AN EVALUATION OF FUNCTIONAL OUTCOMES FOR PATIENTS WITH OPIOID USE DISORDER IN A MEDICATION TREATMENT PROGRAM: WITH A FOCUS ON PREGNANT WOMEN

AN EVALUATION OF FUNCTIONAL OUTCOMES FOR PATIENTS WITH OPIOID USE DISORDER IN A MEDICATION TREATMENT PROGRAM: WITH A FOCUS ON PREGNANT WOMEN

A Dissertation Presented

by

KRISTY PEREIRA

Submitted to the Graduate School of the

University of Massachusetts Amherst in partial fulfillment

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Elaine Marieb College of Nursing

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ABSTRACT

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SEPTEMBER 2023

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Opioid misuse leading to opioid use disorder (OUD is a growing concern in the U.S. Medication Treatment (MT with buprenorphine is considered the gold standard for OUD treatment. Traditionally, *success* in treatment is measured by abstinence from opioids and other drug use. Urine drug screens are used to determine abstinence from opioids and other drug use. There is little evidence on alternative measures to determine treatment success in OUD treatment. The purpose of this descriptive study was to provide evidence that functional outcomes are an important piece in defining treatment success for these individuals. The first study aim was to determine if functional risk score is a better predictor of treatment success when compared to opioid use. The second aim was the same as the first, except analyses were limited to only pregnant patients.

This correlational, retrospective study analyzed EHR data obtained from a multisite, multistate outpatient treatment facility that provided buprenorphine treatment for individuals ≥ 18 years of age from 2016–2018. Included were 416 patients with OUD in MT, of whom 140 were pregnant (Aim 2. Predictors were functional risk score and

opioid use. Outcomes were treatment utilization, medication utilization, and treatment retention.

Findings reveal that functional outcomes were a significant predictor of treatment utilization in almost all models for the entire sample. Opioid use was a more significant predictor of medication utilization for both aims. Functional risk score and opioid use were comparable predictors of treatment retention among the non-pregnant sample. Neither functional risk score nor opioid use were predictors of treatment retention in the pregnant sample.

Treatment success for individuals with OUD in MT has been incorrectly defined. Often, it is speculated that a person who has a positive urine screen and is not abstinent from opioid use 100% of the time is not complying with treatment. The current study findings indicate that functional outcomes were better predictors of treatment utilization when compared to opioid use in both the general and pregnant populations. Incorporating functional outcomes in addition to urine drug screens may provide further insight in gauging treatment success for individuals with OUD in MT.

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LIST OF ABBREVIATIONS

ACOG	American College of Gynecology
AMI	Co-occurring mental illness
AS	Anxiety sensitivity
ASAM	American Society of Addiction Medicine
CBT	Cognitive behavior therapy
CDC	Centers for Disease Control and Prevention
CJS	Criminal justice system
CSV	Comma-separated values
EHR	Electronic health record
HCUP	Healthcare Cost and Utilization Project
MDE	Major depressive episode
MI	Motivational interviewing
MOUD	Medications for opioid use disorder
MRN	Medical record number
MT	Medication Treatment
NAS	Neonatal abstinence syndrome
NCHS	National Center for Health Statistics
NIDA	National Institute on Drug Abuse
NIH	National Institute of Health
NIS	National Inpatient Sample
NSC	National Safety Council
OAT	Opioid agonist treatment
OPR	Oral pain reliever
OUD	Opioid use disorder
SAMHSA	Substance Abuse and Mental Health Services Administration
SMI	Serious mental illness
SUD	Substance use disorders
UDS	Urine drug screen

CHAPTER 1

INTRODUCTION

Background of the Problem

Substance use and mental health issues affect millions of adults in the United States (U.S.) and contribute heavily to the burden of disease, according to the Substance Abuse and Mental Health Services Administration (SAMHSA) and the 2020 National Survey on Drug Use and Health (NSDUH). Their report for national indicators of substance use and mental health among the civilian, noninstitutionalized population aged 12 years or older in the United States, revealed that 40.3 million people in the U.S. aged 12 or older had a past-year substance use. Even more concerning is that among the 40 million, an estimated 9.5 million misused opioids in the past year (SAMHSA.gov/*NSDUH*).

These alarming numbers have contributed to the growing aggregate of overdoses and drug-related deaths. According to the National Center for Health Statistics (NCHS) report on overdose death rates, nearly 841,000 people have died since 1999 from a drug overdose (NIDA.NIH.gov/*Drug overdose death rates*). In 2020, the NCHS reported that more than 90,000 Americans died from drug overdoses, a nearly 30% increase over 2019. Even more alarming is that an estimated 68,000 (75%) of all drug overdose deaths involved an opioid (NIDA.NIH.gov/*Drug overdose death rates*).

The misuse of and addiction to opioids, including heroin and prescription pain relievers, is a serious national crisis that affects public health as well as social and economic welfare (NIDA.NIH.gov/*Drug overdose death rates*). Opioid addiction affects individuals from all different geographic, socioeconomic, and educational backgrounds

(Azadfard et al., 2021). While we have seen a dramatic rise in the increase in opioid use affecting all populations, one group that has been affected by the opioid crisis and continues to remain vulnerable are women of childbearing age (Carter et al., 2019).

Opioid use and misuse in pregnancy has escalated dramatically in recent years, paralleling the epidemic observed in the general population. According to national data obtained from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) database, the number of women with opioid-related diagnoses documented at delivery increased by 131% from 2010 to 2017 (HCUP-US.AHRQ.gov/*NIS*). The rising prevalence of opioid use in pregnancy has led to an increase in associated adverse neonatal outcomes such as neonatal abstinence syndrome (NAS), which, per the American College of Obstetricians and Gynecologists (ACOG), is a drug withdrawal syndrome that opioid-exposed infants experience shortly after birth (ACOG.org/*Opioid use and opioid use disorder in pregnancy*). The number of babies born with NAS in 2017 increased by 82%; seven newborns were diagnosed with NAS for every 1,000 newborn hospital stays, which is approximately one baby diagnosed with NAS every 19 minutes (HCUP-US.AHRQ.gov/*NIS*).

In response to the growing epidemic of opioid misuse, federal agencies in the United States were directed to improve access to medication treatment (MT; SAMHSA.gov/*Medications for SUDS*). MT is the use of approved medications combined with counseling, other behavioral therapies, and patient monitoring, to treat opioid use disorder (OUD). MT programs are designed to provide a "whole patient" approach to the treatment of substance use disorders (SUDs). Treatment and support services should reflect each person's individual needs and preferences. Many people with OUD benefit

from treatment with medication for varying lengths of time, including lifelong treatment. Ongoing outpatient medication treatment for OUD is linked to reduction in morbidity and mortality in addition to better retention and outcomes than treatment without medication (SAMHSA.gov/*Medications for substance use disorders*). Medication and treatment for OUD give people the time and ability to make necessary life changes associated with long-term remission and recovery (e.g., changing the people, places, and things connected with their drug use). Remaining in treatment also allows people with OUD to better manage other aspects of their life, such as parenting, attending school, or working.

According to 2019 estimates, less than 35% of adults with OUD had received treatment for opioid use in the past year (Jones & McCance-Katz, 2019). Despite the strong evidence for the effectiveness of medications in increasing treatment retention and improving well-being for individuals with OUD, numerous barriers including stigma and inadequate professional education and training for providers related to the evidence base for using medication prevent broader access to medication-based treatment, according to *Medications for Opioid Use Disorder Save Lives,* published in 2019 by the National Academies Press (https://www.ncbi.nlm.nih.gov/books/NBK538936/).

ASAM in their recent update recommends UDS during treatment to monitor patients for adherence to prescribed medications and use of alcohol, illicit, and controlled substances (Crotty et al., 2020). However, the challenge with this recommendation is that the measurement of UDS based on the presence or absence of opioids, does not provide adequate information of an individual's progress, success, or ability to be retained in treatment. Research has shown that reliance on UDS as the sole predictor of an individual's treatment success leads to poor patient outcomes and often discharge from

treatment (Hadland & Levy, 2016). Thus, it is vital to understand how measuring functional outcomes (such as supportive contacts, stable employment, finances, and housing), in addition to UDS, can better predict an individual's treatment success for OUD.

Opioid Use Disorder

Over the last decade, opioid use around the world has risen considerably (Patel et al., 2021). According to a report from the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS), in 2020 more than 92,00 Americans died from drug overdoses, a nearly 30% increase over 2019 (Ahmad et al., 2021). Our nation faces a crisis of overdose deaths from opioids, including heroin, illicit fentanyl, and prescription pain relievers (NIDA.NIH.gov/*Drug overdose death rates*). The number of deaths reported represent a mere fraction of the total number of Americans harmed by opioid abuse, misuse, and addiction (SAMHSA.gov/*NSDUH*). An increase in the prescribing of opioids over the past 15–20 years has contributed to rising rates of addiction and mortality due to nonmedical use of prescription opioids (SAMHSA.gov/*NSDUH*). Since the 1990s, when the number of opioids prescribed to patients began to grow, the number of overdoses and deaths from prescription opioids has also increased (CDC.gov/*Drug overdose*).

As opioid use rises, so too does the number of people who suffer from OUD (Patel et al., 2021). OUD is defined in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-V*; American Psychiatric Association, 2013) as a problematic pattern of opioid use leading to clinically significant impairment or distress is a medical condition defined by not being able to abstain from using opioids, and behaviors centered

around opioid use that interfere with daily life. OUDs affect over 16 million people worldwide, over 2.1 million in the U.S., and over 120,000 deaths worldwide annually are attributed to opioids (Chang et al., 2018).

Opioid-related deaths now account for the largest number of accidental deaths in the United States (Seth et al., 2018). In response to the opioid crisis, efforts are aimed at focusing on improved access to treatment and recovery services (NIDA.NIH.gov/*Drug overdose death rates*). Drug addiction is a complex disorder that can involve virtually every aspect of an individual's functioning, in the family, at work, at school, and in the community, per the National Institute on Drug Abuse (NIDA.NIH.gov/*Principles of drug addiction treatment*). Because of addiction's complexity and pervasive consequences, drug addiction treatment typically must involve many components; some of these components focus directly on the individual's drug use; others, like employment training, focus on restoring the person living with addiction to productive membership in the family and society (NIDA.NIH.gov/*Principles of drug addiction treatment*).

Opioid Use Disorder in Pregnancy

Opioid use in pregnancy has escalated dramatically in recent years, paralleling the epidemic observed in the general population (ACOG.org*/Opioid use and opioid use disorder in pregnancy*). According to CDC analyzed data from a 2019 survey in which women self-reported behaviors and experiences before, during, and shortly after pregnancy, about 7% of respondents reported prescription opioid use during pregnancy. Of those, one in five reported misuse of prescription opioids, defined by this survey as getting them from a nonhealthcare source or using them for a reason other than to relieve pain (Ko et al., 2020).

Opioid use by pregnant women represents a significant public health concern given the association of opioid exposure and adverse maternal and neonatal outcomes, including preterm labor, stillbirth, and maternal mortality (Minozzi et al., 2013; Patrick et al., 2012). Maternal opioid use is also associated with an increased risk of NAS, which results from opiate exposure in utero that triggers a postnatal withdrawal syndrome with a constellation of signs and symptoms. These withdrawal symptoms are manifested immediately after birth among babies born to mothers with drug dependence, following abrupt discontinuation of in-utero exposure to the drugs, and includes the use of illegal or prescription opioids (Hudak et al., 2012; Lisonkova et al., 2019).

The rising prevalence of opioid use in pregnancy has led to a sharp increase in NAS. According to data from the 2017 (HCUP)-US.AHRQ.gov/*NIS* survey, the number of babies born with NAS increased by 82% nationally from 2010–2017. The same survey reported that approximately seven newborns were diagnosed with NAS for every 1,000 newborn hospital stays (HCUP-US.AHRQ.gov/*NIS*). These alarming statistics show that nearly 80 newborns are diagnosed with NAS in the U.S. every day, which is equivalent to one baby suffering from opioid withdrawal born approximately every 19 minutes (HCUP-US.AHRQ.gov/*NIS*).

NAS poses significant public health challenges, and the care of babies diagnosed with NAS can be costly to the healthcare system. Caring for a newborn with NAS is associated with prolonged hospital stays and increased medical expenses, which has resulted in an estimated $1.5 billion in related annual hospital charges (Patrick et al., 2015). This alarming increase in these statistics continues to prompt attention from the public, providers, and policymakers to intervene and follow recommendations set forth

by the American College of Obstetrics (ACOG) and American Society of Addiction Medicine (ASAM) collaboratively to guide clinicians in caring for pregnant women with OUD (Carter et al., 2019).

Treatments for Opioid Use Disorder

According to SAMHSA, treatment for SUDs is comprised of multiple service components including individual or group counseling, inpatient/residential treatment, intensive outpatient treatment, case or care management, medication, recovery support services, and 12-step fellowship and peer supports (SAMHSA.gov/*Tip 42*). In the U.S., more than 14,500 specialized drug treatment facilities provide counseling, behavioral therapy, medication, case management, and other types of services to persons with SUDs (NIDA.NIH.gov/*Principles of drug addiction*). MT is defined as the use of the U.S. Food and Drug Administration (FDA)-approved opioid agonist medication (e.g., methadone) partial opioid agonist/opioid antagonist (e.g., buprenorphine), and opioid antagonist medications (e.g., naltrexone). A number of medications are available for the treatment of OUD, both for patients in acute withdrawal and to support long-term recovery (McCarty et al., 2018). These medications help reduce cravings and withdrawal symptoms that come from stopping opioid use (SAMHSA.gov/*Medications for substance use disorders*).

MT for OUD combines counseling and other recovery supports with prescribed medications (SAMHSA.gov/*Medications for substance use disorders*). MT in combination with behavioral therapies, is effective in prevention of relapse of opioid use. Psychosocial interventions such as cognitive behavior therapy (CBT) and motivational interviewing (MI) address the psychosocial contributors to OUD and may help improve retention in care (Jhanjee, 2014) for individuals receiving MT. Other support services

include assessment, coordination, and management of other medical and psychiatric care needs such as provision of general primary care, treatment for other SUDs, pregnancy and HIV or hepatitis C virus (HCV) coinfect (SAMHSA.gov/*TIP 43*).

Comprehensive treatment for patients in MT with OUD includes screening, assessment, and treatment. Despite broad recognition of the importance of MT, it is estimated that only 11% of patients with an OUD are prescribed FDA-approved medications for the disorder (Oesterle et al., 2019). MT has been shown to be a critical component of treatment, and treatment with MT is more effective than treatments that do not use medication in reducing the frequency and quantity of opioid use (Mattick et al. 2009, 2014). Treatment that includes MT also reduces the risk of overdose, improves social functioning, decreases criminal activity, and lowers infectious disease rates (NIDA.NIH.gov/*Principles of drug addiction*). Medications have become an essential component of an ongoing treatment plan, enabling opioid-addicted persons to regain control of their health and their lives (Volkow & McLellan, 2016). Encouraging early enrollment and access to care will facilitate successful outcomes and treatment in the care of patients with OUD.

Available Opioid Use Disorder Treatment for Pregnant Women

The use of pharmacotherapy as part of a comprehensive treatment plan is recommended in treating pregnant women with OUD (Rodriguez & Klie, 2019). OUD in pregnancy can be more problematic than realized due to the barriers that exist for pregnant women seeking treatment for OUD. Among these barriers are social stigma of prenatal substance abuse, lack of provider knowledge in how to care for pregnant women with OUD, potential for legal complications, and many others that may be personal and

individual to each person's situation (Weber et al., 2021). In addressing stigma, widespread stigma creates significant barriers to accessing what people need to survive and thrive, such as care, housing, income, and social services (SAMHSA.gov/*Harm reduction*). Stigma toward people who use drugs is written into our laws, child protective service, and social service system (Wolfson et al., 2021). This stigma is amplified if a person who uses drugs becomes pregnant, and pregnant women often face a higher incidence of legal consequences as a result of their OUD during pregnancy (e.g., pregnant women often face punishment for addiction and loss of custody of child(ren), as a result. many women are reluctant to seek help or disclose their use of opioids (Lester et al., 2004; Stone, 2015).

Support and care for women preconception and at the time of pregnancy plays an important role in improving outcomes for pregnant women (Patrick et al., 2017). Once determined that a pregnant woman has OUD, they should be offered MT consisting of pharmacotherapy and evidence-based behavioral interventions (ACOG/*Opioid use and opioid use disorder in pregnancy*). Pregnancy can serve as a motivating factor for women and provides an important opportunity to identify and treat women with OUD (ACOG/*Opioid use and opioid use disorder in pregnancy*). Each pregnant woman with OUD who is in treatment needs her own individualized plan that is developed in collaboration with her healthcare team (SAMHSA.org/*Clinical guidance for treating pregnant and parenting women with opioid use disorder and their infants*). Women with SUD report high rates of past trauma, including physical and sexual abuse, and need access to gender-specific, family-friendly addiction treatment programs, psychosocial services, and mental health treatment (SAMHSA.org/*Addressing the specific needs of*

women for treatment of substance use disorders). In addition, staff should work collaboratively with women and families to develop a nonjudgmental therapeutic alliance using trauma-informed care approaches (Sweeney et al., 2018). Positive outcomes of treatment in pregnant and parenting women who complete treatment programs include less engagement in criminal activity, higher rates of employment, and lower risk of relapse (Hser et al., 2011).

Pregnant women with OUD face numerous barriers to care, including limited access to treatment, widespread stigma, lack of provider knowledge in how to care for pregnant women with OUD and fear of legal consequences (Saia et al., 2016; Stone, 2015). Current efforts aimed at addressing the opioid epidemic are aimed at improving access to prevention, treatment, and recovery support services have been identified and have included greater recognition of the need for treatment (FDA.gov/*Federal response to opioid crisis*). The intersection of pregnancy and substance use creates a need for a collaborative approach among medical professionals and substance use providers to address the multifaceted needs of the mother, infant, and family (SAMHSA.gov/*A collaborative approach to the treatment of pregnant women with opioid use disorders*). Women who use opioids during pregnancy represent a diverse group, and it is important to recognize the complex needs for pregnant women with OUD. Current measures of treatment success especially for pregnant women with OUD are limited; it is imperative that new ways to define treatment success be developed to care for these women.

Standards and Measures of Treatment Success in Medication Treatment

Medication treatment (MT) is a term addiction professionals have used for years. It refers to short-term medication therapy for alcohol and OUD. These treatments are part

of a larger treatment and recovery plan. MT is used with counseling and behavioral therapy and provides a holistic approach that addresses addiction from several angles (SAMHSA.gov/*Medications for substance use disorders*). During this study, the term MT was used when addressing treatment for individuals with OUD.

Since the inception of MT for opioid addiction, testing for drug use via urine drug screens (UDS) has been the objective measure of treatment efficacy and a tool to monitor treatment compliance and patient progress (SAMHSA.gov/*TIP 43*). It is important to note that assessing patient-centered treatment outcomes (i.e., focusing on attributes that are important to patients and that engage them actively in treatment) should be incorporated along with UDS to assess success in medication treatment. While urine drug testing is an effective tool to measure the presence of drugs, it is often inconsistently administered across programs, does not provide enough data such as how much drug was taken or when it was taken, which are necessary pieces of information that should be gathered when treating an individual for OUD (SAMHSA.gov/*Clinical drug testing in primary care*). The use of drug results may be helpful to providers in suggesting that an individual's dosage needs adjustment or that a more intensive level of care is needed (SAMHSA.gov/*Clinical drug testing in primary care*). However, positive drug tests alone do not confirm that an individual is not engaged in treatment or is not compliant with treatment. Consistent with a harm reduction approach, drug tests should not be used as punishment or as the sole reason to discharge them from treatment (American Society of Addiction Medicine [ASAM], 2017).

Clinical use of drug testing, as the primary indicator of treatment, has led to poor outcomes based on misinterpretation and test limitations (Hadland & Levy, 2016). The

most recent ASAM guidance recommends that "drug testing should be used as a tool for supporting recovery rather than exacting punishment" (ASAM, 2017). The SAMHSA guidance in TIP 63 advised to explain to individuals that testing will help them meet treatment goals and is not performed to render punishments (SAMHSA.org/*Clinical drug testing in primary care*). It is reported that clinicians receive minimal education on UDS and often lack adequate knowledge of how to both choose an appropriate UDS test (Reisfield & Webb, 2007) and interpret results (Starrels et al., 2012). Lack of understanding can lead to misinterpretation of UDS results, failure to identify patterns of harmful drug use, and inappropriate management of individuals seeking treatment. Clinicians may compromise individuals care by denying appropriate treatment or discharging individuals in MT from their practice after inaccurately concluding that they are misusing or diverting opioids owing to a false-positive or false-negative UDS result (Reisfield & Webb, 2007; Starrels et al., 2012).

Unfortunately, misinterpretation of urine drug testing often means penalties for individuals in MT and increased barriers to care. Stigma remains widespread in addiction treatment, resulting in the individual's discharge if they continue to struggle in early phases of stabilization or relapse in later stages (Martin, Bosse, et al., 2018). Due to its inherent limitations and stigmatizing results, drug testing should not be relied upon as the sole measure of an individual's recovery from substance use. Strategies aimed at reducing the negative consequences of drug use can also be a valuable component of treatment for individuals with OUD (Martin, Bosse, et al., 2018). For individuals with OUD, harm reduction strategies include reducing the amount of substance used or the frequency of use. Treatment programs can be developed incorporating harm reduction

principles and clients can receive comprehensive treatment while focusing on positive outcomes co-occurring with their MT treatment. Examining other measures of treatment success that do not solely rely on drug screen information is imperative in successfully caring for individuals receiving treatment for OUD.

Significance of the Study

OUD has affected over 16 million people worldwide (Chang et al., 2018). Among those, over 2.1 million people in the United States have been affected by OUD. OUD includes dependence and addiction with addiction representing the most severe form of the disorder (Vallersnes et al., 2019). Treatment for OUD with approved medications has been shown to reduce OUD and overdose; however, there is no universal treatment standard that exists for MT, and care is delivered in different ways in a variety of settings (Chou et al., 2015). Programs are often not classified according to the threshold or tolerance for ongoing drug use, and policies often have a stringent focus that defines recovery and treatment success solely on abstinence and cessation of drug use (NIDA.NIH.gov/*Principles of drug addiction treatment*). Those who do not meet the proposed criteria are often involuntarily discharged from the program (Cox et al., 2013). There is a popular perception that treatment "fixes" those with SUDs. This perception fails to recognize the nature and complexity of the disorder and the real impact treatment might be having on someone who is identified as noncompliant and not improving in treatment (SAMHSA.gov/*Comprehensive case management for substance abuse treatment/TIP 27*). It is important to identify primary outcomes that identify treatment success for individuals in MT with OUD.

Purpose of the Study

The purpose of this study was to understand if functional outcomes better predict treatment success than drug-use screening alone in a sample of individuals with OUD receiving MT. A secondary aim of this study examined this question in a sample of pregnant women with OUD receiving MT. This paradigm shift in changing how we identify treatment success must include changes in functional status (i.e., functional outcomes) to ensure that proper recognition of improved addiction status is recognized (SAMHSA.gov/*Comprehensive case management for substance abuse treatment/TIP 27*). Nine functional outcome variables were examined in this study, and they included the following: negative social influences (contacts, social supports), unstable housing, criminal justice system (CJS) involvement, unstable finances, unstable employment, custody issues, social stressors, and non-social stressors. The functional outcomes included in this study were extracted and coded from the patient's' electronic health record (EHR). Common themes were noted that patients more often reported the presence of negative aspects that affected their treatment status; thus, the outcomes used to measure treatment success were worded from a negative perspective.

Individuals who stay in treatment are known to have better outcomes with regard to less late drug use, decrease in criminal activity, and increase in employment (Terplan et al., 2015). Pregnant women who stay in care also have higher rates of reunification with their children compared to those who do not complete treatment (Gregoire & Schultz, 2001). The goal for individuals in treatment should be focused on treatment retention, and providers must identify the most effective way to not only facilitate early entry into substance abuse treatment, but to encourage ongoing care. In addition to

identifying additional measures of treatment success among patients in general, it is important to identify treatment success in special populations. Of great importance, is the identification of treatment success in pregnant women who are receiving OUD treatment. Currently, treatment programs that rely solely on UDS as a measure of an individual's treatment success can pose legal and negative ramifications for those individuals receiving treatment and ultimately can lead to discharge from the treatment program. Identifying more valid and reliable ways to measure treatment success including changes in functional status by examining functional outcomes, as previously mentioned in this chapter, has the potential to make changes in policy and to reduce the impact of the current sole use of positive urine screens on treatment plans.

Study Aims and Hypotheses

Outcome Variables

For all aims, indicators of treatment utilization, medication utilization, and treatment retention were used to measure treatment success. Treatment utilization variables included a number of (a) random maintenance visits, (b) maintenance visits, (c) no-show visits, (d) rescheduled visits, (e) other encounters, (f) care interruptions, (g) the total time in care, and (h) time since the last visit. Variables (a) through (h) were adjusted by total time in care in multivariate analyses. Medication utilization was measured by the presence of buprenorphine in a patient's urine. Treatment retention was measured by whether the patient was active in treatment as of January 31, 2018.

To achieve the study goal, the following aims and hypotheses were examined in a sample of patients with OUD receiving MT in a multistate, multisite outpatient treatment program.

Aim 1: To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of patients with OUD receiving MT. (See Figure 1.)

H1a–h: Functional risk score will account for significantly more treatment utilization variance than opioid use across many different treatment utilization variables.

H1i: Functional risk score will account for significantly more medication utilization variance than opioid use.

H1j: Functional risk score will account for significantly more treatment retention variance than opioid use.

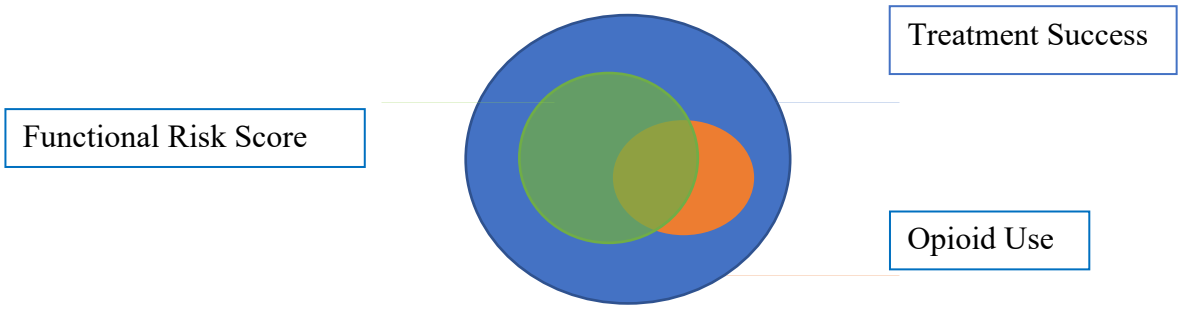

Figure 1: Diagram of Aim 1 hypotheses.

Aim 2: To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of pregnant patients with OUD patients receiving MT.

For this aim, the hypotheses presented in Aim 1 was examined solely in a pregnant sample.

Summary of Study Proposal

Evidence in the literature reflects the opioid public health crisis and nationwide epidemic, but the impact of MT on recovery and outcomes especially in pregnant women is unclear. Currently, there is no universal treatment standard that exists for MT, and these programs are delivered in different ways and in a variety of settings. Understanding

how functional outcomes better predict treatment success when compared to UDS provides an opportunity to improve clinical care of this population. In addition, clarifying these relationships will allow clinicians to intervene more appropriately when presented with individuals with OUD participating in MT.

CHAPTER 2

REVIEW OF LITERATURE AND THEORETICAL FRAMEWORK

This chapter describes the current research and relevant literature related to OUD, as well as current treatment approaches, management, and indicators of treatment success for individuals in MT, with a focus on pregnant women. Following this literature review, an integration of the Ecological Systems Theory (Bronfenbrenner, 1979, 1994) to provide a framework for understanding the multiple levels of a social system and interactions between individuals with OUD and their environment within this system. When working with individuals in treatment for OUD, it is important to examine the individual, relational aspects, community, and societal influences that may impact an individual's success in treatment for OUD.

Introduction

Opioid use and addiction, including heroin and nonmedical use of prescription opioids, is a serious and growing health problem of epidemic proportions (Sharma et al., 2016). Even more concerning is the dramatic rise and prevalence of opioid use in pregnant women. Pregnant women enrolled in MT are of particular interest because prenatal substance use can bring about several deleterious consequences for both mother and baby. Among these consequences, prenatal opioid use has led to an increase in associated adverse neonatal outcomes known as NAS (ACOG/*Opioid use and opioid use disorder in pregnancy*). In response to the concerns of the opioid crisis, comprehensive harm-reduction-based services, such as MT centers, have been developed to provide effective treatment in a nonjudgmental, nonpunitive setting (NIDA.NIH.gov/*Principles of drug addiction treatment*).

