically significant, but not clinically meaningful. Finally, the models for K6 and perceived healthcare quality did not meet the assumptions of linear regression well and some had poor model fit, which limits the reliability of the results for those models.

Despite these limitations, strengths of the study include use of a nationally representative sample of community-dwelling older adults with pain, allowing for generalizations to be made to the population of older US adults (≥50 years) with pain, and the inclusion of many individual-level variables to assess healthcare expenditure, HRQoL, healthcare quality, access to medications, and respect shown by provider among older US adults (≥50 years) with pain.

5.5 Study implications

This study is useful as it provides an up-to-date estimate of the prevalence of pain and opioid use among older adults in the US, which raises awareness of the needs of this population as discussions about the opioid epidemic continue. This study also identifies the factors that are associated with opioid use and those that are not, which may help target interventions to manage pain and improve appropriate opioid use in this population. For example, based on the findings of this study, interventions to reduce healthcare expenditure may be best targeted at all categories except inpatient expenditures, as there was no difference between opioid users and non-opioid users. This study then relates these findings to those of previous studies, and delineates where discrepancies exist among findings that warrant further research as well as what supports or adds to existing knowledge. The findings from this study provide new insight into differences between opioid users and non-opioid users among older US adults with pain, which may help inform evidence-based policies to improve pain management and address the opioid epidemic in this ever-increasing population.

5.6 Future research implications

The findings from this study pose several additional new questions that could be investigated in future. First, it would be interesting to investigate the reasons why there were or were not differences between opioid users and non-opioid users for different dependent variables. In addition, meta-analyses could be conducted to assess pooled data for variables that show inconsistent results in the literature.

This study was a cross-sectional study that assessed healthcare expenditure, HRQoL, healthcare quality, access to medications, and respect shown by provider at one point in time. Future research could involve a longitudinal analysis to observe trends over time, and attempt to predict future trends so that appropriate interventions can be made as necessary.

This study used a sample of older adults (≥50 years) who reported having pain in the past four weeks. Future research could investigate the same questions in a sample with chronic or recurrent pain, or a sample of non-community-dwelling individuals, or a sample outside the US to compare international differences. Alternatively, given the abundance of data available in MEPS dataset, future research could investigate different questions in the same sample. For example, more granular details about healthcare expenditures could be investigated to identify precisely where differences occur between opioid and non-opioid users, or the full set of items related to healthcare quality or healthcare access could be investigated, rather than a few select items, as was the case in this study.

5.7 Conclusions

This study estimated that the number of older US adults (≥50 years) with pain in 2015 was approximately 51 million, and that the estimated prevalence of opioid use among older US adults (≥50 years) with pain in 2015 was approximately 17 million. Opioid use was associated with all personal characteristics, except gender and race.

Adjusted healthcare expenditures were greater among opioid users compared to non-opioid users for all categories of expenditure, except for inpatient expenditures. Adjusted perceived healthcare quality measures and perceived respect shown by healthcare provider measures were greater among opioid users compared to non-opioid users. Adjusted health-related quality of life measures and access to prescription medication measures were not associated with opioid use status. Future research is warranted to investigate reasons why some of these findings exist, and to explore these variables in greater depth, over longer periods of time, and in additional populations.

APPENDICES

IRB Approval letter

THE UNIVERSITY OF ARIZONA
Research, Discovery & Innovation

Human Subjects Protection Program

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P.O.Box 245137
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Date:	April 02, 2019
Principal Investigator:	David Rhys Axon
Protocol Number:	1903444951
Protocol Title:	An investigation of differences in healthcare utilization and expenditure between opioid users and non-opioid users among a nationally representative sample of community-based older adults (>=50) with pain in the United States
Determination:	Human Subjects Review not Required

Documents Reviewed Concurrently:

Regulatory Determinations/Comments:

- Not Research as defined by 45 CFR 46.102(l): As presented, the activities described above do not meet the definition of research cited in the regulations issued by U.S. Department of Health and Human Services which state that "Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research."

The project listed above does not require oversight by the University of Arizona.

If the nature of the project changes, submit a new determination form to the Human Subjects Protection Program (HSPP) for reassessment. Changes include addition of research with children, specimen collection, participant observation, prospective collection of data when the study was previously retrospective in nature, and broadening the scope or nature of the study activity. Please contact the HSPP to consult on whether the proposed changes need further review.

The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).

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