Currently, there is limited information available on ways to measure treatment success for individuals enrolled in MT. UDSs, indicating the absence or presence of drug use have been the gold standard of gauging treatment success in MT programs. UDS results, if positive, can result in punitive measures (e.g., loss of custody of child(ren), loss of job, discharge from program). Clinically, this approach should not be the sole indication of an individual's ability to be successful in treatment as research has shown that harm reduction and treatment retention is key to treating individuals with OUD in MT (Martin et al., 2018).

Other outcomes that would be relevant measures of treatment success are outcomes that indicate how the individual is functioning in their day-to-day life. Such functional outcomes could include improved relationships with people who are supportive of an individual's OUD treatment, decreased/eliminated contact with people who are actively using substances, reduction in criminal activity and/or resolution of criminal justice involvement (e.g., complete probation), maintained or increased stability in housing, finances, employment, regaining or continued custody of children, as well as the absence of social and non-social stressors. Functional outcomes are an important part of a comprehensive evaluation of OUD treatment and present a new way of gauging success beyond a sole reliance on patient abstinence from opioids. This call for evaluating how we measure treatment success has the potential to change the way in which treatment success and recovery from OUD in MT is evaluated.

This chapter presents a review of literature on OUD and current measures of treatment success for individuals enrolled in MT with a focus on pregnant women. The objectives of the search were (a) to identify and distil key literature on current measures

of individuals in MT programs, and (b) to investigate the outcomes of their treatment measures (e.g., retention, compliance, and medication adherence).

History of Opioid Use

Although a detailed orientation of the history of opioid use is beyond the scope of this study, it suffices to say that much of the understanding of opioid use and addiction is in its infancy but continues to evolve. The current opioid addiction crisis that we know today in many ways can be described as a replay of history with America's first epidemic of opioid addiction occurring in the second half of the Nineteenth Century (Kolodny et al., 2015). The use of opioids in history has diverse origins; for centuries, mothers dosed themselves and their children with opium tinctures and patent medicines (Obladen, 2016), soldiers used opium and morphine to treat post-traumatic stress disorder (PTSD) and painful injuries (Carlisle & Golson, 2008).

As the use of opioids for treatment of pain became increasingly prevalent, physicians turned to morphine, an opioid derivative to treat pain and alleviate suffering. Morphine became known as the magic medicine and was used to treat pain as few alternatives to symptomatic treatment existed, cures were scarce, and the etiology of painful conditions was poorly understood. The fascination to treat pain with morphine came to fruition, thus creating a supply and demand for this miracle medicine. The Harrison Narcotics Tax Act of 1914 restricted the use of opioids to pain treatment and outlawed their use for addiction management (The Harrison Narcotics Act (1914). The Harrison Narcotics Act framed opioid dependence and substance abuse in general as a criminal or moral act, rather than as a medical issue. As many as 30,000 physicians, some engaged in unethical practice, some not, were prosecuted under this act (Hamid, 1998).

Opioid addiction remained a difficult-to-treat problem, with very low recovery rates (Velander, 2018).

Fast forward years later to the Twentieth Century, after the Second World War, opioids—synthetic opiates—began to enter the market in greater numbers, including drugs formulated using hydrocodone (later popularized in the 1970s as the narcotic in Vicodin) and oxycodone (the opiate best known today as an ingredient in OxyContin; Kolodny et al., 2015). The spawn of a general worldwide "opiophobia" was created as many doctors', knowing the risks of addiction and dependence, were still conflicted with treating and managing pain despite the known addictive side effects (Jones et al., 2018). Studies surfaced that linked under reliance of opioid analgesics for pain control and resultant undertreatment for pain. Markedly, in 1986 a paper describing the treatment of 38 chronic pain patients concluded that oral pain relievers (OPRs) could be prescribed safely on a long-term basis (Portenoy & Foley, 1986). Despite its low-quality evidence, the paper was widely cited to support expanded use of opioids for chronic noncancer pain (Kolodny et al., 2015).

Opioid use increased gradually, and the first wave of opioid epidemic began in 1995 with the introduction of OxyContin, an extended-release formulation of oxycodone manufactured by Purdue Pharma, which fueled the rapid acceleration of opioid use (Kolodny et al., 2015). The advocacy and campaign for effective pain management and treatment of chronic conditions funded by the Purdue Pharma with support of large organizations such as American Pain Society, the American Academy of Pain Medicine, the Federation of State Medical Boards, the Joint Commission, pain patient groups, and other organizations resulted in the identification and increased aggressiveness in the

treatment of pain with OPRs (Fauber, 2012). The rapid acceleration in opioid use created a rise in opioid use-related deaths as pharmaceutical companies reassured the medical community that patients would not become addicted to prescription OPRs, and healthcare providers began to prescribe them at greater rates. This subsequently has led to widespread diversion and misuse of these medications before it became clear that these medications could indeed be highly addictive (Morone & Weiner, 2013; Van Zee, 2009). The culture change, driven by intent to ensure access to pain relief, had opened the floodgates to the current opioid climate.

In 2010, The second wave of the opioid epidemic started with a rapid increase in deaths from heroin abuse (Dowell et al., 2016). As early efforts to decrease opioid prescribing began to take effect, making prescription opioids harder to obtain, the focus turned to heroin, a cheap, widely available, and potent illegal opioid (Liu et al., 2018). The use of heroin increased in both sexes, the majority of age brackets, and all socioeconomic groups. Heroin is commonly injected, which puts users at risk for injection-related diseases like HIV/AIDS, hepatitis B and C, skin infections, bloodstream infections, and infections of the heart (NIDA.NIH.gov/*Drug facts/Drug use and viral infections*).

A third wave of the opioid epidemic began in 2013 as an increase in deaths related to synthetic opioids like fentanyl began (Liu et al., 2018). More than 72,000 Americans died from drug overdoses in 2017, including illicit drugs and prescription opioids—a twofold increase in a decade (CDC.gov/*NCHS/NVSS/Mortality*). Among the more than 72,000 drug overdose deaths estimated in 2017, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (synthetic opioids) with nearly

30,000 overdose deaths (CDC.gov/*NCHS/NVSS/Mortality*). The increase in fentanyl deaths has been linked to illicitly manufactured fentanyl (not diverted medical fentanyl) used to replace or adulterate other drugs of abuse (CDC.gov/*Increases in fentanyl drug confiscation and fentanyl-related overdose fatalities*).

The increase in injection drug use has also contributed to the spread of infectious diseases including HIV and Hepatitis C (Zibbell et al., 2018). As seen throughout the history of medicine, science can be an important part of the problem and solution when responding to public health crisis. As a result, governmental and regulatory agencies have stepped into institute regulatory measures and societal recommendations that have contributed to a decrease in the number of opioid prescriptions over the years (Jones et al., 2018). Concerted efforts from multiple disciplines, including physicians, legislators, pharmaceutical companies, educators, and the general public are required to continue the battle to combat the opioid crisis (Jones et al., 2018). The issue well known as the opioid crisis has become a public health issue with devastating consequences including increases in opioid misuse and related overdoses, as well as the rising incidence of NAS due to opioid use and misuse during pregnancy (Patrick et al., 2017).

Opioid Use Disorder

Not since the HIV/AIDS epidemic has the United States faced as devastating and lethal a health problem as the current crisis of opioid misuse and overdose and OUD (Bonnie et al., 2017). Opioids, as discussed in the previous section, are a class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and pain relievers available legally by prescription, such as oxycodone (OxyContin®), hydrocodone (Vicodin®), codeine, morphine, and many others

(NIDA.NIH.gov/*Prescription opioids drug facts*). Opioids are often used as medicines because they contain chemicals that relax the body and can relieve pain. Prescription opioids are used mostly to treat moderate-to-severe pain, though some opioids can be used to treat less severe conditions such as coughing and diarrhea (NIDA.NIH.gov/*Prescription opioids drug facts*). Opioids can also make people feel very relaxed and "high," which is why they are sometimes used for nonmedical reasons.

Opioids are a broad group of pain-relieving drugs that work by interacting with opioid receptors in cells located in many areas of the brain, spinal cord, and other organs in the body (Al-Hasani & Bruchas, 2011). Though opioids are mainly prescribed to relieve pain symptoms, they can have negative effects on the body such as depression of breathing due to neuro chemical effects on the brainstem, which can ultimately lead to death if untreated. Although opioids can be generally safe when used as prescribed, they are widely misused and abused, making them incredibly dangerous. Opioids have the potential to cause substance dependence that is characterized by the following: a strong desire to take opioids, impaired control over opioid use, persistent opioid use despite harmful consequences, increased tolerance, and a physical withdrawal reaction when opioids are discontinued (World Health Organization [WHO], 2018). Dependence on prescription opioids includes iatrogenic dependence following the treatment of chronic pain, and dependence following the diversion and theft of prescription opioids from patients, medical facilities, pharmacies, and the manufacturing and distribution chains (WHO, 2018).

In 2019, 9.7 million people self-reported that they had personally misused prescription opioid pain relievers during the previous year (SAMHSA.gov/*NSDUH*). The

most commonly reported reason that prescription opioid pain relievers were misused was to relieve physical pain (65.7%). The misused prescription opioids reported were obtained from a variety of sources. More than half (50.8%) of people who misused pain relievers in the past year said they were obtained from a friend or relative, about one third of respondents (37.5%) reported they received opioids through prescription(s) or stealing from a healthcare provider. About 1-in-15 people who misused pain relievers in the past year (6.2%) bought the last pain reliever they misused from a drug dealer or other stranger (SAMHSA.gov/*NSDUH*).

Opioid overdoses for the first time in U.S. history are a leading cause of preventable deaths surpassing motor vehicle crashes (National Safety Council [NSC], 2018). In 2015 alone, drug overdoses were the leading cause of accidental death, most of which were related to prescription opioids and heroin, far exceeding motor vehicle accidents and gun violence-related deaths combined (CDC.gov/*NCHS/NVSS/Mortality*). Americans now have a 1-in-96 chance of dying from an opioid overdose, according to the council's analysis of 2017 data on accidental death. The probability of dying in a motor vehicle crash is 1-in-103 (NSC, 2018). From 1999 to 2017, more than 700,000 people have died from a drug overdose (CDC.gov/*NCHS/NVSS/Mortality*). There is now also a rise in heroin use and heroin use disorder as some people have shifted from prescription opioids to their cheaper street relative; about 438,000 people aged 12 or older in 2019 had a heroin use disorder, and more than 14,000 Americans died of a heroin overdose in 2019 (NIDA.NIH.gov/*Principles of drug addiction treatment*; SAMHSA.gov/*NSDUH*).

Heroin and prescription opioid misuse is a major health concern. From a diagnostic perspective, it is imperative that the physicians understand, are able to identify OUDs; provide education and strategies for harm reduction, and offer effective, evidence-based treatments. OUD is defined in the DSM-V as a problematic pattern of opioid use leading to clinically significant impairment or distress (American Psychiatric Association, 2013). OUD was previously classified as Opioid Abuse or Opioid Dependence in the DSM-IV and has also been referred to as "opioid addiction." The diagnosis of OUD can be applied to someone who uses opioid drugs and has at least two of the following symptoms within a 12-month period:

- Taking more opioid drugs than intended.
- Wanting or trying to control opioid drug use without success.
- Spending a lot of time obtaining, taking, or recovering from the effects of opioid drugs.
- Craving opioids.
- Failing to carry out important roles at home, work, or school because of opioid use.
- Continuing to use opioids, despite use of the drug causing relationship or social problems.
- Giving up or reducing other activities because of opioid use.
- Using opioids even when it is physically unsafe.
- Knowing that opioid use is causing a physical or problem but continuing to take the drug.
- Tolerance for opioids.
- Withdrawal symptoms when opioids are not taken.

A common misconception is that anyone who is prescribed opioids for pain, regardless of duration will develop an OUD. Edlund et al. (2013) investigated the association between exposure to prescription opioids and the incident of OUD among individuals with a new episode of a chronic noncancer pain condition. In this study, it was determined that even with acute low dose opioids (1–36 mg/day morphine equivalent dose or MED), patients are at increased risk for developing OUD (Edlund et al., 2013). The likelihood of developing OUD ranges from a 3-fold increase for acute low dose

opioids, to a 122-fold increase for chronic high dose opioids (≥ 120mg/day MED) compared to patients who are not prescribed opioids (Edlund et al., 2013).

While it is often the case that people will develop physical tolerance to prescribed opioids, and experience physical withdrawal symptoms if they do not take the drug, the DSM-V explicitly states that these are not applicable if the individual is experiencing these symptoms under appropriate medical supervision. Several terms are commonly used in the literature to describe prescription opioid use patterns. Regular opioid use, including opioids used in a therapeutic context, is associated with physical dependence characterized by a set of signs and symptoms when drug taking is stopped, and tolerance in which more of the drug is needed to achieve the same intensity of effect (Brady et al., 2016).

The amount and duration of use associated with physical dependence is variable, but daily use for more than 2–3 weeks is often accompanied by some withdrawal. Being physically dependent does not necessarily mean that an individual has an OUD, if the individual is taking the medications as prescribed. It is of importance to note the differences in the reporting of statistics for individuals with opioid misuse and those with a diagnosis of opioid abuse or OUD. Definitions of abuse and misuse vary, but generally misuse of opioids is a broad term that captures any use outside of prescription parameters, including misunderstanding of instructions, self-medication of sleep, mood, or anxiety symptoms, and compulsive use driven by an OUD (Brady et al., 2016).

It is important to distinguish between different causes of misuse in order to appropriately address it. Results from the 2020 NSDUH revealed that 9.5 million individuals aged 12 or older used opioids within the past year. Among those who

reported opioid misuse, the vast majority reported the use of prescription pain relievers within the past year (SAMHSA.gov/*NSDUH*). Specifically, 9.3 million people aged 12 or older in 2020 misused prescription pain relievers in the past year compared with 902,000 people who used heroin (SAMHSA.gov/*NSDUH*). In the same report, it was estimated that 2.7 million (1.0%) of people aged 12 or older had an OUD (SAMHSA.gov/*NSDUH*). The number of 2.7 million does not accurately reflect the actual number of individuals who may have a diagnosis of OUD and thus presents a greater issue.

The complex nature of the disorder, reduced access to treatment, combined with a rapidly growing opioid epidemic, has created a public health crisis in the United States and around the world. OUD can affect people of all ages, races, genders, and ethnic backgrounds. In addition, other factors are important to consider when examining opioid use and its impact on individuals affected by OUDs. These variables include trauma exposure, PTSD, anxiety, criminal justice involvement, and use of other drugs and alcohol. Each of these variables will be discussed further in this chapter and will have the potential to contribute valuable information to examining functional outcomes as an indicator of treatment success for individuals with OUD in MT.

Pregnant Women with Opioid Use Disorder

SUDs affect women across all racial and ethnic groups, socioeconomic backgrounds, and rural, urban, and suburban locales (Normile et al., 2018). Women are at highest risk for developing a SUD during their reproductive years (18–44), especially ages 18–29 (Compton et al., 2007). This means, that women who are pregnant or soon to become pregnant are at increased risk for substance abuse. According to survey results from the (2019) NSDUH, 7.2 million women aged 18 or older had a SUD, among women

with an SUD, 4.6 million reported opioid misuse. The survey also shows that almost 99% of the 4.6 million reported prescription pain reliever misuse within the past year (McCance-Katz et al., 2020).

Substance abuse, including the misuse of opioids in pregnancy has increased over the past three decades in the United States, resulting in approximately 225,000 infants yearly with prenatal exposure to illicit substances (Patrick et al., 2012; Patrick et al., 2015). Results from the (2019) NSDUH survey report approximately 112,000 pregnant women aged 15-44 years reported using illicit drugs within the past month, and among those 8,000 reported using opioids as their drug of choice during the previous month (McCance-Katz et al., 2020). According to self-reported data analyzed from the (2019) Pregnancy Risk Assessment Monitoring System (PRAMS) survey, about 7% of women reported using prescription opioid pain relievers during pregnancy (Ko et al., 2020). Study results also showed that among the 7% of respondents, 21.2% reported a misuse (a source other than a healthcare provider or a reason to use other than pain), 27.1% indicated a wanting or needing to cut down or stop using, and 68.1% received counseling from a provider on how prescription opioid use during pregnancy could affect an infant (Ko et al., 2020).

Opioid misuse, which includes use of illicit drugs, including prescription opioids, during pregnancy is a major public health concern. Given that many pregnancies are not recognized until well after the first few weeks and half of all U.S. pregnancies are unplanned, all women who might become pregnant are at risk (Ailes et al., 2015). Newborns exposed to opioids prenatally are at risk to develop NAS, a serious and highly variable condition characterized by central nervous system hyperirritability and

autonomic nervous system dysfunction a costly problem requiring longer newborn lengths of stay and higher hospital charges (Hudak, & Tan, Committee on drugs, et al., 2012). A study by Hirai et al. (2021) which analyzed national and state inpatient HCUP data of birth and deliveries from 2010-2017 shows, that mothers with opioid-related diagnoses (MOD) documented at delivery increased from 3.5 to 8.2 per 1,000 hospitalizations representing an absolute increase of 4.6 per 1,000 delivery hospitalizations and a relative increase of 131%. The same study also shows the estimated rates of NAS significantly increased from 4.0 to 7.3 per 1,000 birth hospitalizations, representing an absolute increase of 3.3 per 1,000 birth hospitalizations and a relative increase of 82% (Hirai et al., 2021).

For the mother-infant dyad, opioid misuse and exposure is associated with adverse outcomes. For example, maternal OUD is associated with severe maternal complications, including mortality, (Admon et al., 2019) and infants diagnosed with NAS have longer and more complicated hospital stays than nonaffected infants (Patrick et al., 2015; Winkelman et al., 2018). The cost of a hospital stay for a newborn with NAS was $8,200 in 2017, compared with $1,000 for other newborn hospital stays which is more than eight-times the increase in cost. The average length of stay for a newborn with NAS was 11 days in 2017, compared with 2 days for other newborn hospital stays which is the equivalent of nearly six-times increase in length of stay.

Rates of NAS and maternal OUD have been shown to vary greatly across states in the US (Hirai et al., 2021). Compared with all birth hospitalizations, neonates with NAS were significantly more likely ($P < .001$) to be non-Hispanic White (77.5% vs. 52.2%), Medicaid-billed (84.0% vs. 46.3%), reside in zip codes in the lowest quartile of median

income (38.1% vs. 28.1%), and live in nonmetropolitan counties (22.1% vs. 13.4%; Hirai et al., 2021). Similarly, compared with all delivery hospitalizations, individuals with MOD were significantly more likely ($P < .001$) to be non-Hispanic White (79.9% vs. 52.5%), aged 25 to 29 years (37.0% vs. 29.2%), Medicaid-billed (77.1% vs. 43.3%), reside in zip codes in the lowest quartile of median income (36.4% vs. 28.1%), and live in nonmetropolitan counties (20.6% vs. 13.4%; Hirai et al., 2021).

During pregnancy, and in the immediate post-partum period, chronic untreated addiction to opioids is associated with lack of prenatal care, increased risk of fetal growth restriction, abruptio placentae, fetal death, preterm labor, and intrauterine passage of meconium (Holbrook & Kaltenbach, 2012). In addition, pregnant women face severe, long-term consequences of drug use, including an increased likelihood of assault and abuse, contracting HIV, or hepatitis, miscarriage, delivering infants with physical and behavioral impairments, postpartum depression, and loss of custody of their children (Dakof et al., 2003; Holbrook & Kaltenbach, 2012; Kissin et al., 2001). Results from the 2019 NSDUH reveal that 34.3 million adult women had a mental illness and/or SUD, an increase of 6.8% over 2018 composed entirely of increases in mental illness (McCance-Katz et al., 2020). A retrospective chart review conducted by Holbrook and Kaltenbach (2012), reported that more than 30% of pregnant women (N = 125) enrolled in substance use treatment program screened positive for moderate to severe depression, and more than 40% reported symptoms of postpartum depression.

Pregnancy provides a unique opportunity to identify and treat women with SUDs (ACOG/*Opioid use and opioid use disorder in pregnancy*). SUDs affect women across all racial and ethnic groups and all socioeconomic groups, and affect women in rural,

urban, and suburban populations. Therefore, it is essential that screening be universal (ACOG/*Opioid use and opioid use disorder in pregnancy*). Results from the 2019 NSDUH survey show that almost 1.5 million women received MT; however, only 726,000 women were diagnosed with an OUD. Screening for substance use should be a part of comprehensive obstetric care and should be done at the first prenatal visit in partnership with the pregnant woman (ACOG/*Opioid use and opioid use disorder in pregnancy*). Women who use opioids during pregnancy represent a diverse group, and it is important to recognize this issue as early detection and referral to treatment can lead to more positive maternal and neonatal outcomes (ACOG/*Opioid use and opioid use disorder in pregnancy*).

In response to this growing concern, harm-reduction based services, such as MT Centers, have been developed to provide effective treatment in a nonjudgmental, nonpunitive setting. Treatment options for pregnant women with opiate addictions include detoxification (Bell et al., 2016) or drug replacement therapy with methadone or buprenorphine (Jones, O'Grady, et al., 2008). Both medications have been found to be compatible with breastfeeding and in utero exposure to either drug has not yet been determined to have deleterious effects on infant development (Jones et al., 2012). For pregnant women with an OUD, opioid agonist pharmacotherapy is the recommended therapy and is preferable to medically supervised withdrawal because withdrawal is associated with high relapse rates (Jones et al., 2017; Jones, O'Grady, et al., 2008; Reddy et al., 2017) ranging from 59% to more than 90% (Saia et al., 2016) and poorer outcomes. Relapse poses grave risks, including communicable disease transmission, accidental overdose because of loss of tolerance, obstetric complications, and lack of prenatal care

(ACOG/*Opioid use and opioid use disorder in pregnancy*). Abrupt discontinuation of opioid use during pregnancy can result in premature labor, fetal distress, and miscarriage (SAMHSA.gov/*Decisions in recovery/Treatment for opioid use disorder medications for opioid addiction handbook*).

Women with OUD may find it especially difficult to reduce or stop substance use without treatment (Terplan et al., 2012). Current efforts to address opioid-related problems have included greater recognition of the need for treatment. While there is clear evidence of a national epidemic, there is little data on best practices to support pregnant women in achieving optimal recovery outcomes (SAMHSA.gov/*Decisions in recovery/Treatment for opioid use disorder medications for opioid addiction handbook*). Pregnancy is a major life transition that can be a time of excitement and anticipation, however this major life transition can create stress caused by physical discomfort, emotional strain and financial difficulties leading to an increase in substance use in pregnancy. Research has shown that not initiating or continuing treatment has high-stake maternal and fetal implications; thus, the negative consequences of the current assessment standards need to be examined.

Barriers to treatment in all populations include poor attendance, early dropout, and drug relapse. Although some research has evaluated the impact of MT on addiction recovery, this examination has not been performed in a pregnant sample. In addition, much of research found has evaluated treatment success solely relying on UDSs using the presence or absence of opioids for determination of recovery or relapse ACOG/*Opioid use and opioid use disorder in pregnancy*). Fear of detection, stigma, and legal ramifications of continued drug use as indicated by positive UDS impacts the common

challenges (retention and relapse) to maintaining addiction recovery for pregnant women receiving MT. Routine urine drug screening is controversial for several reasons. A positive drug test result is not in itself diagnostic of OUD or its severity (ACOG/*Opioid use and opioid use disorder in pregnancy*). Urine drug testing only assesses for current or recent substance use; therefore, a negative test does not rule out sporadic substance use. For some women, UDS can be viewed as punitive and deter women from continuing treatment or cause women to be removed from necessary treatment.

There is a significant need to better understand how treatment success for pregnant women enrolled in MT programs is defined. The impact of evaluating functional outcomes as a measure of treatment success for pregnant women enrolled in MT is critical. Comprehensive addiction treatment programs, that focus on harm-reduction by incorporating the four dimensions of recovery (health, home, purpose, and community) and are tailored to meet women's needs, have been found to lead to improved recovery outcomes for both mother and infant. Recovery-oriented care and recovery support systems help people with mental and SUDs manage their condition successfully.

Demographics of Opioid Use

Opioid-involved overdose death rates in the United States differ by demographic and geographic characteristics. In 2018, 2 million people in the U.S. ages 12 and older, had OUD involving prescription opioids, heroin, or both (NIDA.NIH.gov/*Principles of drug addiction*). With the growing rates of addiction, it is no surprise that our nation faces a crisis of increasing overdose deaths. More than 90,000 people have died since 1999 from a drug overdose (NIDA.NIH.gov/*Drug overdose death rates*). Nearly three

quarters (75%) of these deaths involved a prescription or illicit opioid (NIDA.NIH.gov/*Drug overdose death rates*). These deaths represent a mere fraction of the total number of Americans harmed by opioid misuse and addiction. Overdose deaths have increased in all categories of drugs examined for people ages 12 and older, and includes all races and ethnicities, across all levels of urbanization (Hedegaard et al., 2017). As public health efforts continue to address the opioid epidemic, clinicians, researchers, and public health officials must consider how these epidemics affect groups and individuals differently. In a study by Bagley and colleagues (2020), findings provide an important reminder that failure to consider factors, such as sex and age, in studies of opioid misuse may result in missing important differences with direct implications for prevention and treatment.

Age and Gender

While drug use may begin at a young age, addiction to drugs is not specific to age or gender. Worldwide, about 275 million people (or 5.5% of the global population aged 15–64 years) used drugs at least once in 2019 (SAMHSA.gov/*NSDUH*). Among them, about 62 million people used opioids. Rates of opioid misuse vary by age, with young adults ages 26 years or older having the highest rates of OUD (SAMHSA.gov/*NSDUH*). Results from the 2020 NSDUH show that among people aged 12 or older, 1.0% (or 2.7 million people) had an OUD in the past year (SAMHSA.gov/*NSDUH*). Those results also show that the percentage of adolescents aged 12 to 17 (0.3% or 80,000 people) was lower than the percentages of young adults aged 18 to 25 (0.9% or 286,000 people) or adults aged 26 or older (1.1% or 2.3 million people) that reported past year use.

Although generally associated with adolescents and young adults, the prevalence of opioid use among older adults (age 26+) is steadily increasing. According to a 2020 report from the National Center of Health and Statistics, 5.7% of US adults used one or more prescription opioids in the 30 days prior to sampling between 2015 and 2018 (CDC.gov/*Prevalence of prescription pain medication use among adults: United States, 2015–2018*). The same report shows that prescription opioid use was significantly higher among women than men (women: 6.4% vs. men: 4.9%), and overall use increased with age (20–39 years: 2.8%; 40–59 years: 6.6%; 60+ years: 8.2%). Data also shows that opioid use was higher among women than men for non-Hispanic White (13.7% vs. 9.4%), non-Hispanic Black (12.2% vs. 7.4%), and Hispanic (10.2% vs. 6.8%) adults (CDC.gov/*prevalence of prescription pain medication use among adults: United States, 2015–2018*). These alarming statistics highlight a critical need for prevention and treatment, specifically among middle-aged women.

Increasingly, researchers have begun to consider the role of gender in the opioid epidemic (Silver & Hur, 2020). However, gaps in research comparing sex or gender in relation to addiction is understudied. Twenty years ago, the demographic profile for individuals with OUD would have consisted primarily of White, young adult males but now, we are seeing a separate cohort of incoming OUD patients that are female, older in age and misusing prescription opioids (Sanger et al., 2020).

People may face unique issues when it comes to substance use, as a result of both sex and gender (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). Research has shown that women often use drugs differently, respond to drugs differently, and can have unique obstacles when seeking treatment

(NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). The distinctions between men and women suffering from addiction stem from biological and sociological differences. Biological factors such as, sex chromosomes, hormones, and body size and composition influence how men and women can become addicted to drugs (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). Sociological norms are impacted by society. Examples of these are societal expectations, childcare responsibilities, and stigma (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). Examining opioid use by race/ethnicity and gender offers a closer look at disparities among groups.

Ethnicity and Race

The epidemiology of opioid use points to an evolving epidemic that is impacting every demographic group across the nation, with severe consequences and significant rising rates of OUD and overdose among men and women across the United States (Barbosa-Leiker et al., 2020). Over 35,000 White Americans died from opioid overdose in 2018 (KFF.org/*Opioid overdose deaths by race/ethnicity*). As the epidemic increases, rates for non-Hispanic White adults have risen exponentially when compared with other groups (Mason et al., 2022). While White people continue to experience the highest rates of opioid misuse and deaths from opioid overdose, studies show that some subsets of the American population are disproportionally affected by substance abuse, and access to addiction treatment does differ, often by race and gender (NIDA.NIH.gov/*Access to addiction services by race and gender*). However, according to the research, the ongoing opioid crisis has largely reported its impact on either the White or the total US population and has not focused on trends by race or ethnicity (Alexander et al., 2018). Part of this

could be that there is a lack of effective addiction treatment in rural areas, an estimated 92% of addiction treatment facilities are in urban locations (Hancock et al., 2017).

In general, White Americans have fewer barriers to treatment than some other races in the U.S. However, Americans of any race in rural areas, those in poverty, and those with no health insurance coverage have a difficult time accessing addiction treatment (Hancock et al., 2017; Soni et al., 2018). According to a (2016) HCUP survey that measured opioid-related hospitalizations among women aged 15 or older in the U.S. showed that, overall, White women had the highest rate of opioid-related hospital stays across all income levels (Weiss et al., 2019). The same survey also showed that White and Black women had a similar rate of opioid-related stays in large metropolitan areas, yet in rural areas, Black women had a lower rate of opioid stays compared to White women. (Weiss et al. 2019).

Disparities in to access to quality treatment play a role in every aspect of healthcare and health outcomes, and the opioid crisis is no different (Volkow, 2019). Studies show that minorities and poor people with OUDs remain at a disadvantage when it comes to accessing appropriate treatment and that women face greater barriers to both treatment and overdose reversal than men do (Volkow, 2019). A retrospective cohort study of patients receiving buprenorphine from one large urban clinic found that minority patients were much less likely than Whites to be retained in treatment for at least 1 year (Weinstein et al., 2017).

Racial and ethnic disparities persist across key health and substance use treatment outcomes for mothers and infants (Schiff et al., 2020). Literature has shown that early enrollment and maintenance in MT for pregnant women with OUD has been known to

have better outcomes for mothers and infants however only half of all pregnant women with OUD receive these medications (Harter, 2019; Klaman et al., 2017). The extent to which maternal race or ethnicity is associated with the use of medication to treat OUD is unknown (Schiff et al., 2020). A study conducted by Schiff et al. (2020) examined the impacts of maternal race and ethnicity on treatment of OUD during pregnancy. The study was a retrospective study cohort study that used a population-level statewide data set of pregnant women with OUD (n = 5,247) who delivered a live infant during the study period. The study found that Black non-Hispanic and Hispanic women with OUD were significantly less likely to use any medication for treatment and were less likely to consistently use medication for treatment during pregnancy compared with White non-Hispanic women with OUD. Thus, the study findings illustrate that racial and ethnic disparities do exist in the use of medications for treatment of OUDs during pregnancy and that further investigation is warranted to explore the factors associated with inequitable access to receipt of medication.

Minority groups or people of color may suffer from substance abuse or mental health disorders at high rates part due to difficulties accessing care, the right kind of care not being available, and environmental, social, and financial concerns may be barriers to treatment (SAMHSA.gov/*Highlights by race/ethnicity for the 2021 NSDUH survey*). In addition, previous or current substance misuse, history of mental health diagnoses, longer exposure to opioids, and being prescribed higher opioid doses have been associated with the development of misuse.

Anxiety, Trauma and Post Traumatic Stress Disorder

Co-occurring substance use and mental disorders among people with OUD increases the risk for morbidity and mortality (Jones & McCance-Katz, 2019). Addressing these co-occurring conditions is critical for improving treatment and health outcomes (Jones & McCance-Katz, 2019). Results from the (2020) NSDUH reported that among adults aged 18 or older, (6.7%) or 17.0 million people had a co-occurring mental illness (AMI) and a SUD, and (2.2%) or 5.7 million people had both a serious mental illness (SMI) and a SUD in the past year. The same survey also reported that about half of adults aged 18 or older in 2020 with a co-occurring SUD and AMI in the past year received either substance use treatment at a specialty facility or mental health services in the past year (50.5%), but only 5.7% received both services (SAMHSA.gov/*Highlights by race/ethnicity for the 2021 NSDUH survey*).

According to a study conducted by Jones & McCance-Katz (2019) that analyzed the prevalence of co-occurring substance use and mental health disorders and receipt of mental health treatment among adults aged 18–65 with OUD, found that receiving both mental health and substance use treatment services in the past year was reported by 24.5% of adults with OUD and AMI and 29.6% of adults with OUD and SMI. These findings suggest that expanding access to comprehensive service delivery models that address the substance use and mental health co-morbidities of this population is urgently needed.

Research evidence suggests that the presence of comorbid psychiatric disorders may increase the likelihood of prescription opioid misuse and OUD. According to a (2016) HCUP study on opioid-related hospital stays among women in the U.S., findings

showed that co-occurring mental disorders were present with 56.5% of opioid-related hospital stays compared with only 26.5% of non-opioid-related stays for women, and White women had a somewhat higher percentage of co-occurring mental disorders (59.1%) compared with other racial/ethnic groups (range: 46.4%–52.0%). Co-occurring psychiatric disorders are more prevalent among women than men, (Greenfield et al., 2007) with women more likely to report experiencing a traumatic event and the onset of posttraumatic stress disorder before the development of a SUD (Compton et al., 2000; Copeland et al., 2020; Sonne et al., 2003).

Furthermore, women entering treatment for substance use typically present with a profile of more severe medical, behavioral, psychological, and social problems than men despite a shorter duration of use (Greenfield et al., 2007; Greenfield et al., 2010). A study by Bagley and colleagues (2020) found that among youths and young adults with history of nonfatal opioid overdose, psychiatric comorbidity was more common in girls and young women than their male peers. This is consistent with findings from McHugh et al. (2013) that suggest that among adults with OUD, psychiatric comorbidity is more prominent in women than men. Bagley et al. (2020) found that two-thirds of girls and young women experienced depression or anxiety, and 16% experienced a traumatic stress-related disorder. Furthermore, more than 60% experienced chronic pain, a rate higher than their male peers, which is also consistent with findings from the study of adults with OUD by McHugh et al. (2013).

There is limited recent research on the prevalence of co-occurring disorders, demographic characteristics associated with co-occurring disorders, and receipt of mental health and substance use treatment services among those with OUD (Jones & McCance-

Katz, 2019). A cross-sectional study by Davis et al. (2017) examined the relationship between mental health (mood and anxiety) disorders and prescription opioid use (defined as receiving at least two prescriptions per calendar year) found that adults with mental health conditions receive 51.4% (60 millions of 115 million prescriptions) of the total opioid prescriptions distributed in the U.S. each year. The same study also concluded that when compared with adults without mental health disorders, adults with mental health disorders were significantly more likely to use opioids (18.7% vs. 5.0%; $P < .001$). In adjusted analyses, having a mental health disorder was associated with prescription opioid use overall (odds ratio, 2.08; 95% confidence interval, 1.83–2.35; Davis et al., 2017).

Mood and anxiety disorders are highly associated with nonmedical prescription opioid use (Kissin et al., 2012). Although some of these comorbid conditions precede OUD, others emerge after its onset. Anxiety, chronic pain, or depression may precede or follow development of OUD. A systematic review by Fatséas et al. (2010) using DSM-IV criteria revealed a lifetime prevalence of anxiety among those with an OUD ranging from 26%–35%. Fatséas et al. (2010) reviewed literature to evaluate the prevalence and temporal sequence of co-occurrence of anxiety disorders with opiate dependence in order to better define the relationship between these two disorders and to improve diagnosis and treatment. Their findings concluded that when an anxiety diagnosis precedes the diagnosis of OUD, opioids or other substances are often used to self-medicate in attempts to relieve the symptoms and feelings or anxiety (Fatséas et al., 2010). In the contrary sequence, when the diagnosis of OUD emerges as the primary diagnosis with anxiety

following as a resultant symptom, often it can be resultant of opioid withdrawal through recovery (Fatséas et al., 2010).

The identification of substance-induced- versus independent anxiety disorder has important treatment implications. Given the high rates of relapse among patients with OUD, it is crucial to identify modifiable risk factors for negative treatment outcomes (Baxley et al., 2018). Anxiety sensitivity (AS) is one such risk factor that may be associated with negative OUD treatment outcomes (Baxley et al., 2018). The Baxley et al. study examined the potential impact of AS on the withdrawal process, subsequent treatment engagement, and relapse among individuals with OUD. They found greater AS and that younger age predicted greater fear of withdrawal during detoxification. Contrary to the research hypotheses, AS was not a significant predictor of other treatment outcomes; rather, fear of withdrawal and prior number of opioid detoxifications predicted greater subjective withdrawal severity (Baxley et al., 2018).

PTSD and mental illness have been found to commonly co-occur; in particular, a growing body of literature points to high rates of PTSD among opioid-using populations (Dahlby & Kerr, 2020; Ecker & Hundt, 2018; Roberts et al., 2015). Despite high prevalence rates of PTSD among SUD/OUD populations, patients seeking treatment for substance use are rarely assessed for trauma or offered PTSD-based interventions alongside SUD treatment (Dahlby & Kerr, 2020; Roberts et al., 2015). Studies have shown that there is a high incidence of PTSD, with lifetime prevalence rates ranging from 26–52% among individuals with SUD; Roberts et al., 2015). However, little research is available on rates of PTSD among OUD individuals. Preliminary evidence suggests that rates are equally high among individuals with OUD, with 41% having a lifetime history

of PTSD and 33.2% meeting criteria for a current PTSD diagnosis (Ecker & Hundt, 2018).

A study by Rosic et al. (2021) examined the lifetime prevalence of traumatic events and past-month prevalence of PTSD in patients treated for OUD. The study data aimed to explore the relationship between trauma, PTSD, and treatment outcomes in participants (N = 674) enrolled in MT (Rosic et al., 2021). Results of the study showed that 11% met past-month criteria for PTSD, and 48% reported history of traumatic events with no current PTSD (Rosic et al., 2021). Participants with PTSD were more likely to be female and less likely to be employed or married than those with no trauma history (Rosic et al., 2021).

Studies have shown that while men are more likely to experience a traumatic event within their lifespan, women are two to three times more likely than men to develop PTSD as a result of a traumatic event. (Brady et al., 2016; Olff, 2017). The lifetime prevalence of PTSD is about 10–12% in women and 5–6% in men (Olff, 2017). There are similar differences between the sexes for (comorbid) disorders such as major depression and anxiety disorders (Olff, 2017). It is known that men and women experience different types of traumas, both in private life and at work, with women being exposed to more high-impact trauma (e.g., sexual trauma) than men, and at a younger age (Olff, 2017).

Despite the high prevalence of rates of PTSD among opioid-using populations, patients seeking treatment for substance use are rarely assessed for trauma or offered PTSD-based intervention alongside SUD treatment (Roberts et al., 2015). Research suggests that individuals with opioid dependency and a comorbid diagnosis of PTSD

have poorer recruitment, retention, and adherence, as well as poorer treatment outcomes (Meshberg-Cohen et al., 2021; Schäfer & Najavits, 2007). Recent studies have also found compelling evidence that PTSD symptom severity may undermine opioid agonist treatment (OAT) retention and outcomes, i.e., with every 10% increase in PTSD symptom severity, there is an associated 36% increased risk in OAT interruption, and re-traumatization is associated with double the risk of OAT interruption (Dahlby & Kerr, 2020; Ecker & Hundt, 2018; Schacht et al., 2017).

The acknowledgment and recognition that some people develop mental health problems related to their compulsive drug use, and some people take drugs in an attempt to alleviate symptoms of mental health disorders is important. Mental illness, often undiagnosed, increases the risk for OUD. Patients with a history of depression, PTSD, or anxiety are more likely to suffer from substance abuse, as well as patients with histories of childhood trauma and abuse (Sharma et al., 2016). The acknowledgment and recognition that some people develop mental health problems related to their compulsive drug use, and some people take drugs in an attempt to alleviate symptoms of mental health disorders is important. Several of these studies reveal the need for a complete revamping of the nation's prevention efforts to tailor programs to the unique motivations and vulnerabilities of those with mental health and co-occurring OUD diagnoses. There is an insufficient coordination of care between clinicians and inadequate access to specialists such as mental health and substance use counselors trained in evidence-based treatment. Studies show that the inability to refer to behavioral health and psychosocial services are major barriers for primary care clinicians wanting to treat SUDs

(Hutchinson et al., 2014; Priester et al., 2016). Having collaborative care models aimed at addressing the needs of people who have both OUD and mental health conditions is vital.

Criminal Justice System Involvement

OUDs are highly prevalent among criminal justice populations. (NIDA.NIH.gov/*How is opioid use disorder treated in the criminal justice system?*). Drug-related crimes and seizures of illicit drugs point to a sharp rise in the opioid crisis (Bonnie et al., 2017). One in four individuals with OUDs are involved with the CJS during the course of a year (SAMHSA.gov/*Center for Behavioral Health Statistics and Quality, 2016*), stemming from the debilitating effects of these disorders and the criminal behavior that often accompanies opioid use (Grella et al., 2021). Having an involvement in the CJS has the potential to increase the risk of traumatic experiences and thus can precipitate OUD. Additionally, entering the penal system in the United States while suffering with an OUD can further exacerbate an already difficult situation.

As the opioid epidemic shifts rapidly from prescription opioids to heroin, illicitly manufactured fentanyl, and other illicit drugs, more individuals, many of whom live with OUD, are coming into contact with the CJS (Bonnie et al., 2017). Boutwell et al. (2006) conducted a study analyzing data on arrests, incarcerations, and heroin use estimate that 24–36% of all people with OUD involving heroin pass through U.S. prisons and jails each year, although this figure may be different today owing to changes in the heroin-using population. In a cross-sectional study conducted by Winkleman, Chang, et al. (2018), individuals who reported any level of opioid use were more likely than individuals who reported no opioid use to have physical and mental health conditions and co-occurring substance use. The same study also reported that involvement in the CJS

increased with intensity of opioid use, and any level of opioid use was significantly associated with involvement in the CJS in the past year (Winkelman, Chang, et al., 2018).

Criminal justice-involved populations with OUD have high rates of relapse, future arrests, and death upon release (Soares et al., 2019). The study by Soares (2019) and colleagues reports that while medication for OUD reduces opioid relapse, concerns regarding diversion and stigma limit treatment in CJS populations. Individuals who use opioids have complicated health profiles and high levels of involvement in the CJS. National household-based surveys exclude people who are incarcerated and other institutionalized populations. Thus, trends in the epidemiology of opioid use and misuse, OUD, and overdose in this large, underserved, and particularly vulnerable population often are missed, as is the chance to provide lifesaving treatment and medications to a high-risk population at a high-risk point in time (Bonnie et al., 2017).

OUD is prevalent in criminal justice settings, and improved access to effective treatments and collection of surveillance data with which to track opioid use and associated harms in these settings are needed (Bonnie et al., 2017). A study conducted by Guastaferro and colleagues (2022) explored the relationship between demographics, substance use severity, and access to treatment and OAT receipt. Findings indicate that fewer than 6% of CJS cases received OAT as part of their treatment plan (Guastaferro et al., 2022). Combating the opioid epidemic will require public health interventions that involve CJSs, as well as policies that reduce involvement in the CJS among individuals with SUD.

Other Drugs and Alcohol Use

Interventions to address the U.S. opioid crisis primarily target opioid use, misuse, and addiction, but because the opioid crisis includes multiple substances, the opioid specificity of interventions may limit their ability to address the broader problem of polysubstance use (Compton et al., 2020). Polysubstance use involves the consumption of more than one substance at once. Although polysubstance abuse often refers to abuse of multiple illicit drugs, it is also inclusive of prescription medications used in nonmedical circumstances (American Addiction Centers.org/*Polysubstance use & misuse: The unique treatment needs of polydrug users*). According to the NSDUH (2020), 40.3 million people aged 12 or older (or 14.5% of this population) had an SUD in the past year, including 28.3 million who had alcohol use disorder and 18.4 million who had an illicit drug use disorder. The percentage reported was highest among adults aged 18 to 25 (8.2 million or 24.4%) followed by adults aged 26 or older (30.5 million or 14.0%). The survey results also show that among people aged 12 or older, 5.3 million (53.0%) had past-year marijuana use, 1.5 million (14.7%) had past-month heavy alcohol use, 1.6 million (15.6%) had past-year cocaine use, 873,000 (8.7%) had past-year methamphetamine use, related to their past-year opioid misuse.

A study by Ford and colleagues (2021) examined trends in polysubstance use among adults in treatment for OUD. Their findings showed that treatment admissions between 1992–2017 involving opioid/cocaine and opioid/alcohol co-use decreased while opioid/methamphetamine and opioid/benzodiazepine co-use increased (Ford et al., 2021).The same study also reported that in 2016 to 2017, receipt of medications for OUD was significantly higher for those who used opioids only (38.5%; 95% confidence

interval [CI] 38.4–38.6) compared with individuals who used opioids with cocaine (35.7%; 95% CI 35.6–35.9), methamphetamine (23.9%; 95% CI 23.7–24.2), alcohol (25.0%; 95% CI 24.8–25.2), or benzodiazepines (34.6%; 95% CI 34.3–34.9; Ford et al., 2021).

A study by Winkelman, Chang, et al. (2018) found that among adults who reported varying levels of opioid use, as intensity of opioid use increased, the likelihood of using a given substance increased. Most individuals with prescription opioid misuse, prescription OUD, or heroin use in the past year reported use of one or more additional substances (Winkelman, Chang, et al., 2018). In the same study more than 50% of individuals with a prescription OUD or heroin use also reported using or misusing sedatives or tranquilizers. Lin and colleagues (2021) conducted a retrospective study to compare veteran patients with OUD only to those with additional SUDs and examined association with OUD treatment receipt. Study findings concluded that patients with OUD + 1 SUD and patients with OUD $\geq$ 2 SUDs had lower odds of receiving buprenorphine treatment compared with OUD-only patients.

According to the NSDUH (2020), among women 18 or older with an SUD, one in eight (13.3% or 956,000) struggled with illicit drugs and alcohol in the past year. The (2019) survey also reports that among women 12 or older, 21.0 million (14.8%) used marijuana, 2.1 million (1.5%) used cocaine, 737,000 (0.5%) used methamphetamines, and 231,000 (0.3%) used heroin in the past year (SDUH, 2020). It is also important to examine other substances use in conjunction with opioid misuse. The (2019) NSDUH survey found that among women 12 or older who reported opioid misuse related to other substance use, 2.3 million (49.1%) had past-year marijuana use, 543,000 (11.7%) had

past-year cocaine use, and 307,000 (6.6%) had past-year methamphetamine use related to their opioid misuse in the past year. The same results also evaluated opioid misuse related to major depressive episode (MDE) and serious mental illness (SMI) among women 12 or older, finding showed that 1.3 million (28.7%) had a past-year MDE, 1.1 million (24.7%) had a past-year SMI related to their past-year opioid misuse (SAMHSA.gov/*Highlights for the 2020 NSDUH*).

SUDs including the misuse of substances other than opioids, such as alcohol and methamphetamines affect women across all racial and ethnic groups, socioeconomic backgrounds, and rural, urban, and suburban locales (McHugh et al., 2014). Individuals, including pregnant and parenting women, with OUD also often misuse other substances (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). Polysubstance use has been identified in White women, of reproductive age from predominantly rural areas with lower socioeconomic status (M. Jarlenski et al., 2017). A 2020 study by Jarlenski found that polysubstance use among pregnant women with OUD increased from 60.5% (95% CI 58.3–62.8%) to 64.1% (95% CI 62.8%–65.3%). The study also reported that differential time trends in polysubstance use among women with OUD were found in rural compared with urban counties.

Study findings concluded that large increases in amphetamine use occurred among those in both rural and urban counties (255.4%; 95% CI 90.5–562.9% and 150.7%; 95% CI 78.2–52.7%, respectively), similarly to tobacco use (30.4%; 95% CI 16.9–45.4% and 23.2%; 95% CI 15.3–31.6%, respectively). Results also showed that cocaine use diagnoses declined among women with OUD at delivery in rural (−70.5%; 95% CI −80.4% to −55.5%) and urban (−61.9%; 95% CI −67.6% to −55.1%) counties.

Alcohol use diagnoses among those with OUD declined −57% (95% CI −70.8% to −37.7%) in urban counties but did not change among those in rural counties (Jarlenski et al., 2020).

Increasing prevalence of OUD among women has been accompanied by an increase in adverse pregnancy and birth outcomes, including NAS (Jones, O'Grady, et al., 2008). Effective prevention and treatment strategies exist for opioid misuse and use disorder but are highly underutilized across the United States (NIDA.NIH.gov/*Treatment and recovery*). The continued growth in the opioid epidemic has had the effect of creating silos, so to speak, in that researchers and policymakers, particularly when it comes to treatment, increasingly are focused almost exclusively on OUD, rather than taking a more holistic view of SUDs.

Treatment Options

The opioid epidemic has had a devastating impact on health in the United States. The NSDUH reports that in 2020, 9.5 million people aged 12 years or older misused opioids in the past year (SAMHSA.gov/*Treatments for substance use disorders*). The same survey reported that 2.7 million people reported having an OUD in the past year (SAMHSA.gov/*Treatments for substance use disorders*). Unfortunately the number of individuals who misue opioids is extremely high compared to the number of people who are actually diagnosed with an OUD. Diagnosis and treatment of OUD are an important factor in an indvidual's recovery. Treatment programs can tailor their services to meet the needs of the diverse patient population that has OUD. An emphasis on treatment with medications for opioid use disorder, specifically the FDA-approved medications methadone, buprenorphine, and extended-release naltrexone, is warranted because these

medications have been shown to be highly effective in saving lives (National Academies of Sciences, Engineering, and Medicine. (2019). Among the 2.5 million people aged 12 or older with a past-year OUD, 11.2% (or 278,000 people) received MT in the past year for opioid misuse. (SAMHSA.gov/*Treatments for substance use disorders*). These findings imply that approximately 88.8% of individuals with OUD nationwide who may benefit from MT treatment do not receive it. The treatment gap continues to be an obstacle in addressing OUD in the U.S. Although there has been an increase in the number of individuals seeking treatment, the overall percentages of people with SUDs who need treatment but don't receive it remain exceedingly high, and far above what is seen in the mental health community (Enos, 2018).

According to the 2020 NSDUH, among the 41.1 million people aged 12 or older who needed substance use treatment in the past year, 6.5% (2.7 million) received substance use treatment at a specialty facility in the past year. Despite these alarming statistics, there still remains a very high percentage of individuals who do not seek treatment. In 2020, among 38.4 million people aged 12 or older with a SUD in the past year who did not receive substance use treatment, 97.5% (37.5 million people) did not feel they needed treatment, 1.9% (737,000 people) felt they needed treatment but did not make an effort to get treatment, and 0.5% (211,00 people) felt they needed treatment and made an effort to get treatment (SAMHSA.gov/*Treatments for substance use disorders*).

Among the challenges that come with seeking treatment options are the types of treatment that are not one size fits all and thus should be person-centered and individualized to fit the needs that suit the individual. Some providers and policymakers assume that the best course of treatment for OUD is in an inpatient setting, while much of

the evidence shows that outpatient treatment in the community provides several benefits and an appropriate level of care for many individuals, allowing people to live in their communities, retain employment and/or education, and remain near their support networks, including family and friends (SAMHSA.gov/*Medications, counseling, and related conditions*).

Effective prevention and treatment strategies exist for opioid misuse and use disorder but are highly underutilized across the United States (Bose et al., 2016). A recent report by the National Academies of Science, Engineering and Medicine found that individuals undergoing long-term treatment with methadone or buprenorphine reduced the risk of death 50% (National Academies of Sciences, Engineering, and Medicine. (2019).

Individuals diagnosed with OUD may face challenges with stopping use of opioids on their own. Like many other chronic conditions, OUD can be treated successfully with the right help. There are different types of MT programs; some programs give more structure, while other programs offer more flexibility. Treatment programs can include pharmacotherapies and psychosocial approaches. Pharmacotherapeutic approaches include MT with a variety of medications (methadone, buprenorphine and naltrexone). Psychosocial approaches which include abstinence-based model behavioral interventions that include MI and CBT modalities may be used as stand-alone interventions or in combination with pharmacotherapy. Although some patients have successfully maintained abstinence using only psychosocial approaches, counseling without support for OUD is often associated with a return to use (Smyth et al., 2010).

A study by Wakeman et al. (2020) examined associations between OUD treatment pathways and overdose and opioid-related acute care use as praxis for OUD recurrence. Among (N = 40,885) individuals with OUD who were exposed to six mutually exclusive treatment pathways (no treatment, inpatient detoxification, intensive behavioral therapy, buprenorphine or methadone, naltrexone, and nonintrusive behavioral therapy), findings showed that treatment with buprenorphine or methadone was associated with reductions in overdose and serious opioid-related acute care use compared with other treatments (Wakeman et al., 2020). A review of literature published by Sofuoglu et al. (2018) investigated OUD treatments, including their mechanism of action, efficacy, clinical guidelines in the U.S., and consideration of frequently occurring comorbid conditions. Their literature results concluded that MT is the first-line treatment for patients with OUD and should be provided with behavioral interventions. Findings also concluded that treatment retention remains challenging and proposes that the future studies focus on approaches that best serve the complex needs of patients with OUD, including those with comorbid psychiatric and substance use conditions (Sofuoglu et al., 2018)

Abstinence-Based Model

Abstinence is the most traditional form of addiction treatment. Abstinence-based programs or models are often known as detoxification, or "detox," programs. The goal of these programs is to stop or abstain from all opioid use, often within 30 days or less. While the benefits of these programs may be lower cost to the individual and nonpharmacologic, studies show that people with OUD who follow detoxification with complete abstinence are very likely to relapse, or return to using the drug (Bart, 2012).

Abrupt cessation of opioids after repeated use can produce an intense but rarely life-threatening withdrawal syndrome, which can be understood as an adaptation to maintaining homeostasis or allostatic process (Koob & Volkow, 2016). As withdrawal progresses, tachycardia, tachypnea, hypertension or hypotension, and dehydration can appear. Note that this is distinct from the protracted withdrawal syndrome characterized by dysphoria, craving, and insomnia that reflects brain circuitry neuroadaptations associated with addiction. Symptoms of acute withdrawal (as well as protracted withdrawal) can be a powerful trigger for relapse for individuals with OUD (Blanco & Volkow, 2019), but can also lead to opioid seeking in pain patients in whom acute opioid withdrawal is not properly managed.

Zhu et al. (2018) reported findings from a secondary analysis of original data obtained from a multisite trial study, Starting Treatment with Agonist Replacement Therapies (START) that randomized (N = 1,269) opioid-dependent individuals to receive buprenorphine (n = 740) or methadone (n = 529) in nine sites during 2006–2009. A follow-up study was conducted during 2011–2016 with three assessments 1-year apart. A total of (n = 699) individuals had a follow-up period of 5+ years after the START study randomization and were included in the study. The study examined opioid abstinence according to two categories: (a) individuals who were abstinent from heroin only and (b) individuals who were abstinent from opioids, including both heroin and other opioids (e.g., hydrocodone, oxycodone, other opioid analgesics, excluding methadone or buprenorphine). The study compared abstinent and non-abstinent participants to ascertain if long-term opioid abstinence is associated with improved functioning in other life domains (Zhu et al., 2018). The study found that among individuals seeking medication

treatment for OUD as participants in a clinical trial and followed for at least 5 years, 33.2% achieved stable abstinence from heroin for at least 5 years, and 20.7% were abstinent from heroin and other opioids. Compared to non-abstinent participants, those with long-term abstinence demonstrated lower problem severity at the final follow-up in many key life domains (i.e., drug use, employment, social/family, legal, and psychiatric areas for both abstinent classifications, with additional improvement in medical conditions for those with long-term abstinence from heroin and other opioids). Results also concluded that for both abstinence classifications, older age at opioid initiation, greater social support, and longer duration of treatment were positively associated with stable abstinence (Zhu et al., 2018). It is clear that there is no one-size-fits-all approach to treating persons with OUD, and a combination of both medications and behavioral treatment should be included in the treatment plan for patients in MT for OUD.

Behavioral Interventions

It is known that many OUD diagnoses include other comorbidities such as depression, anxiety, eating disorders, polysubstance use, and many other mental health conditions (Bart, 2012) interventions have been tested in the treatment of SUDs, making them viable options for the treatment of OUDs (American Psychiatric Association, 2013). These interventions include psychotherapies, in particular, MI and CBT.

Motivational Interviewing

MI was developed by Dr. William R. Miller in 1983, when he first referenced the technique in an issue of *Behavioral Psychotherapy* (*Motivational Interviewing - Addiction Center*, n.d.). MI is a conversational person-centered method of communication that targets ambivalence to change by helping people identify their

readiness, ability, and willingness to change (Mumba et al., 2018). When faced with an addiction, one of the most difficult hurdles to overcome is a lack of motivation (Addiction Center.com/*Motivational interviewing*). MI does not focus on the underlying causes of an addiction, such as past traumas or mental illnesses. It is intended to be used in addition to other forms of therapy, such as CBT. Effects of MI include decreased depression, decreased prescription drug misuse, increased self-efficacy, and increased motivation to change (Chang et al., 2015).

The associated increase in abstinence self-efficacy is associated with better outcomes in drug rehabilitation programs as well as an improvement in psychiatric comorbidity symptomology (Chang et al., 2015). MI can be carried out in a variety of settings such as primary care, outpatient clinics, and inpatient rehabilitation programs (Hamera, 2014). A review of literature conducted by Buckner et al. (2021) was conducted to examine extant literature of hospital-based motivation-based interventions for opioid misuse. The need for this review was sought to address the lack of evidence in interventions and techniques to increase intrinsic motivation and opioid misuse. The results concluded that there is a lack of compelling evidence that brief interventions that include motivation-based interventions work in the absence of concurrent pharmacotherapy and/or referral to post discharge treatment providers (Buckner et al., 2021).

Cognitive Behavioral Therapies

CBT is a type of psychotherapy used in treating a variety of mental health conditions (May et al., 2015). CBT has also been associated with improved social functioning and quality of life in various populations (APA, 2013). The mainstay of CBT

is to change patterns of thinking leading to behavioral change that allows individuals to cope better with psychological problems. Specifically for SUDs such as OUDs, CBT focuses on components such as avoidance of stimuli, coping skills training, behavior rehearsal, feedback, and mood regulation (APA, 2013).

Although opioid agonist maintenance is the standard of care for OUD, problems with retention and continued drug use are still common (Moore et al., 2016). A systematic review conducted by Amato et al. (2011) examined treatment efficacy data of 13 different psychosocial interventions in the context of agonist maintenance treatment for OUD. The authors concluded that such interventions do not improve treatment outcomes compared to standard agonist maintenance treatment (Amato et al., 2011). A study by Fiellin et al. (2013) evaluated the impact of CBT on outcomes in primary care, office-based buprenorphine/naloxone treatment of opioid dependence. The study was conducted over a 24-week randomized clinical trial in (N = 141) opioid-dependent patients in a primary care clinic. Study patients were randomized to physician management or physician management plus CBT. Results concluded that among patients receiving buprenorphine/naloxone in primary care for opioid dependence, the effectiveness of physician management did not differ significantly from that of physician management plus CBT (Fiellin et al., 2008).

Several studies have evaluated CBT, which despite demonstrated effectiveness with all other substances of abuse and a range of other psychiatric disorders (Butler et al., 2006, Hofmann & Smits, 2008, McHugh & Otto, 2010), did not improve treatment outcomes for opioid dependent patients receiving buprenorphine. However, a limitation to these studies is that they combined both heroin and prescription opioid dependent

populations and did not examine outcomes based on primary opioid of abuse (Moore et al., 2016). It is hypothesized that given CBT's known effectiveness with other drugs of abuse, CBT may improve treatment outcomes compared to physician management alone for prescription opioid abuse (Moore et al., 2016). In conclusion, the effects of CBT and MT need to be more closely examined for individuals with OUD.

Medication Treatment for Opioid Use Disorder

Medications are central to the treatment of OUD. Medication treatment is primarily used for the treatment of addiction to opioids such as heroin and prescription pain relievers that contain opiates. The prescribed medications operate to normalize brain chemistry, block the euphoric effects of alcohol and opioids, relieve physiological cravings, and normalize body functions without the negative effects of the abused drug (SAMHSA.gov/*Medications for substance use disorders*). Similar to taking medication to manage other chronic illnesses, like diabetes or high cholesterol, studies show that individuals in MT programs are more likely to stay in treatment than those in detox or abstinence-based programs (Moore et al., 2016). As with other chronic medical illnesses, opioid addiction, once developed, has no cure, and requires ongoing monitoring and treatment (McLellan et al., 2000). Therapy alone and abstinence-based models rather than MT have dominated opioid treatment until now (Velander, 2018). Despite detoxification combined with psychosocial treatment, relapse rates remain at 90% or higher (Velander, 2018). These high relapse rates have been confirmed in populations that abuse heroin as well as prescription opioids (Weiss et al., 2011).

Studies show that people with OUD who follow detoxification with complete abstinence are very likely to relapse, or return to using the drug (Bart, 2012; Velander,

2018). While relapse is a normal step on the path to recovery, it can also be life threatening, raising the risk for a fatal overdose (Davoli et al., 2007). Thus, an important way to support recovery from heroin or prescription OUD is to maintain abstinence from those drugs. Someone in recovery can also use medications that reduce the negative effects of withdrawal and cravings without producing the euphoria that the original drug of abuse caused (SAMHSA.gov/*Medications for substance use disorders*). Currently, there are several MT options available for the treatment of opioid dependence, including medication-assisted treatment using full opioid agonists (i.e., methadone), partial μ-opioid agonists (buprenorphine), or opioid antagonists (naltrexone).

Buprenorphine

Buprenorphine was approved for use in the treatment of opioid dependence by the FDA in 2002 (Mcnicholas, 2004). Buprenorphine is a long-acting, high-affinity partial agonist at the mu-opioid receptor (Velander, 2018). As a long-acting agonist, buprenorphine prevents withdrawal and craving and stabilizes opioid receptors (Velander, 2018). As a high-affinity agonist, buprenorphine blocks other opioids from binding, preventing abuse of other opioids (Velander, 2018). As a partial agonist, it has a smaller effect with a ceiling, a low overdose risk, and no intoxication in the opioid dependent (Velander, 2018). Buprenorphine is the first medication to treat OUD that can be prescribed or dispensed in physician offices, significantly increasing access to treatment (SAMHSA.gov/*Medications, counseling, and related conditions*). Unlike methadone treatment, which must be performed in a highly structured clinic, buprenorphine is the first medication to treat opioid dependency that is permitted to be prescribed or dispensed in physician offices, significantly increasing treatment access

(SAMHSA.gov/*Medications, counseling, and related conditions*). Under the Drug Addiction Treatment Act of 2000, qualified U.S. physicians can offer buprenorphine for opioid dependency in various settings, including in an office, community hospital, health department, or correctional facility (SAMHSA.gov/*Medications, counseling, and related conditions*).

Buprenorphine-medication therapy has been shown to be effective in the treatment of opioid dependence both as maintenance medication and for supervised withdrawal from opioids (Johnson & McCagh, 2000; Shulman et al., 2019; Thomas et al., 2014). Studies also show that maintenance treatment with buprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social functioning (Bart, 2012, Fareed et al., 2012; McCance-Katz, 2004; Thomas et al., 2014). Buprenorphine is found to be highly effective for individuals in MT for OUD that have a stable living situation with family and friends who can support them in recovery (SAMHSA.gov/*Recovery and recovery support*). As with all medication used in MT, buprenorphine is prescribed as part of a comprehensive treatment plan that includes counseling and participation in social support programs.

A Swedish study by Kakko et al. (2003) compared patients maintained on 16 mg of buprenorphine daily to a control group that received buprenorphine for detoxification (6 days) followed by a placebo. All patients received psychosocial supports. In this study, the treatment failure rate for placebo was 100% vs. 25% for buprenorphine. More than two opioid-positive urine tests within 3 months resulted in cessation of treatment, so treatment retention was closely related to relapse. Meta-analysis determined that patients on doses of buprenorphine of 16 mg per day or more were 1.82 times more likely to stay

in treatment than placebo-treated patients, and buprenorphine decreased the number of opioid-positive drug tests by 14.2% (Fudala et al., 2003; Kakko et al., 2003; Mattick et al., 2014). Research has also shown that to be effective, buprenorphine must be given at a sufficiently high dose (generally, 16 mg per day or more). Some treatment providers wary of using opioids have prescribed lower doses for short treatment durations, leading to failure of buprenorphine treatment and the mistaken conclusion that the medication is ineffective (MacDonald et al., 2016; Mattick et al., 2014). The length of time a patient receives buprenorphine is tailored to meet the needs of each patient, and in some cases, treatment can be indefinite. To prevent possible relapse, individuals can engage in ongoing treatment with or without MT (SAMHSA.gov/*Medications, counseling, and related conditions*).

Combination Therapies

While it can be noted that MT programs can help treat OUD, there is no one-size-fits-all treatment program. Medication-assisted treatment in combination with counseling and behavioral therapies provides a "whole patient" approach to the treatment of OUD (SAMHSA.gov/*Medications, counseling, and related conditions*). Therefore, having a variety of different programs that tailor to the individual's specific needs is the best option to facilitate treatment entry and success with a working goal toward recovery. Many researchers have argued that exclusive pharmacotherapy or behavioral interventions as treatment modality for OUDs can be ineffective, and to produce better outcomes for individuals experiencing OUDs, a combination of these therapies is needed (Bonnie et al., 2017). Therefore, selecting a combination of medication

and psychosocial treatment that is appropriately targeted and designed to best suit a patient's individual needs is vitally important.

A systematic review conducted by Amato et al. (2011a) evaluated the efficacy of providing social treatment in conjunction with pharmacological detoxification treatments relative to providing pharmacological treatments alone. Findings from the systematic review indicated that psychosocial treatments combined with pharmacological detoxification treatments were effective in increasing rates of levels of treatment attendance, improving rates of treatment completion, reducing opioid use, and facilitating longer-term abstinence (Amato et al., 2011a). Another study by Amato et al. (2011b) evaluated the efficacy of providing specific psychosocial treatments in conjunction with agonist maintenance treatment. Primary outcomes included treatment retention and abstinence during the study period. The review concluded that adding any specific psychosocial support to standard maintenance treatments did not add any benefits for the outcomes considered (Amato et al., 2011b).

Nyamathi et al. (2011) examined the relative effectiveness of 3 MI approaches in reducing drug use among MT clients. MI focused on reduction of drug use individual sessions (MI-S, n = 90), MI delivered in group session (MI-F, n = 79), and a non-MI group, (n = 87). Results showed no significant differences among the groups in drug use during the intervention period or at follow-up (Nyamathi et al., 2011). Two studies examined the efficacy of providing CBT in conjunction with MT. The first study by Kouimatsdis et al. (2012) compared outcomes of participants who were randomly assigned to receive standard MT (n = 31) or standard MT plus CBT (n = 29). Results of the study revealed no significant between-group differences on days of opioid use,

abstinence rates, psychosocial problem severity, quality of life, psychological symptoms, or MT compliance (Kouimatsdis et al., 2012). Another study by Moore et al. (2013) randomly assigned participants to receive MT (n = 18) or MT plus Recovery Line (RL, n = 18) a form of CBT. Study results indicated no significant differences between the groups in MT satisfaction, study retention, self-reported substance use, urinalysis-verified opioid and cocaine abstinence, number of counseling sessions attended beyond the minimum requirement, or coping skills (Moore et al., 2013).

A few studies examined the use of CBT in the context of buprenorphine treatment (Fiellin et al., 2013; Moore et al., 2012). Fiellin et al. (2013) compared the efficacy of providing physician management (PM) alone (PM=71) to PM plus CBT (PM+CBT=70) in a primary care setting. Results concluded that there were no significant differences between the two groups in opioid use and study completion (Fiellin et al., 2013). A similar study by Moore et al. (2012) compared PM with weekly buprenorphine dispensing (PM, n = 28) with PM plus directly observed buprenorphine consumption and CBT (CBT, n = 27). The study found no significant differences between the groups in treatment retention, maximum number of consecutive weeks of opioid abstinence, or participant satisfactions (Moore et al., 2012).

In conclusion, more information about the use of specific medications in combination with specific types of psychosocial interventions during all phases of treatment and among different subpopulations is needed. Continued research is crucial to gain a better understanding of best practices and guidelines in caring for and treating individuals with OUD (Dugosh et al., 2016). Behavioral interventions alone have extremely poor outcomes, with more than 80% of patients returning to drug use

(Velander, 2018). Overcoming the misunderstandings and other barriers that prevent wider adoption of these treatments is crucial for tackling the problem of OUD and the epidemic of opioid overdose in the United States. Regardless of what setting MT is provided in, it is more effective when counseling and other behavioral therapies are included to provide individuals with a whole-person approach.

Barriers to Treatment

Opioid use is widespread, and the need to address barriers to evidence-based treatment is more urgent now than ever. Common reasons cited as barriers to medication treatment include the paucity of buprenorphine-waivered prescribers, low rates of prescribing among waivered physicians, lack of motivation, and stigma associated with both the disease of addiction and use of medications (Hadland et al., 2018; Madras et al., 2020). In a state-level analysis of the supply of physicians waivered to prescribe buprenorphine for OUD, (Knudsen, 2015) found that the average state had eight waivered physicians per 100,000 residents. Insufficient numbers of providers for treatment of OUD have been noted as a significant barrier to the availability of such treatment. McCarty and colleagues (2018) note that contributors to low access to and utilization of treatment with medication include the paucity of trained providers; negative attitudes regarding this form of treatment among providers, patients, and the general public; policy and regulatory barriers, such as utilization management techniques that place limits on dosages; treatment length; cumbersome paperwork for authorization and reauthorization; and minimal counseling coverage.

On April 17, 2018, the FDA held a public meeting where approximately 100 individuals with OUD, caregivers, and other patient representatives provided input on the

most significant health effects and available therapies to manage OUD. A report of key themes was summarized, and participants identified several challenges and barriers to accessing and sustaining MT. They highlighted the impact of stigma on their interactions with healthcare providers and others, particularly when being perceived as "an addict" or when being labeled as "dirty" or "clean" (FDA.gov/*The voice of the patient/Opioid use disorder*). Participants also highlighted challenges in access to MT including long wait times, difficulty finding facilities that provide MT, strict requirements for entry into MT programs, medication cost, and concerns about safety at the facility (FDA.gov/*The voice of the patient/Opioid use disorder*). Within the report, participants described the added challenges to maintaining recovery due to the intensity of withdrawal and craving, the significant pain or mental health needs, and their own difficulty in coming to terms with their illness.

Individuals involved in the CJS also face barriers to effective treatment. While these individuals have high rates of SUD (60–80%), their treatment utilization is low (Hunt et al., 2015). Examining data from the Arrestee Drug Abuse Monitoring II program, Hunt and colleagues (2015) found that those with a history of heroin use had higher drug use and severity and higher rates of treatment utilization than those reporting use of other drugs. However, a minority (34%) of arrestees with drug use histories had received SUD treatment during their lifetime, and only 14% had obtained such treatment during the year prior to their arrest. Receipt of mental health treatment services also is extremely low in this population despite a high prevalence of mental health problems.

There is substantial evidence that supports MT as the first-line treatment for OUD, especially opioid substitution therapy with buprenorphine or methadone as long-

term maintenance of at least 1 year (SAMHSA.gov/*Medications, counseling, and related conditions*). However, patient dropout (typically >50% at 6 months), and provider resistance remain major impediments to effective treatment. To date, few studies have examined patient characteristics that influence key steps in treatment initiation, stabilization, and long-term retention with buprenorphine (Williams et al., 2018). Among the published studies, only few assess outcomes for only 2-3 months of active treatment among highly selected patients in clinical trials (Williams et al., 2018). In a systematic review of existing quality measures relevant to the treatment of OUD and the literature assessing the utility of these measures in community practice. Williams and colleagues (2018) found that despite considerable progress, only seven studies identified quality measures applicable to the treatment of OUD. The study proposes the adoption of a unified quality measurement framework such as an OUD treatment cascade to assist in further refining of existing measures across populations and settings (Williams et al., 2018).

Measuring Treatment Success

ASAM defines addiction as a primary, chronic disease of brain reward, motivation, memory, and related circuitry (ASAM, 2011). Gustin et al. (2015) note the concerted efforts to put addiction treatment on par with the rest of medicine, highlighting addiction as a chronic illness. However, the treatment of addiction is not approached as defined, a chronic disease; the authors also question whether personal philosophies bias our approaches? As any chronic disease with biological, genetic, and physiological bases, addiction would be managed, as a chronic disease, by integrating a combination of treatment paradigms personalized to the specific needs of the patient in order to ensure

the best possible outcomes for the individual, namely an integrated pharma-psychosocial approach to treatment (Martin et al., 2007).

Treatments for OUD must include a comprehensive approach that includes medical, psychosocial, and behavioral management of the disease. Additionally, the clinical criteria defining successful addiction treatment is often based on the patient becoming free of both the drug of abuse and pharmacotherapy that has facilitated abstinence (Gustin et al., 2015). Gustin and colleagues (2015) pose the question, "Why is OUD not held to the same standards of other chronic diseases, e.g., diabetes, wherein insulin treatment continues indefinitely?" For example, medical management of OUD with buprenorphine/naloxone or methadone is often perceived as substituting one addiction for another. This misunderstanding of the contribution of medications to the overall management of OUD can lead to premature discontinuation of medication to the detriment of the patient and thus high rates of relapse (Fiellin et al., 2008; Kakko et al., 2003; Ling et al., 2009).

Assessing patients' symptomatology prior to and after initiation of medication-assisted therapy, demonstrates how effective appropriately administered medications can be at supporting a patient's remission (Gustin et al., 2015). The potential benefits of utilizing medications in patients with OUD include assisting the patient in achieving remission from the disease, allowing the individual to engage in active recovery (Parran et al., 2010), and increasing retention in treatment. For example, a patient who has been stable on buprenorphine/naloxone for an extended period, and over the course of 3 years that individual became employed, found stable housing, regained custody of his/her children, yet is still being maintained on low doses of buprenorphine/naloxone (Gustin et

al., 2015). Shouldn't this be considered a treatment success? Or are we allowing misconceptions of the role of medication in the process of recovery to bias how we direct patients through treatment? Gustin et al. (2015) suggest a promotion of individualized care, and to begin to consider whether discontinuing a medication that has allowed the patient to rebuild his/her life from the depth of their addiction is worth the risk of destroying the quality of life due to relapse. In addition, there are significant consequences that can occur if certain medications are abruptly discontinued without appropriately being tapered or monitored. There are many other examples of similar decision making in medicine-that are known for example, depression can lead to suffering and suicide, elevated blood pressure is associated with increased rates of myocardial infarction, stroke, and renal failure and so patients are continued on antidepressants or antihypertensives throughout a lifetime with little hesitation (Gustin et al., 2015).

Recent guidelines indicate there is little consistent evidence to evaluate the effectiveness of MTs (Sanger et al., 2018). Reviews evaluating MT effectiveness have found great variability in outcomes between studies, (Hedrich et al., 2012; Mattick et al., 2009) making it difficult to establish a real treatment effect. Each study evaluated, measures a different set of treatment outcomes that define success in arbitrary or convenient terms (Sanger et al., 2018). This poses a substantial limitation in addiction research that must be overcome to reach a consensus on which treatment outcome domains should be the goals, how those outcome domains should be measured and what works for opioid addiction management (Sanger et al., 2018). Who decides on what outcome is important? Some might consider abstinence the ultimate goal of addiction

treatment, while a patient may desire control over their opioid use or symptom management to be the goal of treatment (Sanger et al., 2018).

Additionally, researchers must consider how trial design is influenced by selection of outcomes (Sanger et al., 2018). If the outcome for such trials was reduced criminal activity, reduced incidence of infectious diseases, reduced homelessness or other social advantage, the intervention may be helpful for only certain groups of patients (Sanger et al., 2018). Regardless, without the identification of a measurable treatment outcome that has an impact and significance to patients, services, and the population as a whole, all the investment in trials will continue to result in inadequate and inconsistent "effectiveness" with limited, if any, external validity (Sanger et al., 2018). There needs to be a set of established MT outcomes, so that healthcare providers and their patients, pharmacotherapeutics developers, policy makers, researchers, budget holders and service users are able to evaluate the true effectiveness of these therapies (Sanger et al., 2018).

Individuals with OUD go through various stages of both addiction and treatment cycles, as personal, social, and environmental changes influence treatment overtime. The cycles of treatment, abstinence, and relapse, which can be termed a "treatment career," may vary widely in length, pattern, and ultimate outcome (Knudsen, 2015). A longitudinal dynamic approach is needed to identify and understand key factors influencing drug use and its treatment over time. Like the treatment of many chronic conditions (e.g., diabetes, hypertension, mental illness), treatment for drug dependence is beset with problems of patient compliance with intervention protocols (Hser et al., 1997). As in any condition requiring long-term management, interruptions in, or failure to comply with, treatment contributes to the inability to measure treatment success after any

single intervention episode (Hser et al., 1997). Unlike the management of other chronic conditions, where a longer time frame for recovery is accepted, evaluations of treatment for drug dependence tend to focus narrowly on single episodes of treatment (Hser et al., 1997).

While it is important to determine outcomes for any single intervention, a research approach that evaluates the patterns and outcomes of multiple, sequential interventions provides a fuller understanding of the effectiveness of treatment over time (Hser et al., 1997). Measurement of the dimensions of an individual's treatment career is inherently difficult. A systematic review evaluating the effectiveness of different MATs for OUD suggests the literature has no consistent definition of a "successful" addiction treatment outcome, and thus most trials assessing therapy effectiveness use a variety of end points (Dennis et al., 2015). Treatment attrition continued opioid use, criminal activities, quality of life, and economic costs are among the long list of outcomes used across trials aimed to establish treatment effectiveness in the OUD literature (Sanger et al., 2018).

Treatment Retention

A primary outcome in treating opiate dependence is retention in treatment because retention is associated with better outcomes such as decreased drug use, improved social functioning, and quality of life, and reduced mortality (Bart, 2012; Hser et al., 1997). Several studies have found that patients treated with medication were more likely to remain in therapy compared to patients receiving treatment that did not include medication (Mattick et al., 2009). A systematic review of literature conducted by Timko et al. (2015) to identify factors associated with the outcome of retention in MT for opiate

dependence (2010–2014), found better retention rates for participants who received naltrexone and buprenorphine than patients who received placebo or no medication. Results also found a wide variability in retention rates, and only a single study examined retention in MT for longer than 1 year, demonstrating the need for longer-term follow up is needed (Timko et al., 2016)

A second systematic review of the literature conducted by Matitick, and colleagues (2014) found that buprenorphine at high doses (generally, 16 mg per day or more) were 1.82 times more likely to stay in treatment than placebo-treated patients, and buprenorphine decreased the number of opioid-positive drug tests by 14.2% (the standardized mean difference was -1.17; Fudala et al., 2003; Kakko et al., 2003; Mattick et al., 2009). Some treatment providers wary of using opioids have prescribed lower doses for short treatment durations, leading to failure of buprenorphine treatment and the mistaken conclusion that the medication is ineffective (Lamb et al., 2016; MacDonald et al., 2016; Mattick et al., 2014).

The Swedish study by Kakko et al. (2003) compared patients maintained on 16 mg of buprenorphine daily to a control group that received buprenorphine for detoxification (6 days) followed by placebo. All patients received psychosocial supports. In this study, the treatment failure rate for placebo was 100% vs. 25% for buprenorphine. More than two opioid-positive urine tests within 3 months resulted in cessation of treatment, so treatment retention was closely related to relapse. Of patients not retained in treatment, there was a 20% mortality rate. Longer treatment with buprenorphine is associated with better outcomes, and treatment discontinuation leads to high rates of relapse (Bell et al., 2009).

Treatment Compliance

A troubling fact about drug treatment is that client compliance to treatment is generally poor. While client engagement in treatment (attendance, adherence to program rules, etc.) is understudied, it is well known that dropout rates (particularly from outpatient programs) are often high, and subsequent relapse to drug use and related negative behaviors is common among dropouts from all types of treatment (NIDA, 2018). The reasons that people relapse or return to drug use are varied, and each reason is personal to each individual who experiences this gradual return to substance use (https://serenityatsummit.com/resources/what-is-relapse/). However, regardless of the reason, a person may often be unaware of what they are experiencing. By the time a person realizes they are experiencing a relapse, they may return to using the substance of choice.

While the definition of a drug relapse makes it seem that a person has consciously made the decision to go back to using, it is usually not that simple (https://serenityatsummit.com/resources/what-is-relapse/). The chronic nature of addiction can mean that relapse, or a return to drug use after an attempt to stop, can be part of the process. This process known as "Iterative relapse" is the most common path, an expectation to be managed and addressed, and an indication to refine problem-solving strategies and care (Martin, Bosse, et al., 2018). Iterative relapse is also common in other chronic diseases (such as hypertension and type 2 diabetes), and only a minority of patients follow medical recommendations (McLellan et al., 2000).

According to The WHO, adherence to long-term therapy for chronic illness is estimated to be 50% (WHO, 2003). The WHO (2013) also reports that medication

adherence rates are even lower among persons who experience poverty or lack social support, suggesting that a shortage of resources is a contributing factor. In other chronic conditions, we speak not of "relapse" but of "noncompliance," "nonadherence," and "uncontrolled disease." (Martin, Bosse, et al., 2018). Clinically shaming or discharging patients who are labeled as nonadherent is not customary and despite overwhelming evidence that punitive consequences are ineffective, individuals with OUD continue to be criminalized (Martin, Bosse, et al., 2018; Volkow, 2021). Equally ineffective is identification of patients who experience relapse as "failing medical treatment" (Martin, Bosse, et al., 2018). Relapse is recognized as a common expected part of care for SUDs (NIDA.NIH.gov/*Principles of drug addiction treatment*). This does not mean that relapse should be ignored; rather, it should lead to thoughtful, patient-centered refinements in care, such as avoidance of social media, family supervision of buprenorphine administration, and support as patients seek employment or stable housing (Martin, Bosse, et al., 2018).

Tkacz et al. (2012) conducted a study to examine the effect of compliance with buprenorphine on reducing relapse among a sample of patients in treatment for OUD. Study findings demonstrated the effectiveness of buprenorphine for the prevention of relapse in a national sample of OUD patients. Compared to noncompliant patients, buprenorphine-compliant patients were 10 times less likely to report opioid use. Enhancing compliance with medication treatment is essential for patient recovery. Furthermore, discerning the reasons for noncompliance may serve as an avenue for increasing compliance rates for individual patients (Tkacz et al., 2012). Because

addiction can affect so many aspects of a person's life, treatment should address the needs of the whole person to be successful.

Further research on treatment compliance for individuals with OUD enrolled in MT programs is needed. Although literature highlights the importance in evaluating an individual's compliance to an appropriate treatment regimen, the concept of treatment compliance can be viewed as stigmatizing and thus for the purposes of this study, the concept of "treatment utilization" replaces this term.

In addition, further research focusing on replacing the existing language used to describe how an individual utilizes treatment and encompasses elements such as treatment length, time, and adaptation to events that affect outcomes for individuals with OUD is necessary.

Medication Adherence

The most commonly utilized medication for the treatment of OUD is buprenorphine/naloxone. There has been a great deal of debate, as well as conflicting studies, relative to how long patients should be treated in order to achieve optimal outcomes and avoid relapse (Gustin et al., 2015; Martin, Chiodo, et al., 2018). Time constraints that are placed on treatment are often unrealistic and can lead to challenges in treatment outcomes. In addition, providers often are not understanding that the course of treatment should be dependent upon the individual patient's needs, attitudes, and overall stability. A fixed dose reduction or tapering scheduling is not always effective for the majority of patients.

Medication adherence has been linked to improved outcomes across a variety of chronic diseases states (DiMatteo et al., 2002.). Adherence with buprenorphine has been

shown to reduce the incidence of subsequent relapse among an opioid dependent sample (Tkacz et al., 2012). The Tkacz et al. study (2012) found that adherence with buprenorphine medication treatment may reduce the risk for expensive hospital-based services, and ultimately lead to a reduction in overall healthcare expenditure. Although literature highlights the importance in evaluating an individual's adherence to their medication regimen, the concept of medication adherence in MT can be viewed as stigmatizing, and thus for the purposes of this study, the term "medication utilization" replaces the term medication adherence and refers to an individual's ability to utilize buprenorphine for treatment of OUD

Measurement of Opioid Use Using Urine Drug Screens

UDSs remain the current gold standard for measurement of medication adherence and treatment compliance in MT programs (SAMHSA.gov/*TIP 43*). Despite its limitations, urine drug testing is dominant in MT programs because obtaining specimens is relatively easy and testing is affordable (SAMHSA.gov/*TIP 43*). As with any medical test, it is imperative for clinicians to understand how to interpret test results as misinterpretation allows for negative repercussions and penalties for the patient (Martin, Chiodo, et al., 2018).

Stigma remains widespread in addiction treatment, and often providers will label urine results as "clean" or negative for drug use and/or "dirty" indicative of positive findings consistent with drug use. Although these are common terms in describing results that show use of addictive substances, misinterpretation can result in discharge if a patient continues to struggle in early phases of stabilization or have relapse in later stages (Martin, Chiodo, et al., 2018). Drug tests are often misinterpreted as they are designed to

detect whether a substance has been used within a particular window of time. In addition, drug tests do not provide an accurate of measure of patterns over time, which should be considered (Baxter et al., 2017). Drug testing provides another source of information to complement self-report, collateral report, and provider assessment. Having an additional, alternative means of assessing a patient's recent substance use is important to treatment planning and ongoing treatment adjustment (Baxter et al., 2017)

The most recent guidance from the ASAM recommends that "drug testing should be used as a tool for supporting recovery rather than exacting punishment" (Baxter et al., 2017). Some researchers may also believe that the implied risk of discovery through drug screens may prevent relapse, especially when consequences of a positive screen are severe (Mass.gov./*Bureau of Substance Abuse Services [BSAS]*). However, we already know that more than half of individuals in treatment are likely to use substances while in treatment or shortly thereafter, and that most people need at least 3 months in treatment to achieve abstinence (Mass.gov./*BSAS*). Recent guidelines for opioid treatment programs mandate that programs administer UDS during treatment to monitor patients for adherence to prescribed medications; however, a positive drug screen result alone cannot justify adverse consequences, including discharge (SAMHSA.gov/*Federal guidelines for opioid treatment programs*).

While there is research that provides evidence of UDS results as an important tool for individuals in treatment, UDS alone does not add to our knowledge or understanding of why an individual may have returned to using substances (Hadland & Levy, 2016; SAMHSA.gov/*Federal guidelines for opioid treatment programs*). Relatedly, there is very limited empirical evidence about whether the use of drug testing in addiction

treatment settings leads to improved clinical outcomes (SAMHSA.gov/*Federal guidelines for opioid treatment programs*; Wakeman et al., 2020). As care for patients with OUD using MT evolves to be more patient-centered, with less stigma and more privacy, providers should be able to integrate measurement of recovery outcomes with UDS for ongoing care of patients in recovery (Madras et al., 2020).

Two systematic reviews conducted by Blum et al. (2014) and Dupouy et al. (2014), illuminated the currently unrealized role of drug tests in addiction treatment. Blum et al. (2014) looked at whether drug test results are useful indicators of patients' progress in treatment and concluded that testing for both prescribed addiction medications and illicit drug use can improve a provider's ability to determine the effectiveness of the current treatment approach. However, a systematic review of patient charts concluded that drug testing does not appear to change the way patients are managed by their treatment providers, although it was unclear whether these results were due to provider behavior or actual lack of effect of drug testing on management or outcome of patients in addiction treatment (Dupouy et al., 2014). The decision to use any tool in healthcare should be grounded in the principles of improved patient care and outcomes (Baxter et al., 2017). Evidence is limited that the use of drug testing in addiction treatment improves patient outcomes. Due to its inherent limitations, drug testing should not be relied upon as the sole measure of a patient's substance use (Baxter et al., 2017).

Drug testing should be accurately interpreted, used to support positive patient outcomes rather than cause patient harm, and discussed in a nonjudgmental manner (Martin, Chiodo, et al., 2018). Demonstrating that functional outcomes are a better

measure of treatment retention, medication adherence and treatment success when compared to using UDSs will not replace other measures of effectiveness, including in-treatment assessments, but it would add to those measures. It also means that among healthcare providers, there must be a general recognition that the goal for patients with significant SUDs should focus on harm reduction. Harm reduction measures for individuals with OUD in MT should focus on decreased use vs. complete abstinence from alcohol and other drugs and accompanying steps toward recovery and an improved quality of life (SAMHSA.gov/*Recovery and recovery support*).

Functional Outcomes

OUD is a major public health problem and is now the leading reason for addiction treatment, second to alcohol (SAMHSA.gov/*Facing addiction in America*). Fortunately, medications (i.e., pharmacotherapies) are available to aid recovery from OUD and are becoming more widely available. In the United States, federally approved pharmacotherapies include methadone, buprenorphine (e.g., suboxone), and naltrexone. Medication treatment programs are designed to lifesaving treatments that help individuals recover from OUD. We know that they help to reduce opioid use, but what do we know about their effects on other aspects of life and everyday functions? The impact of MT on functional outcomes has been measured in a variety of different ways (cognitive function, occupational function, physical function, behavioral/social function, and neurologic function); however, there is minimal research on functional outcomes as a measure of medication treatment success for individuals in treatment for OUD (Maglione et al., 2018).

The systematic review conducted by Maglione et al., (2018) synthesizes evidence on the effects of MAT for OUD on functional outcomes, including cognitive (e.g., memory), physical (e.g., fatigue), occupational (e.g., return to work), social/behavioral (e.g., criminal activity), and neurological (e.g., balance) function. While many of the reviews looked at physical (fatigue) and cognitive outcomes (memory, attention), study results concluded that weaknesses in the body of evidence prevent strong conclusions about the effects of MT for OUD on functional outcomes. This lack of relevant data was not entirely unexpected, as studies of interventions for SUD tend to focus on reduction or cessation of substance use, treatment retention, and harm reduction (Maglione et al., 2018). Maglione et al. (2018) made future suggestions to add more rigorous studies of functional effects that would strengthen the body of literature.

This review evaluates the research conducted to date that examines the effects of OUD pharmacotherapies on functioning in various aspects of one's life, including physical, social, occupational (i.e., work-related functioning), and neurocognitive outcomes. The outcomes of the Maglione et al. (2018) review are limited to the inclusion criteria set forth by the author. Therefore, they do not extend to pregnant women, inpatient treatment populations, or adolescents. Further studies are needed to determine whether these functional outcomes extend to broader patient populations. Thus, there is a need to better understand how these lifesaving treatments affect everyday functions like social relationships and cognitive skills that might play an important role for measurement of MT outcomes.

Theoretical Framework

Given the complexity of OUD, it is challenging to understand it from the perspective of a single theory, guiding framework, or conceptual model. The examination of several viewpoints may be necessary in order to grasp the complex nature and progression of OUD. For the purposes of this study, Bronfenbrenner's' ecological systems theory and SAMHSA's working definition of recovery were used to guide this study. Bronfenbrenner's foundational work, the ecological systems theory (1979), also called the development in context or human ecology theory, identifies five environmental systems with which an individual interacts. The theory offers a framework through which community psychologists examine individuals' relationships within communities and the wider society. SAMHSA's working definition of recovery from mental disorders and/or SUBs identifies a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential (SAMHSA.gov/*Recovery and recovery support*). Through recovery support, SAMHSA identified four major dimensions of recovery that help guide an individual with OUD through recovery.

Bronfenbrenner's theory provides the overarching conceptual framework for this study by defining the social contexts for investigation, specifying the need for an inclusive, multidimensional view of these social contexts, and suggesting relationships of the contexts when evaluating functional outcomes for individuals with OUD in MT. Bronfenbrenner posited that human development processes are influenced by individual characteristics, as well as features in one's immediate and more distant environments. Over the course of a lifetime, development progresses through a series of increasingly

complex and reciprocal interactions between an individual and the people, things, and symbols in their environment.

Research designed to investigate this developmental progression is described as aligning with a process-person-context model (Bronfenbrenner, 1994) and is endemic in our current understanding of psychological health and illness. The fundamental acknowledgement that individuals live within a wider, often complex set of interrelated systems underpins this study. Moving beyond an acknowledgement of ecological influences that operationalizes this understanding of a person within their environment is what drives the need for other measures of treatment success such as functional outcome evaluation through a more individualized, person-centered approach.

Although Bronfenbrenner's work focuses on the quality and context of the child's environment, there seems to be consensus that children are influenced, first and foremost, by their parents and immediate family structures, as well as other social domains, such as peers, school, and neighborhood influences. Bronfenbrenner defines person-environment interrelations in terms of the individual, micro-, meso-, exo-, macro-and chronosystems. For example, Bronfenbrenner suggests an approach to examining interrelations among social contexts is to posit that "In ecological research, the principal main effects are likely to be interactions" (Bronfenbrenner, 1977, page 518).

A social ecological framework can be utilized to examine how the impact of functional outcomes among individuals with OUD in MT can be a better indication of treatment success. The theory foundation can help to examine the phenomenon of drug use, in light of the numerous influences and interactions, within the various social contexts of the population studied. Application of this theory could also be used to

demonstrate how an individual's progress in treatment for OUD is influenced by individual characteristics, as well as features in one's immediate and more distant environments. Determinants of mental health and SUDs include individual, social, and societal factors, and their interaction with each other. Thus, SUDs including OUD, need to be understood from biological, psychological, and sociocultural perspectives. Study variables included that define the individual are age, race, gender, and ethnicity.

In addition to Bronfenbrenner's ecological systems theory, SAMHSA's working definition of recovery was incorporated to assist in the exploration of how functional outcomes impact an individual with OUD in MT. This perspective is vital for individuals with mental and/or substance use conditions, as it incorporates a holistic perspective that addresses the whole person and their community, and is supported by peers, friends, and family members (SAMHSA.gov/*Recovery and recovery support*). SAMHSA's working definition of recovery defines recovery as a process of change through which individuals improve their health and wellness, live self-directed lives, and strive to reach their full potential (SAMHSA.gov/*Recovery and recovery support*).

There are four major dimensions that support a life in recovery. These dimensions include health, home, purpose, and community. The model is guided by the belief that the process of recovery is highly personal and occurs via many pathways that may include clinical treatment, medications, faith-based approaches, peer support, family support, self-care, and other approaches. The model also recognizes that the process of recovery is characterized by continual growth and improvement in one's health and wellness in addition to managing setbacks, as a natural part of life (SAMHSA.gov/*Recovery and recovery support*). The working definition and set of principles for recovery has helped

create a standard, unified working definition that helps advance recovery opportunities for all Americans, and helps to clarify these concepts for peers, families, funders, providers, and others.

SAMHSA's working definition of recovery complements Bronfenbrenner's theory by adding the value of recovery and recovery-oriented systems of care that are widely accepted by states, communities, healthcare providers, peers, families, researchers, and advocates (SAMHSA.gov/*Recovery and recovery support*). It is also important to incorporate SAMHSA's working definition due to the limitations of secondary data that support the study aims and hypotheses included in this study. Both SAMHSA's definition of recovery and Bronfenbrenner's theory were used to guide interpretation of the results within the current state of the science and inform future research.

Bronfenbrenner's Ecological Systems Theory

The Microsystem

This system is the individual's immediate or direct environment, it refers to the institutions and groups that most immediately and directly impact the individual's development including family, friends, classmates, teachers, and neighbors. At this level, an individual is able to build social networks and thereby gain a valuable source of support. It is this system where we have direct social interactions with these social agents. Social environment plays a big role in terms of positive vs. negative contacts and supports. These close relationships have extraordinary power to normalize or stigmatize behaviors and to support or hinder optimal individual development. For individuals with OUD in MT, these interactions directly influence an individual's treatment outcomes.

Currently, the treatment guidelines and measures of success assess the presence or absence of support systems but do not go into greater detail to examine the impact it may have on an individual's treatment status. When assessing medication utilization, individuals who do not disclose their status due to fear of stigmatization or negative repercussions may face challenges in accessing care and thus may not receive the social support from friends or family who may encourage them to attend clinic appointments or remind them to take their medication. Bronfenbrenner's theory states that we are not mere recipients of the experiences we have when socializing with these people in the micro system environment, but we are contributing to the construction of such environment (Bronfenbrenner, 1977).

Several studies have shown that positive social and family support are associated with relatively good treatment adherence (DiMatteo et al., 2002; Tkacz et al., 2012). Nondisclosure and stigma disrupt the ability to form social networks in the microsystem. Inadequate interactions within the microsystem may result in a cascade of disruption throughout all tiers of systems of the ecological model (Bronfenbrenner, 1975). In the case of evaluating functional outcomes for individuals in treatment for OUD, each of the functional outcomes and some of the covariates presented and available in the study data directly influence the individual and thus are included in this system. These variables include supports, community, counseling, finances, and housing.

The Mesosystem

Bronfenbrenner describes the mesosystem as the connections or "a system of microsystems." The mesosystem consists of the relations that microsystems have with one another; it is made up of the connections between contexts. The interrelations

between these systems and the resulting impact on the individual comprise the mesosystem. This interaction of the different microsystems involves linkages between home and work, or social supports/contacts and family. If an individual's social contacts or supports are actively involved in their lives and support them in treatment, then the individual is more likely to stay in treatment and thus their outcomes are affected positively through harmony and like-mindedness (e.g., increase in treatment retention, decreased drug use). However, if the individual's social contacts or supports are negative and openly criticize them, then the individual experiences disequilibrium and conflicting emotions, leading to the potential development of negative outcomes (e.g., increased drug use, decrease in treatment retention, involvement with criminal justice). The variables that can impact an individual's mesosystem are the presence or absence of counseling, interactions between a person's home, or workplace, and their engagement and experiences for treatment of OUD. It is challenging to identify variables measured that directly influence the individual's mesosystem; however, several of the variables identified in the microsystem could be included as interconnections that comprise an individual's mesosystem.

The Exosystem

This system pertains to the indirect environment and thus involves linkages between two or more settings, also described as the environment in which the microsystems are embedded—one of which may not contain the individual but affects them indirectly, nonetheless. Other people and places that the individual may not directly interact with may still have an effect on the individual, comprise the exosystem. The exosystem consists of settings that individuals do not have direct contact with, but still

influence the individual. Currently, the variables in this study that pertain to the exosystem are other drugs and alcohol, employment, finances, social and non-social stress, custody of children, CJS involvement, as well as MT.

The Macrosystem

The macrosystem represents the social and cultural patterns that examine policies, laws, values, and trends that comprise the broad cultural, political, economic, and societal/environmental backdrop of an individual's life (Bronfenbrenner, 1979, 1994). This system is the largest and most distant collection of people that still exercise significant influence on the individual. Further evaluation of geographical areas in which people with OUD seek treatment, evaluation of religious and cultural patterns and values may be important and thus included as functional outcomes for individuals with OUD in MT. The impact of political decision making on statewide policies and governmental laws might influence how treatment for individuals with OUD is delivered. For example, a mother's/parent's involvement in the judicial system due to criminal justice involvement could be a possible component in an individual's macrosystem. Other larger issues such as evaluating how state, government and national laws, for example, may help or hinder access to treatment for people with OUD would be important to explore.

It is known that pregnant women, in particular, face social stigma regarding their addiction (Saia et al., 2016; Stone, 2015). A qualitative study conducted by Brakenhoff and Slesnick (2015) analyzed 12 sessions of family therapy using thematic analysis to identify common themes that arose during substance abusing mothers and their children's discussion during family therapy. Results from the study found that mothers who were interviewed regarding their experiences of social stigma toward their addiction were not

directly discussed; rather during the interviews, it was noted that some of the mothers appeared to act defensively when they were and made frequent statements to justify or minimize the impact their addiction had on their children (Brakenhoff and Slesnick, 2015). Societal expectations and perceptions may influence a mother's desire to maintain a positive image, thus leading to a decrease in treatment utilization and negative treatment outcomes. Variables in this study which include CJS involvement and child custody issues as part of an individual's macrosystem could directly influence an individual's success in treatment for OUD.

The Chronosystem

Bronfenbrenner describes this system as allowing for the influence "of changes (and continuities) over time" within the person's environment and the impact of such changes of their development (Bronfenbrenner, 1986: p. 724). A dimension of time may include age, a change in family structure such as with pregnancy, treatment status, in addition to societal changes with economic cycles or wars. Bronfenbrenner's model can be used for individuals with OUD in MT and evaluating function outcomes as predictors of treatment success. Similar to the theoretical underpinning that guides this study, Ungar (2013) expanded Bronfenbrenner's model in their studies of resilience to include a focus on the success of individuals and groups to secure resources leading to healthy development, even in adverse circumstances.

Hewell and colleagues (2017) studied systemic and individual factors in medication-assisted treatment for opioid abuse, and they reported findings supporting the construct of recovery capital (including personal recovery capital, family and social recovery capital, and community recovery capital), as well as suggesting the interactional

relationship of such resources. The Hewell et al. study (2017) found that advising providers to be educated about multiple ecological influences and to be flexible in their approaches influences the utilization and ever-changing sources of recovery capital available to their clients. This system would help evaluate an individual's change in functional status over time. Age and pregnancy are variables included in this study that could influence an individuals' initiation, engagement, retainment, and success in treatment for OUD.

SAMHSA's Working Definition of Recovery

For individuals with OUD, recovery signals a dramatic shift in the expectation for positive outcomes for individuals who experience mental, and substance use conditions or the co-occurring of the two (SAMHSA.gov/*Recovery and recovery support*). There is an expectation that when an individual with mental and/or substance use seeks help, they will fully recover and overcome their addiction. The process of recovery is highly personal and occurs in many different pathways. A universal, one-size-fits-all approach does not work for every individual seeking treatment for their OUD. As a result, SAMHSA has developed a standard, unified working definition in hopes of helping advance recovery opportunities for all Americans by clarifying concepts leading to treatment and recovery support services (SAMHSA.gov/*Recovery and recovery support*).

SAMHSA defines recovery as a process of change through which individuals improve their health and wellness, live-self-directed lives, and strive to reach their full potential (SAMHSA.gov/*Recovery and recovery* support). Recovery is important to identify because it signals a dramatic shift in the expectation for positive outcomes for individuals who experience mental health challenges, and substance use or the co-

occurring of the two (SAMHSA.gov/*Recovery and recovery support*). Through the recovery support strategic initiative, SAMHSA has delineated four major dimensions that support a life in recovery. The four major dimensions include health, home, purpose, and recovery (SAMHSA.gov/*Recovery and recovery support*).

Recovery is characterized by continual growth and improvements in one's health and wellness and focused around managing setbacks. Setbacks are a natural part of life and with OUD, we know that setbacks or iterative relapses are a natural part of life. Recovery support systems promote a partnership for people in recovery from mental health and OUD. These support systems promote individual, program, and system level approaches that foster health, and resilience; increase housing to support recovery; reduce barriers to employment, education, and other life goals; and secure necessary social supports in their chosen community (SAMHSA.gov/*Recovery and recovery support*).

Health, the first dimension of recovery is focused on overcoming or managing one's disease(s) or symptoms by making informed, healthy choices that support physical and emotional well-being. Home is a stable and safe place to live, purpose is engaging in meaningful daily activities such as a job, school, volunteerism, family caretaking, independent income and resources that assist in one's integration into society. Community is centered around the relationships and social networks that provide support, friendship, love, and hope (SAMHSA.gov/*Recovery and recovery support*). Along with the four dimensions of recovery are guiding principles of recovery. These guiding principles include hope, person-driven, many pathways, holistic peer support, relational, culture, addresses trauma, strengths/responsibility, and respect (SAMHSA.gov/*Recovery and recovery support*).

Theoretical Framework Summary

Study variables that are characteristic of an individual include gender, race, ethnicity, and mental health (i.e., anxiety and history of PTSD or trauma). Upon examining how an individual's microsystem, or most immediate environment, which includes such variables as family and friends, housing, contacts, and social supports, which can help providers in tailoring treatment that is both individualized and focused. The second system, which is the mesosystem, focuses on community and evaluates how interactions between two or more environments where an individual exists can interact and directly influence treatment success. The way in which the individual comes in contact and interacts with these influences within the mesosystem affects all aspects of their treatment for OUD. For example, an individual with OUD in MT, who has positive supports, may be encouraged to seek counseling, while continuing to hold a job which allows for engagement, retention, and success in treatment.

Evaluation of an individual's exosystem, contains variables with linkages that may exist between two or more settings, one of which the individual may not directly interact with but may still have an effect on the individual. The influence of drugs and alcohol in an individual's social environment, finances, employment, social and non-social stress, custody issues, CJS involvement, and MT are all variables that may or may not directly influence an individual's ability to be successful in treatment for OUD. An individual's macrosystem that views social and cultural values may impact the individual. Study variables such as religious and cultural beliefs, stigma, bias, in addition to local, state, and federal-level healthcare policy and regulations have significant impact on our cultural understanding of addiction, treatment, and outcomes.

Lastly, evaluation of an individual's chronosystem that includes variables such as age, pregnancy, and treatment status could help in developing a comprehensive treatment plan, along with the systems already outlined. The future study data helps plan for challenges that are likely to occur over time and demonstrates the influence of both change and consistency in an individual's environment. The chronosystem and studying changes over time has the potential to add an important piece of time to the study evaluation. Evaluation of the study variables that are available in the EHR and supported by the aims and hypotheses that demonstrate how functional outcomes are a better indicator of treatment success can be further enhanced with Bronfenbrenner's ecologic systems theory. Viewing treatment success by the perception of the individual (individual level), allows for a less stigmatizing, person-centered approach, supporting a better way of defining treatment success in this vulnerable population.

While existing strategies to the opioid crisis proposed by public health leaders tackle specific aspects of the problem, a feasible solution must use an approach broader in nature. Bronfenbrenner's social ecological systems theory (1979) is a useful framework to conceptualize the underlying mechanisms and risk factors associated with the opioid abuse epidemic (see Figure 2 at end of the chapter). As a whole, the theory identifies a reciprocal deterministic relationship between the individual and their environment. According to Conn and Marks (2017), "Environmental contexts interact with the individual to promote healthy behaviors or create risks of maladaptive ones such as substance misuse" (p. 185). The individual is at the core of each of the levels of the social ecological model, with their internalized attitudes, beliefs, experiences, and health (Carney, 2017). The individual influences his or her surroundings as much as his or her

surroundings influence the individual. Moreover, all of the levels of the model elicit an impact on the individual (Carney, 2017).

In conclusion, the complex nature of the current opioid-use crisis sees no single solution. Rather, it demands a multifaceted approach as prescribed in the social ecological systems theory. Social ecological approaches have been used for addiction and have informed all aspects in delivery of care for this complex issue. Bronfenbrenner's theory provides the overarching conceptual framework by establishing a developmental perspective, defining the social contexts for investigation, specifying the need for an inclusive, multidimensional view of these social contexts, and suggesting relationships of the contexts to each other in evaluating functional outcomes for individuals in treatment for OUD.

Significance

Currently, there is no universal treatment standard that exists for MT, and these programs are delivered in different ways and in a variety of settings. Programs are often not classified according to the threshold or tolerance for ongoing drug use, and policies are often stringent focusing on complete abstinence and cessation of drug use, leading to involuntary discharge from the program. There is a popular perception that treatment "fixes" those with SUDs. This perception fails to recognize the nature and complexity of the disorder. Common measures of addiction treatment success assess outcome measures solely on the reduction in the use of a specific drug. Urine is tested for medication adherence and treatment compliance; if urine tests are positive, it can be assumed treatment compliance is an issue and hence results in discharge from the program based on these results.

Within this proposal are suggestions to augment current measures (urine screens) of medication utilization and treatment success with functional outcome measures that address the social and psychological aspects of an individual's treatment course. This suggested change is a more robust and comprehensive measure of gauging treatment success for individuals in MT for OUD that this research addresses. The data from such a comprehensive outcome evaluation has the potential to guide changes in treatment to improve retention, medication utilization, and treatment outcomes. This process of change begins by redefining the initial primary goal of addiction treatment as being both total abstinence from the use of opioids and improved quality of life. It also begins with identifying practical strategies for how functional patient outcomes can be used to assess and predict treatment success for individuals with OUD enrolled in MT.

It is also important to recognize that women with OUD need treatment for their opioid use not only for their own health but for the health of their unborn child, which is just one factor among many that fosters a healthy pregnancy. The rate of NAS is increasing worldwide, and these substance-exposed infants will continue to have developmental, health, and educational concerns in addition to the impact the family experiences. Women with SUD are an understudied population, limiting our current understanding of this group and appropriate intervention approaches. This is extremely troubling due to the known implications associated with not receiving proper care for SUDs during pregnancy as it is suspected that prenatally drug-exposed infants, especially those exposed to opioids, hold the highest risk for adverse neonatal outcomes than any other classes of substances. This change in the evaluation of care, can increase the quality of treatment, generate a new way of monitoring care, and deliver more consistently the

outcome widely sought but seldom achieved: a sustained addiction- and substance-free, healthy lifestyle with better outcomes for both mother and infant.

Demonstrating that functional outcomes are a better measure of treatment retention, medication utilization, and treatment success when compared to using UDS will not replace other measures of effectiveness, including in-treatment assessments, but it would add to those measures. It would ensure that the standard measure of treatment effectiveness is improvement in drug use, and it would encourage addiction treatment programs and clinicians to focus on the individual's strengths as the expected outcome of treatment.

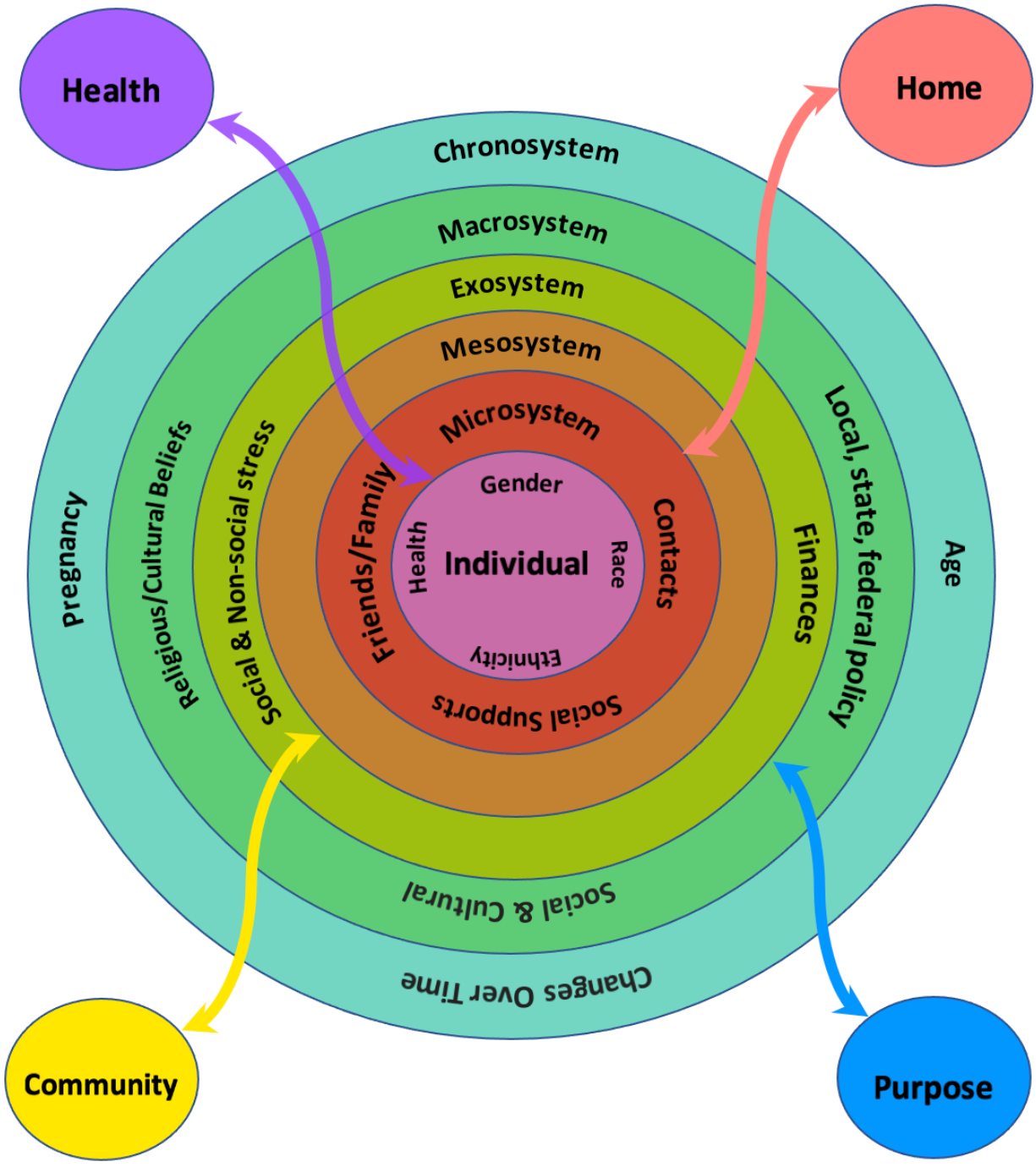

Figure 2: Bronfenbrenner's ecological systems theory model & SAMHSA's four dimensions of recovery adopted to evaluate functional outcomes for individuals with OUD in medication treatment.

CHAPTER 3

METHODS

This chapter provides an overview of the research methodology that was utilized in the study. The sections included are research purpose, design, setting, sample, operational definition and measurement of variables, procedures, data analysis, and limitations.

Research Purpose

The purpose of this study was to understand if functional outcomes better predict treatment success and medication utilization when compared to opioid use in a sample of individuals with OUD receiving MT, with a focus on pregnant women.

Research Design

This study utilized a correlational retrospective analysis of EHR data.

IRB Approval

IRB approval from the University of Massachusetts Amherst was received prior to transfer of patient data and analyses described below.

Setting and Sample

Data was obtained from EHR of patients currently receiving addiction treatment at a multistate, multisite, office-based outpatient addiction treatment center. The treatment center employs evidence-based treatment for a range of SUDs; however, most patients receive treatment for an OUD. Upon admission, each patient undergoes a biopsychosocial assessment and receives an individualized treatment plan. Patients who meet criteria for OUD according to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-V*; American Psychiatric Association, 2013) receive MT at the

centers. Most often, MT consists of buprenorphine/naloxone, with the exception of pregnant patients who are treated with buprenorphine only. For the study, de-identified patient data was included for all patients ages 18 and older who (a) met criteria for OUD diagnosis, (b) received treatment between January 1, 2016, and January 31, 2018, and (c) received MT with any form of buprenorphine.

Electronic Health Records/Retrospective Chart Review

The Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 that was signed into law as part of the "stimulus package" represents the largest U.S. initiative to date that is designed to encourage widespread use of EHRs (Menachemi & Collum, 2011). EHRs are defined as "a longitudinal electronic record of patient health information generated by one or more encounters in any care delivery setting" (Menachemi & Collum, 2011). The growing availability of EHRs provides opportunities to enhance patient care, embed performance measures in clinical practice, and facilitate clinical research (Cowie et al., 2017). The current utilization of EHR is commonly referred to as "clinical data reuse" or "retrospective chart review" (Meystre et al., 2017).

The retrospective chart review (RCR), also known as the medical record review, is a widely applicable research methodology that can be used by healthcare disciplines as a means to direct subsequent prospective investigations (Vassar & Holzmann, 2013). Retrospective chart review is a useful method when data has been recorded in case notes or a structured database and an analysis of the data elements needs to be done (Sarkar & Seshadri, 2014). RCR entails studying data that has already been recorded and involves summarizing the data, subjecting it to appropriate statistical analysis and

drawing inferences (Sarkar & Seshadri, 2014). Reuse of clinical data is essential to fulfill the promises for high quality healthcare, improved healthcare management, reduced healthcare costs, population health management, and effective clinical research (Meystre et al., 2017).

Advantages of EHR Chart Review

Conducting a chart review has several advantages. Potential benefits of EHR chart reviews include enhancing clinical outcomes (e.g., improved quality, reduced medical errors), organizational outcomes (e.g., financial, and operational benefits), and societal outcomes (e.g., improved ability to conduct research, improved population health, reduced costs; Menachemi & Collum, 2011). Among the many benefits, chart reviews typically require less time in terms of data collection and extraction when compared to prospective studies (Sarkar & Seshadri, 2014). A few other advantages include the opportunity to assess a large sample at limited cost, enables easy collection of information, minimizes recall bias for an event in the past and it also reduces the need for intrusion into patients' time for assessment as part of the study (Sarkar & Seshadri, 2014).

Disadvantage of EHR Chart Review

Despite the benefits of EHR chart review functionalities, several potential disadvantages can be identified. These include variation in the manner in which data has been gathered and recorded in the charts that limits the extraction and interpretation of the variables (Sarkar & Seshadri, 2014). Data abstractors, or those who code and maintain the data, may not always be consistent and therefore increase the likelihood that data is retrieved in an inconsistent manner (Vassar & Holzmann, 2013). Another issue is

that some records may be incomplete or lost in the course of time, leading to missing data (Sarkar & Seshadri, 2014). Many sources of data such as patient report of symptoms, exams, patient history, procedures, treatment, and medications are vital when reviewing and reporting information from an EHR. Additionally, this requires knowledge in several different fields; namely, clinical specific area, data mining, text mining, medical records, hospital, and clinical procedures (Pereira et al., 2015). As RCRs continue to be a popular research methodology within the clinical sciences, identifying common pitfalls can assist researchers produce quality research using valid and reliable data (Vassar & Holzmann, 2013).

Data Mining Electronic Health Records

EHRs contain both structured and unstructured data. The process by which one reviews the structured content is referred to as data mining. The most basic definition of data mining is the analysis of large data sets to discover patterns and use those patterns to forecast or build predictive models (Crockett & Eliason, 2017). Structured EHR data, such as encoded diagnosis and medication information, are the easiest data sources to process, but advances in data mining methods has made it possible to also use the narrative parts or "unstructured" pieces of patient records (Jensen et al., 2012). The free text of an EHR is a rich resource, in which providers are able to record events or information history as told to them by their patients. These free text fields are unstructured, so there is little to no standardization of the content, format, or quality of these notes. Consequently, transforming these free text fields into useful, quantified data remains a difficult problem (A. A. Thomas et al., 2014).

Advantages of Data and Text Mining

Data mining holds great potential for the healthcare industry to enable health systems to systematically use data and analytics to identify inefficiencies and best practices that impact and improve the delivery of care and health outcomes (Jensen et al., 2012). Textual, unstructured, or free text data is often found in the form of written notes of medical healthcare providers. Extracting this data has the opportunity to provide useful data that may not be contained in the basic, formalized EHR. Healthcare facilities and groups use data mining tools to reach better patient-related decisions. Patient satisfaction is improved because data mining provides information that will help staff with patient interactions by recognizing usage patterns, current and future needs, and patient preferences (Raghupathi & Raghupathi, 2014).

Disadvantages of Data Mining

Data mining possesses great potential for the healthcare industry, but it also comes with some concerns; one major concern is that massive amounts of patient data being shared during the data mining process may leave some patients worried that their personal information could fall into the wrong hands (Lee & Yoon, 2017). A second concern is that there is still a large proportion of healthcare data in an unstructured format. Unstructured texts store a lot of valuable medical information but lack common structural frameworks, and there are many errors, such as improper grammatical use, spelling errors, local dialects, and semantic ambiguities that increase the complexity of data processing and analysis (Sun et al., 2018). As a result, it was necessary to find ways to blend structured and unstructured data to obtain maximum value and facilitate

meaningful use of this data and get insights into patient outcomes, increase treatment effectiveness and patient satisfaction (Sarwar et al., 2022).

Identification of Setting and Sample Size

The sample was obtained from EHR information provided for individuals with OUD who were over 18 years of age and received medication treatment with buprenorphine at a multistate, multisite MT facility from January 1, 2016, through January 31, 2018. All patients were screened and met the criteria for OUD according to the *DSM-V*. Individuals who were under the age of 18 and treated for OUD with other medications or modalities were excluded from this study.

Sample Size and Power Analysis

Determination of the sample size consists of the following factors: the total sample size of the population being studied, significance level, power, and effect size. Using G*Power 3.1.9.2, power analyses were performed to estimate the required sample size for this study. For Aim 1, assuming a small effect size of 0.02, power of 0.80, an alpha level of 0.05, and with 10 predictors, the power to identify even a small effect size was statistically significant. The second study aim which focused solely on pregnant women (n = 140) was significantly underpowered and considered to be more of an exploratory aim of the study. It is important to note that there was an oversampling of women in this study as enough pregnant women were needed for Aim 2 which focused on pregnant women.

Operational Definition of Variables

All variables of interest in this study were obtained from patients' EHR data. The data had already been provided to Dr. Chiodo in CSV format. All CSV tables had been

converted to SPSS files and merged by patient medical record number (MRN). All MRN and other identifying information were removed prior to data transfer and analysis. A description of all study variables and how they were operationalized is provided below.

Predictors (IVs)

The main predictors evaluated in this study were functional risk score and opioid use.

Predictor 1: Functional Risk Score

The functional risk score is operationalized as the sum of nine pre-identified factors that may increase a patients' risk for leaving or discontinuing treatment. Functional risk scores were obtained from coding EHR provider text entries documented during patient visits. The functional risk score was created using the following constructs: 1. Negative social support (risk = yes = 1; no = 0), 2. Negative contact (risk = yes = 1; no = 0) 3. Unstable housing (risk = yes = 1; no = 0), 4. CJS involvement (risk = yes = 1; no = 0), 5. Unstable finances (risk = yes = 1; no = 0), 6. Unstable employment (risk = yes = 1; no = 0), 7. Child custody issues (risk = yes = 1; no = 0), 8. Social stressors (risk = yes = 1; no = 0), 9. Non-social stressors (risk = yes = 1; no = 0). Patients were assigned a risk score of "1" for each positive factor, this coding happened for each visit giving each patient visit a risk score of 0-9. All risk score across all visits were summed to create the total risk score.

Reliability of the Functional Risk Scores

To ensure reliable coding, three training sessions occurred. In these training sessions, two RAs coded provider documentation for 10 patients. To code these 10 patients, a total of 1425 individual risk scores were coded. As mentioned, a total of three

rounds of coding took place, in which both RAs independently coded the same 10 patients in each round (N = 30). After each round of coding, data was compared, key phrases and information was presented and discussed, all discrepancies were resolved, and an information log was created to support the decision of assigning a risk code.

Evaluating the difference in risk scores between the RAs is important to determine the overall reliability of the results. The question of consistency, or agreement among the individuals collecting, or analyzing the data, immediately arises due to the variability among human observers (McHugh, 2012). Well-designed research studies must therefore include procedures that measure agreement among the various data collectors (M. L. McHugh, 2012). To achieve this goal, study designs typically involve training the data collectors, and measuring the extent to which they record the same scores for the same phenomena.

When evaluating the reliability of risk score for this study, Cohen's kappa was used. Cohen's kappa was used instead of percent agreement (the number of agreement scores divided by the total number of scores) since percent agreement does not account for chance agreement (McHugh, 2012). Cohen's kappa takes into account the possibility that raters actually guess on at least some variables due to uncertainty (McHugh, 2012). Like most correlation statistics, the kappa can range from −1 to +1. It should be noted that both percent agreement and kappa have strengths and limitations (McHugh, 2012). The percent agreement statistic is easily calculated and directly interpretable. Its key limitation is that it does not take account of the possibility that raters guessed on scores and thus the possibility of overestimating the true agreement among raters is not discounted. The kappa was designed to take account of the possibility of guessing, but the

assumptions it makes about rater independence and other factors are not well supported, and thus it may lower the estimate of agreement excessively (McHugh, 2012). In providing the best results, it is advised for researchers to calculate both percent agreement and kappa. If there is likely to be much guessing among the raters, it may make sense to use the kappa statistic, but if raters are well trained as in this study, little guessing is likely to exist and thus the researcher may safely rely on percent agreement to determine interrater reliability (McHugh, 2012).

Reliability was evaluated after the third round of coding and before disagreement resolution. A reliability coefficient was obtained for each risk score. All risk scores had scores that were > 0.9 (i.e., > 90% agreement), demonstrating an almost high rate of reliability resolution.

Predictor 2: *Opioid Use*

Patients' opioid drug use was measured by percent of UDSs that were positive for opioids. Patients provided urine at each visit and also when called in randomly to do so. UDS evaluate the presence of an extensive list of opioids, including heroin, morphine, hydrocodone, hydromorphone, and oxycodone. A variable was constructed to determine the percent of opioid tests that were positive for each patient by dividing the total number of opioid positive tests by the total number of opioid tests conducted.

Outcome Variables

The Outcome Variables in this study were treatment utilization, medication utilization, and treatment retention. There is no standard definition that defines treatment utilization; therefore, multiple variables were used to examine treatment utilization. Medication utilization was calculated by taking the number of positive buprenorphine

urine tests/total number of tests that yield percent positive UDSs. This provided an indication of medication utilization while an individual was in treatment (% buprenorphine + UDS). Treatment retention was measured as (yes/no) and looked at the patients that remained active in treatment as on January 31, 2018.

Treatment Utilization

Several types of encounters were recorded in the EHR each time the patient was scheduled for a visit. These types of visits where an encounter is created include one-to-one provider visits (initial visit, induction visit, maintenance visit) and random UDS visits. Evaluating the frequency at which a patient misses a scheduled provider visit or random UDS provides the opportunity to examine an individual's treatment utilization. The following variables operationalized treatment utilization: (a) number of maintenance visits, (b) number of random maintenance visits, (c) number of no-show visits, (d) number of rescheduled visits, (e) number of other encounters, (f) number of care interruptions, (g) total time in care, and (h) time since last visit, in the multivariate analyses. Because patients who have been in treatment longer would be expected to have higher rates of treatment utilization, treatment utilization variables (a)–(h) were adjusted by total time in care, which is the amount of time the patient had been in care.

Number of Maintenance Visits

Initial visits occurred when a patient sought to initiate treatment at the treatment center. This also included patients who had been in treatment previously and sought to be re-initiated into treatment following a care interruption (described further below); as such, it was possible for someone to have more than one initial visit.

Number of Random Maintenance Visits

This was measured by the total number of times a patient did not show for a random UDS visit.

Number of No-Show Visits

The number of times a patient did not show for a scheduled appointment, the appointment was identified as a "no-show visit."

Number of Rescheduled Visits

This variable was constructed by calculating the total number of times a patient rescheduled their maintenance visit.

Number of Other Encounters

Other patient encounters were any other encounters with the treatment center staff and recorded in the EHR that were not provider visits or random UDS visits. For example, calling regarding a prescription or to check on insurance was coded as other encounter. The frequency of contact with treatment center staff may also be an indicator of patient engagement in treatment. Total number of other encounters were summed for each patient

Number of Care Interruptions

A patient was considered to be a patient if they have been seen within the past 30 days. A stoppage in treatment was considered a care interruption. The number of care interruptions was a composite variable of several variables available in the database: induction visits, rejoin visits, and initial visits. Each time a patient began treatment, there was an initial intake visit. If a patient had been out of care for a significant period of time, the treatment center considered the first visit a patient returns as an "initial visit." An

induction visit took place when a patient came to the treatment center to begin MT following the initial visit. During the induction visit they received their first dose of MT. If the amount of time a patient had been out of care was of a short enough duration that the treatment center considered no need for additional education and intake information, the first visit back to care was labeled as a "re-join" visit and the patient was immediately placed back on MT. The number of care interruptions was the total number of initial, induction, and re-join visits.

Total Time in Care

The amount of time a patient was active in care from the study start date January 1, 2016, through January 31, 2018, divided by the total number of care interruptions (30 days outside of treatment) yielded the total time in care.

Time Since the Last Visit

Time since last visit indicated the number of days since the last clinical visit and was calculated by subtracting the last date of service from the current date. The last time a patient received treatment divided by number of care interruptions (if applicable) yielded time since last visit.

Medication Utilization

Medication utilization was defined as *taking buprenorphine* for MT as was outlined in the treatment protocol developed by the healthcare provider according to the substance use treatment plan. The presence and levels of buprenorphine were also examined in UDS at each visit. For the purposes of data analysis, buprenorphine utilization was operationalized as percent of UDS positive for buprenorphine. To construct this variable, the total number of buprenorphine positive UDS was divided by

the total number of UDS completed, resulting in a ratio of the number of buprenorphine positive tests: total number of buprenorphine tests.

Treatment Retention

Patients who were still active in treatment on January 31, 2018, were considered retained in treatment.

Covariates

Covariates that were included in the analyses included: age, gender (male/female), ethnicity (Hispanic/Latino/non-Hispanic/Latino), race (White/non-White), and pregnancy (yes/no). Other variables known to influence MT outcomes were extracted from both structured and unstructured data fields in the patient's record including history of anxiety (yes/no), history of PTSD and trauma exposure (PTSD/trauma) (yes/no), history of involvement in the CJS (yes/no), and other drug/alcohol use (% positive).

Anxiety

During patient intake, patients provided an extensive medical and social history. There are several locations in the EHR where data related to anxiety history can be entered by a provider. Each of these fields is in free text format. After translating all text data to lowercase, syntax was written to identify cases with a diagnosis of anxiety. The following phrases were identified in the text fields and flagged as positive for anxiety: anxiety, etc. In addition, a patient with any anxiety diagnosis code was identified as positive for anxiety.

History of PTSD/Trauma

Similar to anxiety, during patient intake, patients provide an extensive medical and social history. There are several locations in the EHR where data related to PTSD or

trauma history can be entered by a provider. Each of these fields is in free text format. Text conversion was performed and any case where a provider identified a history of PTSD was identified as PTSD positive.

The following phrases were identified in the text fields and flagged as trauma positive: *stabbed, gunshot, traumatic, abused, hostage, victim of, rape, traumatic abuse, childhood abuse, history abuse, intimate partner violence, domestic violence, gun shot, bullet wound, trauma history, physical abuse, sexual abuse, emotional abuse, assaulted, abuse as child, stab wounds, beat up, being shot, verbal abuse, bullet lodged, shrapnel, stab injury, sexually abused, physically abused, mugging, traumatic experiences, emotionally abused, domestic violence, past sexual trauma, violent incident, abusive relationship, stabbing victim, molested*, *and kidnapped.*

In addition, a patient with a diagnosis code consistent with trauma was identified as positive for trauma and a patient who identified as having PTSD was also identified positive for trauma. Since many patients identified as having both PTSD and trauma, a composite variable was constructed merging PTSD positive and anxiety positive cases. Analyses was performed using composite PTSD/Anxiety variables.

Other Drug and Alcohol Use

Patients' drug use was measured by percent of UDS that are positive for alcohol and other drugs. Patients provided urine at each visit and also when called in randomly to do so. Percent positive other drug and alcohol variables were included as covariates in all analyses. The drugs examined included THC, benzodiazepines, alcohol, cannabis, amphetamines, and cocaine. These variables were constructed using the same method as percent positive opioid drug use and percent positive buprenorphine.

History of Involvement in Criminal Justice System

The national treatment provider evaluated patient involvement in the CJS (i.e., probation, awaiting trial, and past incarceration) each quarter when the treatment plan was evaluated. This data was identified via check boxes. Providers were able to check either that there were "pending criminal charges" or "resolved criminal charges." If a patient was positive for either, they were identified as involved with the CJS. In addition, several patients were identified as being involved in the CJS through a separate database for patients who were part of a study performed by the treatment center location. All patients in the "Jail Database" were identified as positive for CJS involvement.

Measurement of Variables

All variables were obtained from the EHR. Level of measurement for all predictor and outcome variables was continuous, with the exception of treatment retention, which was dichotomous.

Procedures

The Addiction Research and Education Foundation (AREF)—a nonprofit organization led by Dr. Chiodo—had access to patient data from a multisite, multistate outpatient treatment center that was provided to Dr. Chiodo in individual CSV data tables. Dr. Chiodo imported all data tables into SPSS v25 and merged them into a data file. Files were merged based on patient MRN. Before providing the data for analysis, Dr. Chiodo removed all identifying patient information including MRN, and a study ID was created for each patient. IRB approval from the University of Massachusetts Amherst was received prior to data transfer. The data was transferred to an iron-key password

secured and locked data file. Data was then analyzed, and analyses were performed to evaluate study aims.

Data Analysis

Prior to beginning study analyses, all variable distributions were evaluated for normality or data entry errors. All necessary variable transformations were performed prior to analysis. After completion of distribution evaluation, descriptive statistics were calculated for all variables. Prior to multivariate analyses, bivariate analyses were performed. Bivariate analyses included Pearson Product Moment Correlations and t-tests, depending on the level of measurement of the variables being examined. All multivariate analyses utilized hierarchical multiple linear regression or hierarchical logistic regression. All control variables were included in all the regression models. The multivariable analyses are described below.

Aim 1: To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of patients with OUD in MT.

> H1a-h: Functional risk score will account for significantly more treatment utilization variance than opioid use across many different treatment utilization variables.
>
> H1i: Functional risk score will account for significantly more medication utilization variance than opioid use.
>
> H1j: Functional risk score will account for significantly more treatment retention variance than opioid use.

For Aim 1, multiple linear regression was performed to examine relationships between opioid use, functional risk score variables, and treatment utilization variables. For each of the treatment utilization variables multilinear regressions were performed the two predictor variables: opioid use and functional risk score. Step (1) all covariates were entered into the regression model, Step (2) drugs and alcohol variables were entered into

the model, Step (3) each treatment regression model included opioid use & functional outcomes to comprise total risk score variable. A significant regression coefficient (***β***) was used to determine if opioid use or functional risk significantly predicted treatment utilization.

Lastly, an R to Z transformation was done to compare the 95% confidence intervals of the Beta weights. An overlap of > 50% was considered statistically significant difference between the amount of variance accounted for by the regression models. The same procedure was done for hypotheses H1a.-h. and H1i.

For H1j. logistic regression was used to examine the relationships between opioid use, functional risk score variables, and treatment retention. For each of the (TU) variables, multilinear regressions were performed for the two predictors: opioid use and functional risk score. The same method was done as with H1.- Hi. except odds ratios between the two regressions were compared to determine the outcome.

Aim 2: To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of pregnant women with OUD in MT.

Analysis for this aim was limited to only pregnant patients and included data only during their pregnancy. The analytic plan was identical to what was presented in Aim 1.

Limitations

Several limitations may have impacted this study. The first is that this study was a retrospective collection of data that presented outcomes from a risk perspective thus, a prospective study evaluating positive outcomes that influence and individuals' ability to be successful in treatment would be warranted. The second limitation is the potential errors in data entry such as (omission of data, missed flagged phrases and data for race and ethnicity, as well as typographical or grammatical errors that would otherwise be

pertinent to the data collection process). Another limitation is that the patient health information (PHI) documents may have lacked authenticity, in that parts of a document might have been incomplete or missing because of age. Incomplete documentation can lead to the inability and verification of information and thus present challenges in determining bias. Lastly, documents and data may not be representative of the wider population and thus can limit generalizability of the study.

Protection of Human Subjects

Approval for this study was obtained from the University of Massachusetts Amherst Investigational Review Board committee (see Appendix A) and the Addiction Research and Education Foundation (see Appendix B). Upon admission to one of the multisite treatment centers, patients provide informed consent that includes permission to use their de-identified EHR data for research purposes. The data utilized for the purpose of this study was de-identified to prevent any personal health information from being linked to the study participant. In addition, all data obtained and analyzed was stored in locked areas or on password-protected computers. The computer that contains this program was password protected and was only accessible to the researcher. The measures in place greatly reduced the potential of breach in confidentiality and reduced human subject risk.

CHAPTER 4

RESULTS

This chapter outlines the results of the study including sample characteristics, distribution evaluation, bivariate, and multivariate analyses. This chapter provides results based on the predictor variables (functional risk score and opioid use) and the dependent variables (treatment utilization, medication utilization, and treatment retention). Multivariate analyses are presented for each study aim.

Sample Characteristics

Variables collected on the demographic form at the beginning of the survey included sex assigned at birth, race, ethnicity, and state that patient received treatment for OUD. The study sample consisted of (N = 416) patients, due to the variability in patient age, outliers for age were windsorized resulting in an age range from 20 to 73 years (M = 38.1, SD = 10.7) for the sample. The majority of the sample identified as female (63.7%), White (93.6%) and non-Hispanic (86.5%). All patients in the sample resided in and received treatment within the state of Massachusetts. Among the patient sample, slightly over one third (33.7%,) reported being pregnant during their time in treatment (see Table 1). The age range among pregnant women that reported they were ever pregnant while in treatment in the sample was (M = 31.5, SD = 6.2). It is important to note that there was a higher percentage of females due to the oversampling of women for Aim 2. All patients included in this sample received buprenorphine for treatment of OUD.

Other variables relevant to the study of individuals in treatment for OUD and functional outcomes were also collected, these include PTSD/trauma, pregnancy, CJS involvement, and anxiety. Just over one third of the sample, (36.5%), had reported a

history of PTSD or trauma (PTSD/trauma) while enrolled in treatment. As mentioned in Chapter 3, PTSD diagnosis and reported trauma were combined into one variable to create a composite variable PTSD/trauma due to similar constructs. There was further evidence of psychiatric comorbidity as slightly over half of the sample (55.8%) reported symptoms of anxiety and just over one third of patients (36.1%) acknowledged they had been involved with the criminal justice system while in treatment (see Table 1).

Table 1: Characteristics of sample.

Variable	N	%
Sex (% female)	416	63.7
Race (% White)	282	93.6
Ethnicity (% non-Hispanic)	304	86.5
Pregnant during treatment (% pregnant)	416	33.7
History of PTSD/trauma	416	36.5
Reported Anxiety (% yes)	416	55.8
Criminal Justice System (% yes)	416	36.1

Drugs and Alcohol Use

Drugs and alcohol use was reported by evaluating the percent of UDS results that were positive for drug and alcohol use (see Table 2). results showed that 8.9% (*SD* = 12.7%) tested positive for the presence of benzodiazepines, 13.5% (*SD* = 21.7%) for alcohol, 32.1% (*SD* = 38.9%) for cannabis, 4.6% (*SD* = 12.6%) for amphetamines, and 14.4% (*SD* = 24.1%) for cocaine. Initially, other drugs and alcohol use variables were not normally distributed. Analyses for non-normal distributions were performed using log-transformed variables.

Table 2: Other drug and alcohol use.

Substance (% positive)	Min	Max	Mean	SD
Benzodiazepine	0.0	67.0	8.9	12.7
Alcohol	0.0	100.0	13.5	21.7
Cannabis	0.0	100.0	32.1	38.9
Amphetamine	0.0	79.0	4.6	12.6
Cocaine	0.0	100.0	14.4	24.1

Predictor Variables

Functional Risk Score

Nine individual functional outcomes were scored and totaled for each patient encounter to create the functional risk score (see Table 3). The nine outcomes include negative social supports, negative contacts, unstable housing, criminal justice involvement, unstable finances, unstable employment, custody of children, social stressors, and non-social stressors. Among individuals that reported having little to no support socially while active in treatment, just over half the sample, 58.9% (M = 0.65, SD = 3.30), reported having no support from friends, family, or a significant other while in treatment. Among those outcomes that were reported, just about a quarter, 23.1% (M = 2.66, SD = 5.78), of individuals with OUD did mention having negative contacts while in treatment. Some examples of this include contact with individuals that led to drug use or being surrounded by individuals who actively engage in the use of drugs or alcohol.

Among those that reported unstable housing while in treatment, almost half, 42.3% (M = 2.75, SD = 7.29), of individuals reported periods where their living situation was unstable. Examples of this include the patient reporting they lost housing, eviction, living in a shelter, renting a room, staying in different places (i.e., couch surfing), being homeless, or living in a hotel. CJS involvement was reported by a third, 34.3% (M = 1.50, SD = 3.86) of individuals in treatment. This variable was further defined by past and current CJS involvement. The percentage reported reflected current criminal justice involvement which was defined by; being on house arrest, awaiting trial, being probation, incarceration, or any involvement with police such as having their license revoked, or arrests by law enforcement. Unstable finances were reported by just over a third, 37.3%

(*M* = 0.94, *SD* = 1.90) of individuals in treatment. Key phrases of unstable finances such as being in debt, behind on payment, financial stress or burden and difficulty in paying copays were reported by individuals as markers for unstable finances.

Unstable employment was reported by over half, 66.3% (*M* = 3.86, *SD* = 6.30), of the sample while in treatment. Key phrases mentioned to support this outcome were unemployment, disability, quit work, being fired, recent layoff, lost job or working seasonally. Custody issues were reported by slightly over one third, 38.7% (*M* = 2.92, *SD* = 7.53), of the sample, key phrases that supported custody issues while in treatment were lost custody of children, Department of Children and Family (DCF) involvement, and unable to see children. The final two outcomes are social stressors, which were reported by 95.2% (*M* = 15.31, *SD* = 17.86) of the sample and non-social stressors, which were reported by 98.8% (*M* = 16.88, *SD* = 14.85) of the sample. Social stressors were identified as stressors dealing with people issues. Examples are a fight with family, friends, or significant other, illness of family members that affects the individual in treatment, childcare issues, or if the provider noted a presence of increased social stressors during the visit encounter. Non-social stressors were identified as health problems of the individual in treatment (being ill, having pain, new or existing medical diagnoses, hospitalizations, surgeries etc.), transportation, insurance, or pharmacy issues, as well as reports of anxiety or depression. The scores for each patient and each encounter were summed to create a total risk score.

Table 3: Functional outcome scores descriptive statistics.

Functional Risk Score Variables (% reported sum)	Min	Max	Mean	SD	% Ever
Negative Social Supports	0.00	61.0	0.65	3.30	23.1
Negative Contacts	0.00	72.0	2.66	5.78	58.9

Unstable Housing	0.00	112.0	2.75	7.29	42.3
Criminal Justice System	0.00	35.0	1.50	3.86	34.3
Unstable Finances	0.00	14.0	0.94	1.90	37.3
Unstable Employment	0.00	41.0	3.86	6.30	66.3
Custody Problems	0.00	85.0	2.92	7.53	38.7
Social Stress	0.00	110.0	15.31	17.86	95.2
Non-Social Stress	0.00	80.0	16.88	14.85	98.8
Total Functional Risk Score	0.00	318.0	47.47	44.86	N/A

Opioid Use

Patients' opioid drug use was measured by evaluating the percentage of opioids that were present in an individual's urine. Among the patients in the sample the average opioid use was 7.8% (SD = 10.2%).

Outcome Variables

Treatment Utilization

Several variables were used to evaluate treatment utilization (see Table 4). These include: number of random maintenance visits (M = 1.4, SD = 1.6), number of maintenance visits (M = 68.5, SD = 49.8), number of no-show visits (M = 6.3, SD = 6.6), number of rescheduled visits (M = 8.7, SD = 9.8), number of other encounters (M = 53.6, SD = 33.4), number of care interruptions (M = 0.8, SD = 1.3), total time in care (M = 2.1, SD = 1.5), and time since the last visit (M = 3.6, SD = 1.6). Distributions of the treatment utilization variables were evaluated for normality and outliers prior to analysis. Care interruptions were analyzed using stem-and-leaf plot and boxplot methods. This resulted in the identification of 30 extreme outliers with > 7 care interruptions. Therefore, care interruptions were windsorized (adjusted: M = 0.8, SD = 1.3; range 0–7).

Due to the non-normal distribution, skewness, and kurtosis, the number of random maintenance visits, the number of maintenance visits, the number of "no show" visits, the number of rescheduled visits, and the number of other encounters were all log-

transformed. All analyses were performed using transformed variables. Number of care interruptions was further described by evaluating the number of interruptions in care including discharges, rejoins, and other lapses in an individual's treatment course. A patient was considered to be an active patient if they had been seen within the past 30 days. A stoppage in treatment was considered a care interruption. There was on average, a little less than half of patients, 43.5% (M = 0.8, SD = 1.3) who reported at least one interruption in their care.

Table 4: Treatment utilization descriptive statistics.

Treatment Utilization Variables	Mean	SD	Min	Max
Number of random maintenance visits	1.4	1.7	0.0	8.0
Number of maintenance visits	68.5	49.8	5.0	316.0
Number of no-show visits	6.3	6.6	0.0	34.0
Number of rescheduled visits	8.7	9.8	0.0	76.0
Number of other encounters	53.6	33.4	3.0	244.0
Number of care interruptions	0.8	1.3	0.0	6.0
Total time in care years	2.1	1.5	0.3	7.3
Time since last visit	0.23	0.39	0.0	1.5

Medication Utilization

As previously mentioned, medication utilization was determined by evaluating the percent of UDS results that were positive for buprenorphine. Results showed that the majority of the patients were positive for buprenorphine 94.9%, (SD = 0.08%). This indicates that almost all patients enrolled in treatment utilized medication for OUD. Since medication utilization was not normally distributed, analyses were performed using a log-transformed variable.

Treatment Retention

Treatment retention was determined by evaluating the number of patients who were still active in treatment as of January 31, 2018. Among the patients in the sample (N=416), 70.4% of patients were still active in treatment as of January 31, 2018.

Relationship Between Gender and Sample Characteristics

The relationship between gender and other study sample characteristics (race, ethnicity, PTSD/trauma, anxiety, and CJS involvement) was examined via a chi-square analysis (see Table 5). Results identified a significant relationship between gender and ethnicity, PTSD, and anxiety. Specifically, women in treatment for OUD, were more likely to identify as non-Hispanic (93.8% vs. 73.9%; $\chi^2 = 23.9$, $p < 0.001$), and report more anxiety (61.5% vs. 45.7%; $\chi^2 = 9.8$, $p = 0.002$), and PTSD/trauma (45.3% vs. 21.1%; $\chi^2 = 24.1$, $p < 0.001$), when compared to men in the sample. There were no significant relationships between gender and race ($\chi^2 = 3.7$ $p = 0.452$), and CJS involvement ($\chi^2 = 0.1$ $p = 0.742$).

Table 5: Relationship between gender and sample characteristics.

Variable	Gender		χ^2	**p**
	Males (n = 153)	Females (n = 263)		
Race (% White)	92.4	94.2	3.7	0.452
Ethnicity (% Non-Hispanic)	73.9	93.8	23.9	**<0.001**
History of PTSD/trauma (%Yes)	21.1	45.3	24.1	**<0.001**
Reported Anxiety (% Yes)	45.7	61.5	9.8	**0.002**
Criminal Justice System (% Yes)	37.1	35.5	0.1	0.742

Relationship Between Gender and Medication Utilization, and Drugs and Alcohol Use

The relationship between gender and drugs and alcohol use was evaluated via independent t-test (see Table 6). Results identified a significant relationship between gender and alcohol use. In this sample, men had a higher percentage of alcohol use compared to women in this sample (17.1% vs. 11%; $t = 2.7$, $p < 0.001$). In contrast there was no relationship found between gender and benzodiazepine ($t = -0.8$, $p = 0.850$), cannabis ($t = 0.2$, $p = 0.090$), amphetamines ($t = -0.7$, $p = 0.270$), or cocaine ($t = 1.4$, $p = 0.199$). To determine if there were any differences between gender and medication utilization, and opioid use, an independent sample t-test was performed (See Table 6), and findings show that there were no significant relationships between gender and buprenorphine ($t = -0.4$, $p = 0.705$), and opioid use ($t = 0.7$, $p = 0.514$).

Table 6: Relationship between gender and medication utilization, and drugs and alcohol use.

Variable (% positive)	N	Mean	SD	t	p
Benzodiazepine					
Male	151	8.3	12.6	-0.8	0.850
Female	265	9.0	12.7		
Alcohol					
Male	151	17.1	24.0	2.7	**<0.001**
Female	265	11.0	18.6		
Cannabis					
Male	151	32.0	38.9	0.2	0.709
Female	265	31.2	38.1		
Amphetamine					
Male	151	4.2	10.6	-0.7	0.270
Female	265	5.1	13.5		
Cocaine					
Male	151	16.7	24.1	1.4	0.199
Female	265	13.3	23.5		
Opioid Use					
Male	151	8.2	9.7	0.7	0.514
Female	265	7.6	10.5		
Buprenorphine Use					
Male	151	0.9	0.1	-0.4	0.705
Female	265	1.0	0.1		

Relationship Between Gender and Functional Risk Score

The relationship between gender and functional risk score was evaluated using independent sample t-tests (see Table 7)**.** In the study sample, women reported more custody problems (3.68 vs. 1.57; $t = -2.9$, $p = 0.004$) than men in the sample. In contrast, men reported more unstable finances (1.21 vs. 0.79; $t = 2.2$, $p = 0.030$), and unstable employment (5.15 vs. 3.11; $t = 3.1$, $p = 0.002$). There were no significant relationships found between gender and social support, ($t = 0.8$, $p = 0.416$), negative contacts ($t = 0.1$, $p = 0.954$), housing issues ($t = 1.6$, $p = 0.105$), CJS issues ($t = -0.2$, $p = 0.877$), social stress ($t = -0.0$, $p = 0.998$), non-social stress ($t = 1.8$, $p = 0.078$), or total functional risk score ($t = 1.0$, $p = 0.329$).

Table 7: Relationship between gender and functional risk score.

Variable	N	Mean	SD	t	p
Negative Social Supports					
Male	151	0.83	5.12	0.8	0.416
Female	265	0.55	1.44		
Negative Contacts					
Male	151	2.67	0.33	0.1	0.954
Female	265	2.64	0.40		
Unstable Housing					
Male	151	3.51	10.39	1.6	0.105
Female	265	2.31	4.65		
Criminal Justice System					
Male	151	1.46	3.63	-0.2	0.877
Female	265	1.52	3.99		
Unstable Finances					
Male	151	1.21	2.00	2.2	**0.030**
Female	265	0.79	1.81		
Unstable Employment					
Male	151	5.15	6.87	3.1	**0.002**
Female	265	3.11	5.82		
Custody Problems					
Male	151	1.57	6.62	-2.9	**0.004**
Female	265	3.68	7.91		
Social Stress					
Male	151	15.30	18.91	-0.0	0.998

Female	265	15.30	17.27		
Non-Social Stress					
Male	151	18.58	16.51	1.8	0.078
Female	265	15.91	13.74		
Total Functional Risk Score					
Male	151	50.31	48.49	1.0	0.329
Female	265	45.84	42.66		

Relationship Between Gender and Treatment Utilization

To determine if there were any differences between gender and treatment utilization an independent group t-test was performed (see Table 8). Results showed that males in the sample had more maintenance visits (81.6 vs. 61.0; $t = 3.9$, $p < 0.001$), spent longer time in care (0.9 vs. 0.8; $t = 3.2$, $p = 0.001$), and had longer periods of time in between visits (0.3 vs. 0.2; $t = 2.8$, $p = 0.005$) when compared to females in the sample. There were no significant relationships found between gender and attendance at random maintenance visits ($t = 0.7$, $p = 0.475$), no-show visits ($t = 1.8$, $p = 0.070$), rescheduled visits ($t = 1.1$, $p = 0.261$), other encounters ($t = 1.1$, $p = 0.276$), or care interruptions ($t = 0.6$, $p = 0.537$).

Table 8: Relationship between gender and treatment utilization.

	N	Mean	SD	t	p
Number of random maintenance visits					
Male	151	1.5	1.6	0.7	0.475
Female	265	1.4	1.5		
Number of maintenance visits					
Male	151	81.6	54.8	3.9	**<0.001**
Female	265	61.0	45.1		
Number of "no-show" visits					
Male	151	7.1	7.3	1.8	0.070
Female	265	5.8	6.1		
Number of rescheduled visits					
Male	151	9.4	22.0	1.1	0.261
Female	265	8.3	9.2		
Number of other encounters					

Male	151	56.0	33.7	1.1	0.276
Female	265	52.3	33.2		
Number of care interruptions					
Male	151	0.9	1.3	0.6	0.537
Female	265	0.8	1.2		
Total time in care years					
Male	151	0.9	1.5	3.2	**0.001**
Female	265	0.8	1.5		
Time since last visit					
Male	151	0.3	0.4	2.8	**0.005**
Female	265	0.2	0.4		

Relationship Between Gender and Treatment Retention

To determine if there were any differences between gender and treatment retention, a chi-square analysis was performed (see Table 9). Results show that females had a higher rate of treatment retention when compared to males in the sample (75.5 vs. 61.6; $\chi^2 = 8.9$, $p = 0.003$).

Table 9: Relationship between gender and treatment retention.

	Gender			
Variable (% retained)	Males	Females	χ^2	p
Treatment Retention	61.6	75.5	8.9	**0.003**

Relationship Between Age and Sample Characteristics

The relationship between age and study demographic variables were evaluated via t-tests (see Table 10). A significant relationship was identified between age and pregnancy (31.5 vs. 40.9; $t = 8.4$, $p < 0.001$). Women who were pregnant while in treatment were on average younger than women who were not pregnant during treatment. No significant relationships were found between age and gender, ($t = 5.3$, $p = 0.090$), race ($t = 1.3$, $p = 0.402$), ethnicity ($t = 0.9$, $p = 0.972$), PTSD/trauma ($t = 0.2$, $p = 0.344$), anxiety ($t = -1.2$, $p = 0.713$), or CJS involvement ($t = -0.2$, $p = 0.096$).

Table 10: Relationship between age and sample characteristics.

Variable	N	Mean	SD	t	p
Gender					
Male	151	41.7	10.7	5.3	0.090
Female	265	36.1	10.2		
Race (% White)					
White	264	37.6	10.8	1.3	0.402
Non-White	18	41.0	13.0		
Ethnicity (% Non-Hispanic)					
Hispanic	41	39.3	10.5	0.9	0.972
Non-Hispanic	263	37.7	10.7		
History of PTSD/Trauma (% yes)					
No	264	38.2	10.4	0.2	0.344
Yes	152	38.0	11.2		
Reported Anxiety (% yes)					
No	184	37.4	10.8	-1.2	0.713
Yes	232	38.7	10.7		
Criminal Justice System (% yes)					
No	266	38.0	11.1	-	0.096
Yes	150	38.2	10.2	0.2	
Pregnancy (% yes)					
No	123	40.9	11.0	8.4	**<0.001**
Yes	140	31.5	6.2		

Relationship Between Age and Medication Utilization, and Drugs and Alcohol Use

The relationship between age and other drugs and alcohol use variables was analyzed by computing the Pearson product-moment correlation coefficient (see Table 11). There was a positive correlation between age, benzodiazepines, alcohol, and cannabis use showing that as age increased, benzodiazepine use ($r = 0.18$, $p < 0.001$) and alcohol use ($r = 0.12$, $p < 0.05$) also increased. In contrast, there was a negative relationship between age and cannabis use showing that as age increased, cannabis use decreased ($r = -0.10$, $p < 0.05$). No relationships were found between age and opioid use ($r = -0.14$, $p = 0.78$), and buprenorphine use ($r = 0.00$, $p = 0.952$).

Table 11: Relationship between age and drugs and alcohol use.

Variable (% positive)	r
Benzodiazepine	**0.18*** **
Alcohol	**0.12***
Cannabis	**- 0.10***
Amphetamine	0.06
Cocaine	0.07
Opioid Use	-0.14
Buprenorphine	0.00

*p<0.05. **p<0.01. ***p<0.001.

Relationship Between Age and Functional Risk Score

To examine the relationship between age and several functional outcome variables, a correlation analysis was performed (see Table 12). There was a significant negative relationship between age and several functional outcome variables, showing that as age increased negative social supports (r = -0.19, p < 0.01), negative contacts (r = -0.19, p < 0.01), unstable housing (r = -0.23, p < 0.01), custody problems (r = -0.40, p < 0.01), and total functional risk (r = -0.14, p < 0.01) decreased. There was no significant relationship between age and CJS (r = -0.14, p = 0.07), unstable finances (r = 0.06, p = 0.42), unstable employment (r = -0.05, p = 0.38), social stress (r = -0.05, p = 0.29), or non-social stress (r = -0.08, p = 0.13).

Table 12: Relationship between age and functional risk score.

Variable	r
Negative Social Support	**-0.19****
Negative Contacts	**-0.19****
Unstable Housing	**-0.23****
Criminal Justice System	-0.14
Unstable Finances	0.06
Unstable Employment	-0.05
Custody Problems	**-0.40****
Social Stress	-0.05
Non-Social Stress	-0.08
Total Functional Risk Score	**-0.14****

*p<0.05. **p<0.01. ***p<0.001.

Relationship Between Age and Treatment Utilization

To determine if there were differences between age and treatment utilization, a correlation analysis was performed (see Table 13). Significant relationships were found between age and several treatment utilization variables showing that as age increased, attendance at random maintenance visits ($r = 0.16$, $p < 0.01$), maintenance visits ($r = 0.25$, $p < 0.01$), and total time in care ($r = 0.22$, $p < 0.01$) increased. No significant relationships were found between age and number of "no show" visits ($r = -0.02$, $p = 0.726$), reschedule visits ($r = -0.03$, $p = 0.574$), other encounters ($r = -0.08$, $p = 0.089$), care interruptions ($r = -0.01$, $p = 0.834$), or time since last visit ($r = -0.06$, $p = 0.263$).

Table 13: Relationship between age and treatment utilization.

Variable	r
Number of random maintenance visits	**0.16****
Number of maintenance visits	**0.25****
Number of "no-show" visits	-0.02
Number of rescheduled visits	0.03
Number of other encounters	0.08
Number of care interruptions	0.01
Total time in care years	**0.22****
Time since last visit	0.06

*p<0.05. **p<0.01. ***p<0.001.

Relationship Between Age and Treatment Retention

To determine if there was a relationship between age and treatment retention, an independent samples t-test was performed (see Table 14). Results show that there was no significant relationship found between age and being retained in treatment ($t = 1.7$, $p = 0.916$).

Table 14: Relationship between age and treatment retention.

Variable (% retained)	N	Mean	SD	t	p
Treatment Retention					
Yes	293	37.5	10.9	1.7	0.916
No	123	39.5	10.2		

Relationship Between Pregnancy and Sample Characteristics

The relationship between pregnancy and study variables was evaluated via chi-square analysis (see Table 15). There was no significant relationship found between pregnancy and study demographic variables.

Table 15: Relationship between pregnancy and sample characteristics.

		Pregnancy Status			
Variable (%)	N	Non-Pregnant	Pregnant	χ^2	p
Race (% White)	189	43.8	56.2	0.0	0.916
Ethnicity (% Non-Hispanic)	192	90.9	96.2	2.2	0.135
History of PTSD/trauma (% Yes)	263	41.9	47.1	0.7	0.396
Reported Anxiety (% Yes)	263	66.9	57.1	2.7	0.102
Criminal Justice System (% Yes)	263	37.1	35.0	0.1	0.723

The Relationship Between Pregnancy and Medication Utilization, and Drugs and Alcohol

The relationship between pregnancy and drugs and alcohol use was evaluated via independent samples t-test (see Table 16). Pregnant patients were found to have lower rates of benzodiazepine (6.7% vs. 12.2%; $t = 3.5$, $p < 0.001$), and alcohol use (7.9% vs. 14.0%; $t = 2.7$, $p < 0.01$), than patients who had not been pregnant at some point during treatment. No differences were found between pregnancy and cannabis ($t = 1.6$, $p = 0.120$), amphetamines ($t = 0.5$, $p = 0.622$), or cocaine use ($t = -0.06$, $p = 0.952$). The relationship between pregnancy and opioid use, and medication utilization was also evaluated via an independent samples t-test (see Table 16). Analyses show that there was no significant relationship between pregnancy and opioid use ($t = 1.6$, $p = 0.109$), or medication utilization ($t = -1.1$, $p = 0.25$).

Table 16: Relationship between pregnancy and opioids, and drugs and alcohol use.

Variable (% positive)	N	Mean	SD	t	p
Benzodiazepine					
Non-Pregnant	123	12.2	14.4	3.5	**<0.001**
Pregnant	140	6.7	10.4		
Alcohol					
Non-Pregnant	123	14.0	22.6	2.7	**<0.01**
Pregnant	140	7.9	11.6		
Cannabis					
Non-Pregnant	123	35.3	40.3	1.6	0.120
Pregnant	140	27.8	36.2		
Amphetamine					
Non-Pregnant	123	5.6	14.6	0.5	0.622
Pregnant	140	4.7	12.5		
Cocaine					
Non-Pregnant	123	12.9	24.0	-0.1	0.952
Pregnant	140	13.1	22.4		
Opioid Use					
Male	123	0.9	0.1	1.6	0.257
Female	140	1.0	0.1		
Buprenorphine Use					
Male	123	0.08	0.1	-1.1	0.109
Female	140	0.07	0.1		

Relationship Between Pregnancy and Functional Risk Score

The relationship between pregnancy and functional risk score was evaluated via independent sample t-test (see Table 17). There was a significant relationship between pregnancy and several functional risk score variables showing that women who were not pregnant during treatment reported more incidences of negative social supports ($t = 3.0$, $p = 0.003$), negative contacts ($t = 2.4$, $p = 0.018$), unstable finances ($t = 3.1$, $p = 0.002$), social stress ($t = 4.5$, $p < 0.001$), non-social stress ($t = 3.6$, $p < 0.001$), and had higher total functional risk scores ($t = 3.7$, $p < 0.001$) when compared to pregnant women in treatment. In contrast, pregnant women had more custody issues ($t = -2.3$, $p < 0.001$) when compared to women who were not pregnant while in treatment. There were no

significant relationships found between pregnancy status and unstable housing (t =1.8, p = 0.060), CJS issues (t = 0.7 p = 0.478), and unstable employment (t = 1.8, p = 0.079).

Table 17: Relationship between pregnancy and functional risk score.

Variable	N	Mean	SD	t	p
Negative Social Supports					
Non-Pregnant	123	0.85	1.92	3.0	**0.003**
Pregnant	140	0.30	0.77		
Negative Contacts					
Non-Pregnant	123	3.71	8.90	2.4	**0.018**
Pregnant	140	1.69	3.18		
Unstable Housing					
Non-Pregnant	123	2.90	5.65	1.8	0.069
Pregnant	140	1.83	3.53		
Criminal Justice System					
Non-Pregnant	123	1.72	4.52	0.7	0.478
Pregnant	140	1.37	3.50		
Unstable Finances					
Non-Pregnant	123	1.17	2.34	3.1	**0.002**
Pregnant	140	0.46	1.10		
Unstable Employment					
Non-Pregnant	123	3.80	6.28	1.8	0.079
Pregnant	140	2.54	5.38		
Custody Problems					
Non-Pregnant	123	2.50	6.11	-2.3	**< 0.001**
Pregnant	140	4.78	9.14		
Social Stress					
Non-Pregnant	123	20.47	20.10	4.5	**< 0.001**
Pregnant	140	10.89	12.99		
Non-Social Stress					
Non-Pregnant	123	19.22	15.73	3.6	**< 0.001**
Pregnant	140	13.14	11.07		
Total Functional Risk Score					
Non-Pregnant	123	56.35	48.47	3.7	**< 0.001**
Pregnant	140	36.98	34.77		

Relationship Between Pregnancy and Treatment Utilization

The relationship between pregnancy and treatment utilization was evaluated via independent samples t-tests (see Table 18). There was a significant relationship between non-pregnant patients and several treatment utilization variables with women who were

not-pregnant during treatment having had more random maintenance visits (1.7 vs. 1.2, $t = 2.5$, $p = 0.012$), maintenance visits (75.7 vs. 48.3, $t = 5.0$, $p < 0.001$), "no show" visits (6.7 vs. 5.1, $t = 2.2$, $p = 0.032$), rescheduled visits (10.7 vs. 6.2, $t = 4.1$, $p < 0.001$), other encounters (58.5 vs. 47.1, $t = 2.8$, $p = 0.005$), and spending longer time in care (2.5 vs. 1.6, $t = 5.1$, $p < 0.001$), and having longer periods of time in between visits (0.3 vs. 0.8, $p < 0.001$) when compared to patients who were pregnant while in treatment. In contrast, patients who were pregnant in treatment had more time between visits when compared to non-pregnant patients in the sample (0.8 vs. 0.3, $t = 5.1$, $p < 0.001$). There was no significant relationship found between pregnancy and the number of interruptions in care ($t = 1.7$, $p = 0.100$).

Table 18: Relationship between pregnancy and treatment utilization.

	N	Mean	SD	t	p
Number of random maintenance visits					
Non-Pregnant	123	1.7	1.6	2.5	**0.012**
Pregnant	140	1.2	1.4		
Number of maintenance visits					
Non-Pregnant	123	75.7	49.9	5.0	**<0.001**
Pregnant	140	48.3	36.4		
Number of "no show" visits					
Non-Pregnant	123	6.7	6.3	2.2	**0.032**
Pregnant	140	5.1	5.9		
Number of rescheduled visits					
Non-Pregnant	123	10.7	9.9	4.1	**<0.001**
Pregnant	140	6.2	7.7		
Number of other encounters					
Non-Pregnant	123	58.5	34.8	2.8	**0.005**
Pregnant	140	47.1	40.0		
Number of care interruptions					
Non-Pregnant	123	0.9	1.3	1.7	0.100
Pregnant	140	0.7	1.1		
Total time in care years					
Non-Pregnant	123	2.5	1.5	5.1	**<0.001**
Pregnant	140	1.6	1.3		
Time since last visit					
Non-Pregnant	123	0.3	0.4	5.1	**<0.001**
Pregnant	140	0.8	0.2		

Relationship Between Pregnancy and Treatment Retention

The relationship between pregnancy and treatment retention was evaluated via chi-square analysis (see Table 19). There was a significant relationship between pregnancy and treatment retention (88.6% vs. 61.3%; $\chi^2 = 26.6$, $p < 0.001$), showing that pregnant patients had higher rates of being retained in treatment when compared to non-pregnant patients in the sample.

Table 19: Relationship between pregnancy and treatment retention.

		Pregnancy			
Variable (% retained)	N	Pregnant	Non-pregnant	χ^2	p
Treatment Retention	264	88.6	61.3	26.6	**<0.001**

Analysis of Study Aims

Analysis of Aim 1

The first aim of this study was to determine if functional risk score (negative social support, negative contacts, unstable housing, CJS, unstable finances, unstable employment, custody problems, social stress, non-social stress, and total risk) was a better predictor of treatment success when compared to opioid use in a sample of patients with OUD receiving MT. It was hypothesized that the functional risk score would account for more variance in treatment utilization (maintenance visits, random maintenance visits, no-show visits, rescheduled visits, other encounters, care interruptions, total time in care, and time since last visit), medication utilization (% buprenorphine positive), and treatment retention (yes/no retained) when compared to opioid use.

Demographics included in multivariate analyses are gender (male/female), race (% White), ethnicity (% non-Hispanic), age, pregnancy (yes/no). Covariates included

PTSD/trauma (yes/no), anxiety (yes/no), history of CJS involvement (yes/no), and drug and alcohol use (% positive). Although sample information was provided describing the sample, race and ethnicity were not used in analyses due to high rates of missing data. Because of the high rate of homogeneity of the sample (93.6% White; 86.5% non-Hispanic) it likely did not have an impact on the study results. The lack of diversity, however, does limit study generalizability which is discussed in the study limitations.

Total time in care was included as a covariate for the following treatment utilization variables: number of random maintenance visits, number of maintenance visits, number of no-show visits, number of rescheduled visits, number of other encounters, and number of care interruptions. Total time in care was included as the rates of these variables increase as a patient is in care for longer durations. Total time in care was not used as a covariate when the treatment utilization variables examined were total time in care, time since the last visit, medication utilization, and retention (see Chapter 3).

Aim 1

Aim 1. To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of patients with OUD in MT.

H1a.-h: Functional risk score accounts for significantly more treatment utilization variance than opioid use.

H1a: Functional risk score accounts for significantly more random maintenance visits than opioid use.

H1b: Functional risk score accounts for significantly more maintenance visits than opioid use.

H1c: Functional risk score accounts for significantly more no-show visits than opioid use.

H1d: Functional risk score accounts for significantly more rescheduled visits than opioid use.

H1e: Functional risk score accounts for significantly more other encounters than opioid use.

H1f: Functional risk score accounts for significantly more care interruptions than opioid use.

H1g: Functional risk score accounts for significantly more total time in care than opioid use.

H1h: Functional risk score accounts for significantly more time since last visit than opioid use.

H1i: Functional risk score accounts for significantly more medication utilization variance than opioid use.

H1j: Functional risk score accounts for significantly more treatment retention variance than opioid use.

Number of Random Maintenance Visits

Multiple linear regression was used to examine the relationship between the number of random buprenorphine maintenance visits a patient had and each of the functional risk scores, including the total risk score (see Table 20). The results identified that opioid use was a significant predictor in every regression model. These results show that as opioid use increased, patients did not attend their random maintenance visits. Functional risk was not a predictor of random buprenorphine maintenance visits in any of the regression models.

Table 20: Opioid use, functional risk score, and random maintenance visits.

Number of Random Maintenance Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	-0.13	**0.028**	0.02	-0.06	0.253	0.00
Negative Contacts	-0.13	**0.035**	0.02	-0.08	0.197	0.01
Unstable Housing	-0.15	**0.014**	0.02	-0.10	0.054	0.01
Criminal Justice System	-0.14	**0.018**	0.02	-0.04	0.381	0.00
Unstable Finances	-0.13	**0.028**	0.01	-0.09	0.143	0.01
Unstable Employment	-0.14	**0.015**	0.02	-0.07	0.191	0.01
Custody Problems	-0.15	**0.011**	0.02	-0.05	0.375	0.00
Social Stress	-0.15	**0.015**	0.02	-0.05	0.484	0.00
Non-Social Stress	-0.15	**0.016**	0.02	-0.03	0.723	0.00
Total Functional Risk Score	-0.14	**0.024**	0.02	-0.12	0.086	0.01

Number of Maintenance Visits

Multiple linear regression was used to examine the relationship between the number of buprenorphine maintenance visits a patient had and each of the functional risk scores, including the total risk score. The results identified that functional risk score was a significant predictor of buprenorphine maintenance visits in all treatment models (see Table 21). These findings show that patients who had higher functional risk scores had more maintenance treatment visits. In contrast, opioid use was related to maintenance visits only in the regression models with unstable housing (β = 0.06, p = 0.052, $_pr^2$ = 0.01) and custody problems (β = 0.07, p = 0.028, $_pr^2$ = 0.02).

Table 21: Opioid use, functional risk score and maintenance visits.

Number of Maintenance Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.04	0.262	0.00	0.12	**<0.001**	0.07
Negative Contacts	0.00	0.957	0.00	0.27	**<0.001**	0.23
Unstable Housing	0.06	**0.052**	0.01	0.07	**0.020**	0.02
Criminal Justice System	0.06	0.083	0.01	0.06	**0.047**	0.01
Unstable Finances	0.05	0.142	0.01	0.10	**0.005**	0.03
Unstable Employment	0.06	0.059	0.01	0.06	**0.045**	0.01
Custody Problems	0.07	**0.028**	0.02	0.09	**0.002**	0.04
Social Stress	0.05	0.101	0.01	0.24	**<0.001**	0.15
Non-Social Stress	0.04	0.188	0.01	0.24	**<0.001**	0.14
Total Functional Risk Score	0.04	0.245	0.01	0.28	**<0.001**	0.19

Number of No-Show Visits

Multiple linear regression was used to examine the relationship between the number of no-show visits a patient had and each of the functional risk scores, including total risk score. The results identified that opioid use was a significant predictor of no-show visits in all regression models (see Table 22). These findings show that patients with increased opioid use had more no-show visits during their time in treatment. Similarly, functional risk was significantly related to the number of no-show visits a

patient had with unstable housing (β = 0.12, p = 0.023, $_pr^2$ = 0.02), CJS (β = 0.11, p = 0.041, $_pr^2$ = 0.02), custody problems (β = 0.11, p = 0.051, $_pr^2$ = 0.01), social stress (β = 0.21, p = 0.004, $_pr^2$ = 0.03), non-social stress (β = 0.27, p < 0.001, $_pr^2$ = 0.05), and total risk score (β = 0.29, p < 0.001, $_pr^2$ = 0.06), showing that as functional risk score went up, patients did not show for did not show for their treatment visits.

Table 22: Opioid use, functional risk score, and number of no-show visits.

Number of No-Show Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.17	**0.008**	0.03	0.06	0.299	0.00
Negative Contacts	0.18	**0.005**	0.03	0.01	0.859	0.00
Unstable Housing	0.18	**0.004**	0.03	0.12	**0.023**	0.02
Criminal Justice System	0.17	**0.007**	0.03	0.11	**0.041**	0.02
Unstable Finances	0.17	**0.006**	0.03	0.05	0.444	0.00
Unstable Employment	0.18	**0.004**	0.03	0.10	0.091	0.01
Custody Problems	0.19	**0.002**	0.03	0.11	**0.051**	0.01
Social Stress	0.17	**0.006**	0.03	0.21	**0.004**	0.03
Non-Social Stress	0.16	**0.012**	0.02	0.27	**<0.001**	0.05
Total Functional Risk Score	0.16	**0.014**	0.02	0.29	**<0.001**	0.06

Number of Rescheduled Visits

Multiple linear regression was used to examine the relationship between the number of rescheduled visits a patient had and each of the functional risk scores, including the total risk score. The results identified that opioid use was a significant predictor of rescheduled treatment visits across all treatment models (see Table 23). These findings show that as a patient's opioid use increased, they were more likely to reschedule their visits while in treatment. Similarly, functional risk was related to rescheduled visits and was significant with the following models; with unstable housing (β = 0.14, p = 0.013, $_pr^2$ = 0.02), unstable finances (β = 0.17, p = 0.014, $_pr^2$ = 0.02), custody problems (β = 0.16, p = 0.006, $_pr^2$ = 0.03), social stress (β = 0.30, p < 0.001, $_pr^2$ = 0.06), non-social stress (β = 0.40, p < 0.001, $_pr^2$ = 0.10), and total risk score (β = 0.35,

$p < 0.001$, $_pr^2 = 0.08$), showing that as functional risk score went up, so did the frequency of rescheduling.

Table 23: Opioid use, functional risk score, and number of rescheduled visits.

Number of Rescheduled Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.16	**0.016**	0.02	0.06	0.293	0.00
Negative Contacts	0.15	**0.025**	0.02	0.10	0.142	0.01
Unstable Housing	0.17	**0.008**	0.03	0.14	**0.013**	0.02
Criminal Justice System	0.16	**0.013**	0.02	0.08	0.129	0.01
Unstable Finances	0.14	**0.026**	0.02	0.17	**0.014**	0.02
Unstable Employment	0.17	**0.009**	0.03	0.05	0.376	0.00
Custody Problems	0.18	**0.004**	0.03	0.16	**0.006**	0.03
Social Stress	0.15	**0.014**	0.02	0.30	**<0.001**	0.06
Non-Social Stress	0.13	**0.033**	0.02	0.40	**<0.001**	0.10
Total Functional Risk Score	0.13	**0.032**	0.02	0.35	**<0.001**	0.08

Number of Other Encounters

Multiple linear regression was used to examine the relationship between the number of other encounters a patient had and each of the functional risk scores, including the total risk score. The results identified opioid use as a significant predictor of the number of other encounters a patient had while in treatment with unstable housing ($\beta = 0.11$, $p = 0.048$, $_pr^2 = 0.01$), unstable employment ($\beta = 0.11$, $p = 0.051$, $_pr^2 = 0.01$), and custody problems ($\beta = 0.12$, $p = 0.028$, $_pr^2 = 0.02$; see Table 24). Similarly, functional risk was related to other encounters and was significant with the following models; with unstable housing ($\beta = 0.16$, $p = 0.001$, $_pr^2 = 0.04$), finances ($\beta = 0.14$, $p = 0.021$, $_pr^2 = 0.01$), custody problems ($\beta = 0.14$, $p = 0.006$, $_pr^2 = 0.03$), social stress ($\beta = 0.26$, $p < 0.001$, $_pr^2 = 0.06$), non-social stress ($\beta = 0.35$, $p < 0.001$, $_pr^2 = 0.11$), and total risk score ($\beta = 0.32$, $p < 0.001$, $_pr^2 = 0.09$). These results show that patients with increased opioid

use and higher functional risk scores had higher rates of total other encounters while in treatment.

Table 24: Opioid use, functional risk score, and number of other encounters.

Number of Other Encounters (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.09	0.155	0.01	0.10	0.055	0.01
Negative Contacts	0.10	0.082	0.01	0.05	0.414	0.00
Unstable Housing	0.11	**0.048**	0.01	0.16	**0.001**	0.04
Criminal Justice System	0.10	0.069	0.12	0.07	0.149	0.01
Unstable Finances	0.10	0.114	0.01	0.14	**0.021**	0.01
Unstable Employment	0.11	**0.051**	0.01	0.05	0.339	0.00
Custody Problems	0.12	**0.028**	0.02	0.14	**0.006**	0.03
Social Stress	0.10	0.079	0.01	0.26	**<0.001**	0.06
Non-Social Stress	0.08	0.156	0.01	0.35	**<0.001**	0.11
Total Functional Risk Score	0.08	0.157	0.01	0.32	**<0.001**	0.09

Number of Care Interruptions

Multiple linear regression was used to examine the relationship between the number of interruptions in care a patient had while in treatment and each of the functional risk scores, including the total risk score. The results identified opioid use as a significant predictor of rescheduled treatment visits across all treatment models (see Table 25). These results show that as opioid use increased, the number of interruptions in care also increased. In contrast, functional risk did not predict the number of care interruptions a patient had while in treatment.

Table 25: Opioid use, functional risk score, and number of care interruptions.

Number of Care Interruptions (Sum)	Opioid Use			Functional Risk Score		
	β	\ p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.28	**<0.001**	0.06	0.03	0.587	0.00
Negative Contacts	0.31	**<0.000**	0.07	-0.11	0.147	0.01
Unstable Housing	0.29	**<0.000**	0.06	0.09	0.119	0.01
Criminal Justice System	0.28	**<0.000**	0.06	0.06	0.317	0.00
Unstable Finances	0.30	**<0.000**	0.06	-0.08	0.297	0.00
Unstable Employment	0.29	**<0.000**	0.06	0.08	0.213	0.01
Custody Problems	0.29	**<0.000**	0.06	-0.03	0.633	0.00
Social Stress	0.29	**<0.000**	0.06	-0.05	0.566	0.00
Non-Social Stress	0.30	**<0.000**	0.06	-0.07	0.382	0.00
Total Functional Risk Score	0.29	**<0.000**	0.06	-0.02	0.778	0.00

Total Time in Care

Multiple linear regression was used to examine the relationship between total time in care and each of the functional risk scores, including total risk. The results identified that both opioid use and functional risk were predictors of total time in care, with opioid use significant across all regression models and functional risk significant with all but CJS (β = 0.06, p = 0.247, $_pr^2$ = 0.01) and custody problems (β = 0.06, p = 0.294, $_pr^2$ = 0.00 (see Table 26). Results of these analyses show that as opioid use increases total time in care decreases and as functional risk score increases, total amount of time in care increases.

Table 26: Opioid use, functional risk score, and total time in care.

Total Time in Care (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	r^2
Negative Social Supports	-0.16	**0.008**	0.03	0.20	**<0.001**	0.05
Negative Contacts	-0.20	**<0.001**	0.04	0.41	**<0.001**	0.17
Unstable Housing	-0.12	**0.045**	0.01	0.14	**0.011**	0.02
Criminal Justice System	-0.13	**0.035**	0.02	0.06	0.247	0.01
Unstable Finances	-0.17	**0.002**	0.03	0.45	**<0.001**	0.22
Unstable Employment	-0.13	**0.036**	0.02	0.27	**<0.001**	0.09
Custody Problems	-0.12	**0.056**	0.01	0.06	0.294	0.00
Social Stress	-0.11	**0.022**	0.02	0.58	**<0.001**	0.36
Non-Social Stress	-0.14	**0.006**	0.03	0.56	**<0.001**	0.33
Total Functional Risk Score	-0.14	**0.005**	0.03	0.57	**<0.001**	0.36

Time Since Last Visit

Multiple linear regression was used to examine the relationship between the amount of time between treatment visits and each of the functional risk scores, including the total risk score. The results identified opioid use was a significant predictor of the time since last treatment visit in all treatment models and functional risk only with non-social stress, (β = -0.17, p = 0.010, $_pr^2$ = 0.02) and total risk score (β = -0.21, p = 0.002,

$_pr^2$ = 0.04; see Table 27). These findings show that as opioid use increased, the time since last treatment visit also increased. In contrast, functional risk score was generally not related to the amount of time since a patient's last treatment visit.

Table 27: Opioid use, functional risk score, and time since last visit.

Time Since Last Visit (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.20	**0.005**	0.02	-0.01	0.098	0.01
Negative Contacts	0.20	**0.004**	0.03	-0.11	0.092	0.01
Unstable Housing	0.18	**0.010**	0.02	-0.10	0.105	0.10
Criminal Justice System	0.18	**0.010**	0.02	-0.00	1.000	0.00
Unstable Finances	0.20	**0.006**	0.02	-0.12	0.066	0.01
Unstable Employment	0.18	**0.009**	0.02	-0.10	0.101	0.01
Custody Problems	0.18	**0.011**	0.02	-0.41	0.510	0.00
Social Stress	0.18	**0.010**	0.02	-0.12	0.065	0.01
Non-Social Stress	0.19	**0.007**	0.03	-0.17	**0.010**	0.02
Total Functional Risk Score	0.19	**0.007**	0.03	-0.21	**0.002**	0.04

Relationship Between Opioid Use, Functional Risk Score, and Medication Utilization

Multiple linear regression was used to examine the relationship between medication utilization and each of the functional risk scores, including the total risk score. The results identified opioid use as a significant predictor of buprenorphine utilization as treatment for their OUD across all treatment models, showing that as opioid use increased, medication utilization with buprenorphine decreased (see Table 28). In contrast, functional risk was related to medication utilization only in the regression models with negative contacts (β = 0.21, p < 0.001, $_pr^2$ = 0.04), social stress (β = 0.14, p = 0.018, $_pr^2$ = 0.01), and total risk score (β = 0.12, p = 0.043, $_pr^2$ = 0.01).

Table 28: Opioid use, functional risk score, and medication utilization.

Medication Utilization (% buprenorphine +)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	-0.47	**<0.001**	0.20	0.05	0.304	0.00
Negative Contacts	-0.50	**<0.001**	0.22	0.21	**<0.001**	0.04
Unstable Housing	-0.03	**<0.001**	0.20	0.01	0.880	0.00
Criminal Justice System	-0.46	**<0.001**	0.04	-0.01	0.163	0.00
Unstable Finances	-0.47	**<0.001**	0.19	-0.02	0.627	0.00
Unstable Employment	-0.46	**<0.001**	0.20	0.05	0.335	0.00
Custody Problems	-0.47	**<0.001**	0.19	0.02	0.634	0.00
Social Stress	-0.47	**<0.001**	0.21	0.14	**0.018**	0.01
Non-Social Stress	-0.47	**<0.001**	0.20	0.08	0.147	0.01
Total Functional Risk Score	-0.03	**<0.001**	0.20	0.12	**0.043**	0.01

Relationship Between Opioid Use, Functional Risk Score Variables, and Treatment Retention

Logistic regression was performed to examine the relationship between treatment retention and each of the functional risk scores, including the total risk score. Results identified opioid use was a significant predictor of treatment retention across all treatment models showing that as opioid use increased, probability of being retained in treatment decreased (see Table 29). In contrast, functional risk was related to treatment retention only with negative contacts (OR = 1.5), unstable finances (OR = 2.1), non-social stress (OR = 1.5), and total risk score (OR = 1.6). These results show that as functional risk went up, the probability of being retained in treatment increased.

Table 29: Opioid use and functional risk score on treatment retention.

Retention (Sum)	Opioid Use			Functional Risk Score		
	B	p	OR	B	p	OR
Negative Social Supports	-4.92	**.008**	.007	.323	.223	1.382
Negative Contacts	-5.18	**.005**	.006	.391	**.043**	1.479
Unstable Housing	-4.51	**.013**	.011	-.019	.895	.981
Criminal Justice System	-4.41	**.016**	.012	-.079	.645	.924
Unstable Finances	-5.00	**.007**	.007	.719	**.008**	2.052

Unstable Employment	-4.54	**.013**	.011	.169	.250	1.185
Custody Problems	-4.29	**.019**	.014	.264	.091	1.302
Social Stress	-4.41	**.016**	.012	.268	.065	1.307
Non-Social Stress	-4.59	**.012**	.010	.413	**.027**	1.512
Total Functional Risk Score	-4.64	**.012**	.010	.459	**.012**	1.583

Aim 1 Results

The first aim of this study was to determine if functional risk score was a better predictor of treatment success than opioid use for patients with OUD enrolled in MT. The study findings showed that within the general population included in this study, opioid use was a better predictor of treatment utilization and medication utilization (see Table 30) in two of the nine regression models, and these include, number of care interruptions and time since last visit. In comparison, when evaluating other treatment utilization measures, functional risk score was a better predictor of treatment utilization in six of the nine regression models (see Table 30), which include number of buprenorphine maintenance, number of random maintenance visits, number of no-show visits, number of rescheduled visits, number of encounters, and total length of time patients were in care during their treatment course.

These results show that functional outcomes are predicting how patients utilize treatment as much as if not better than opioid use. It is expected that opioid use is a better predictor of medication utilization. Measuring buprenorphine levels via UDS shows whether a patient in treatment is utilizing their medication. When evaluating interruptions in care, opioid use as the sole predictor is likely due to a bias. Patients who are positive for opioids are typically viewed as being non-compliant with treatment standards and thus discharged from treatment as a result of their opioid use resulting in more frequent interruptions in their care. In evaluating treatment retention, both opioid use and functional risk score were equivalent predictors of treatment retention (see Table

30). Results of aim 1 provide evidence that functional outcomes should be included as measures of treatment success for patients with OUD in MT.

Table 30: Aim 1 results.

Treatment Utilization Variables	Opioid Use	Functional Risk Score
Number of random maintenance visits		*
Number of maintenance visits		*
Number of "no-show" visits		*
Number of rescheduled visits		*
Number of other encounters		*
Number of care interruptions	*	
Total time in care		*
Time since the last visit	*	
Medication utilization	*	
Treatment retention	**N/A**	**N/A**

Analysis of Aim 2

The second aim of this study was to determine if functional risk score (negative social support, negative contacts, unstable housing, CJS, unstable finances, unstable employment, custody problems, social stress, non-social stress, and total risk) was a better predictor of treatment success when compared to opioid use in a sample of pregnant patients with OUD receiving MT. It was hypothesized that the functional risk score would account for more variance in treatment utilization (maintenance visits, random maintenance visits, no-show visits, rescheduled visits, other encounters, care interruptions, total time in care, and time since last visit), medication utilization (% buprenorphine positive), and treatment retention (yes/no retained) when compared to opioid use.

See Aim 1 (Chapter 3) for detailed analyses.

Aim 2

Aim 2. To determine if functional risk score is a better predictor of treatment success when compared to opioid use in a sample of pregnant patients with OUD in MT.

H2a.-h: Functional risk score accounts for significantly more treatment utilization variance than opioid use.

H2a: Functional risk score accounts for significantly more random maintenance visits than opioid use.

H2b: Functional risk score accounts for significantly more maintenance visits than opioid use.

H2c: Functional risk score accounts for significantly more no-show visits than opioid use.

H2d: Functional risk score accounts for significantly more rescheduled visits than opioid use.

H2e: Functional risk score accounts for significantly more other encounters than opioid use.

H2f: Functional risk score accounts for significantly more care interruptions than opioid use.

H2g: Functional risk score accounts for significantly more total time in care than opioid use.

H2h: Functional risk score accounts for significantly more time since last visit than opioid use.

H2i: Functional risk score accounts for significantly more medication utilization variance than opioid use.

H2j: Functional risk score accounts for significantly more treatment retention variance than opioid use.

Number of Random Maintenance Visits

Multiple linear regression was used to examine the relationship between the number of random maintenance visits pregnant patients had and each of the functional risk scores, including the total risk score (see Table 31). These results show that neither opioid use

nor functional risk sore predict the number of random maintenance visits a pregnant patient had while in treatment.

Table 31: Opioid use, functional risk score, and number of random maintenance visits.

Number of Random Maintenance Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	pr2	β	p	pr2
Negative Social Supports	-0.04	0.711	0.10	-0.17	**0.032**	0.44
Negative Contacts	-0.10	0.496	0.14	-0.10	0.348	0.20
Unstable Housing	-0.10	0.327	0.20	-0.05	0.536	0.13
Criminal Justice System	-0.11	0.309	0.21	0.05	0.534	0.00
Unstable Finances	-0.12	0.287	0.22	0.04	0.673	0.00
Unstable Employment	-0.11	0.288	0.22	-0.16	0.055	0.40
Custody Problems	-0.11	0.321	0.21	-0.05	0.546	0.13
Social Stress	-0.10	0.374	0.20	-0.10	0.372	0.20
Non-Social Stress	-0.10	0.465	0.20	-0.11	0.297	0.22
Total Functional Risk Score	-0.07	0.482	0.15	-0.15	0.133	0.31

Number of Maintenance Visits

Multiple linear regression was used to examine the relationship between the number of maintenance visits a pregnant patient had and each of the functional risk scores, including the total risk score. The results identified that functional risk score was a significant predictor in all models except with unstable housing ($\beta = 0.04$, $p = 0.447$, ${}_pr^2 = 0.01$), criminal justice system involvement ($\beta = 0.03$, $p = 0.581$, ${}_pr^2 = 0.00$), and unstable finances ($\beta = 0.06$, $p = 0.298$, ${}_pr^2 = 0.01$; see Table 32). These results show that as functional risk score goes up, pregnant women have more maintenance visits while in MT. In contrast, opioid use was not a predictor of maintenance visits in any of the regression models (see Table 32).

Table 32: Opioid use, functional risk score, and number of maintenance visits.

Number of Maintenance Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	-0.04	0.587	0.11	0.17	**0.001**	0.12
Negative Contacts	-0.06	0.360	0.19	0.26	**<0.001**	0.20
Unstable Housing	0.03	0.677	0.00	0.04	0.447	0.01
Criminal Justice System	0.03	0.692	0.00	0.03	0.581	0.00
Unstable Finances	0.01	0.914	0.00	0.06	0.298	0.01
Unstable Employment	0.04	0.579	0.00	0.18	**<0.001**	0.12
Custody Problems	0.03	0.621	0.00	0.18	**<0.001**	0.14
Social Stress	-0.00	0.954	0.01	0.26	**<0.001**	0.21
Non-Social Stress	-0.05	0.419	0.17	0.33	**<0.001**	0.26
Total Functional Risk Score	-0.04	0.440	0.16	0.35	**<0.001**	0.35

Number of No-Show Visits

Multiple linear regression was used to examine the relationship between the number of no-show visits pregnant patients had and each of the functional risk scores, including total risk. The results identified functional risk score as a significant predictor of the number of no-show visits pregnant patients had while in treatment with unstable housing ($\beta = 0.19$, p = 0.027, $_pr^2 = 0.05$), unstable employment ($\beta = 0.19$, p = 0.045, $_pr^2 = 0.04$), non-social stress ($\beta = 0.24$, p = 0.045, $_pr^2 = 0.04$), and total risk score ($\beta = 0.26$, p = 0.017, $_pr^2 = 0.06$; see Table 33). In contrast, opioid use was not a predictor of no-show visits in any of the regression models (see Table 33). These results show that as functional risk went up, pregnant patients had more no-show visits.

Table 33: Opioid use, functional risk score, and number of no-show visits.

Number of No-Show Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.11	0.383	0.01	0.08	0.372	0.01
Negative Contacts	0.12	0.326	0.01	0.05	0.647	0.00
Unstable Housing	0.13	0.245	0.01	0.19	**0.027**	0.05

Criminal Justice System	0.13	0.275	0.01	0.15	0.113	0.03
Unstable Finances	0.20	0.095	0.03	- 0.20	0.060	0.00
Unstable Employment	0.14	0.214	0.02	0.19	**0.045**	0.04
Custody Problems	0.14	0.243	0.01	0.06	0.478	0.01
Social Stress	0.12	0.318	0.01	0.16	0.117	0.03
Non-Social Stress	0.08	0.486	0.01	0.24	**0.045**	0.04
Total Functional Risk Score	0.09	0.467	0.01	0.26	**0.017**	0.06

Number of Rescheduled Visits

Multiple linear regression was used to examine the relationship between the number of rescheduled visits pregnant patients had and each of the functional risk scores, including the total risk score. The results identified a positive relationship between opioid use and the number of times a treatment visit was rescheduled with unstable housing (β = 0.27, p = 0.031, ${}_pr^2$ = 0.05), criminal justice system involvement (β = 0.26, p = 0.035, ${}_pr^2$ = 0.05), unstable employment (β = 0.27, p = 0.030, ${}_pr^2$ = 0.05), custody problems (β = 0.27, p = 0.026, ${}_pr^2$ = 0.05), and social stress (β = 0.24, p = 0.049, ${}_pr^2$ = 0.04; see Table 34). Similarly, functional risk score was a significant predictor of rescheduled visits with; custody problems (β = 0.19, p = 0.035, ${}_pr^2$ = 0.05), social stress (β = 0.22, p = 0.039, ${}_pr^2$ = 0.05), non-social stress (β = 0.36, p = 0.004, ${}_pr^2$ = 0.09), and total risk score (β = 0.30, p = 0.008, ${}_pr^2$= 0.07; see Table 34). These results show that as opioid use increased and functional risk score went up, pregnant patients were more likely to reschedule their treatment visits.

Table 34: Opioid use, functional risk score, and number of rescheduled visits.

Number of Rescheduled Visits (Sum)	Opioid Use			Functional Risk Score		
	β	p	${}_pr^2$	β	p	${}_pr^2$
Negative Social Supports	0.20	0.105	0.03	0.20	0.074	0.03
Negative Contacts	0.21	0.100	0.03	0.18	0.111	0.03
Unstable Housing	0.27	**0.031**	0.05	0.14	0.122	0.03
Criminal Justice System	0.26	**0.035**	0.05	0.11	0.262	0.01

Unstable Finances	0.23	0.077	0.03	0.12	0.276	0.01
Unstable Employment	0.27	**0.030**	0.05	0.06	0.557	0.00
Custody Problems	0.27	**0.026**	0.05	0.19	**0.035**	0.05
Social Stress	0.24	**0.049**	0.04	0.22	**0.039**	0.05
Non-Social Stress	0.19	0.123	0.03	0.36	**0.004**	0.09
Total Functional Risk Score	0.21	0.087	0.03	0.30	**0.008**	0.07

Number of Other Encounters

Multiple linear regression was used to examine the relationship between the number of other encounters pregnant patients had and each of the functional risk scores, including the total risk score. The results identified that opioid use was a significant predictor of the number of other patient encounters with all treatment models except with negative social supports in the model ($\beta = 0.21$, p = 0.068, ${}_pr^2 = 0.04$; see Table 35). In contrast, functional risk was related to the number of other encounters with negative social supports ($\beta = 0.23$, p = 0.005, ${}_pr^2 = 0.08$), social stress ($\beta = 0.21$, p = 0.031, ${}_pr^2 = 0.05$), non-social stress ($\beta = 0.36$, p = 0.002, ${}_pr^2 = 0.10$), and total risk score ($\beta = 0.31$, p = 0.002, ${}_pr^2 = 0.10$; see Table 35). These findings indicate that as opioid use increased and functional risk went up, the number of other encounters pregnant patients had while in treatment also increased.

Table 35: Opioid use, functional risk score, and number of other encounters.

Number of Other Encounters (Sum)	Opioid Use			Functional Risk Score		
	β	p	${}_pr^2$	β	p	${}_pr^2$
Negative Social Supports	0.21	0.068	0.04	0.23	**0.005**	0.08
Negative Contacts	0.23	**0.045**	0.04	0.19	0.063	0.04
Unstable Housing	0.30	**0.010**	0.07	0.12	0.138	0.02
Criminal Justice System	0.28	**0.011**	0.07	0.16	0.069	0.04
Unstable Finances	0.23	**0.046**	0.04	0.18	0.063	0.04
Unstable Employment	0.30	**0.010**	0.10	0.03	0.709	0.00
Custody Problems	0.30	**0.008**	0.07	0.14	0.090	0.03
Social Stress	0.27	**0.016**	0.06	0.21	**0.031**	0.05
Non-Social Stress	0.21	**0.052**	0.04	0.36	**0.002**	0.10
Total Functional Risk Score	0.23	**0.035**	0.05	0.31	**0.002**	0.10

Number of Care Interruptions

Multiple linear regression was used to examine the relationship between the number of interruptions in care a pregnant patient had and each of the functional risk scores, including the total risk score. In general, the results show that neither opioid use nor functional risk had a significant effect on the number of care interruptions pregnant women had while in treatment.

Table 36: Opioid use, functional risk score, and number of care interruptions.

Number of Care Interruptions (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.14	0.309	0.01	0.12	**0.044**	0.04
Negative Contacts	0.30	**0.036**	0.05	-0.23	0.062	0.39
Unstable Housing	0.22	0.107	0.03	-0.10	0.571	0.12
Criminal Justice System	0.22	0.117	0.03	0.10	0.476	0.01
Unstable Finances	0.20	0.174	0.02	0.10	0.525	0.00
Unstable Employment	0.23	0.104	0.03	0.10	0.524	0.00
Custody Problems	0.22	0.109	0.03	-0.10	0.356	0.20
Social Stress	0.25	0.072	0.03	-0.21	0.088	0.35
Non-Social Stress	0.30	**0.027**	0.05	-0.36	**0.009**	0.53
Total Functional Risk Score	0.27	0.056	0.04	-0.22	0.089	0.35

Total Time in Care

Multiple linear regression was used to examine the relationship between pregnant patient's total time in care and each of the functional risk scores, including the total risk score. The results identified opioid use was a significant predictor of the total amount of time a pregnant patient was in care only with; unstable finances (β = -0.24, p = 0.043, $_pr^2$ = 0.42) in the regression model (see Table 37). In contrast, functional risk score was significant with negative contacts (β = 0.36, p < 0.001, $_pr^2$ = 0.11), unstable finances (β = 0.47, p < 0.001, $_pr^2$ = 0.23), unstable employment (β = 0.28, p = 0.005, $_pr^2$ = 0.08),

social stress (β = 0.43, p < 0.001, $_pr^2$ = 0.20), non-social stress (β = 0.61, p < 0.001, $_pr^2$ = 0.33), and total risk score (β = 0.52, p < 0.001, $_pr^2$ = 0.27; see Table 37).

Table 37: Opioid use, functional risk score, and total time in care.

Total Time in Care (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	-0.15	0.269	0.23	0.12	0.229	0.01
Negative Contacts	-0.21	0.097	0.34	0.36	**<0.001**	0.11
Unstable Housing	-0.11	0.415	0.17	0.08	0.412	0.01
Criminal Justice System	-0.10	0.434	0.16	-0.05	0.663	0.10
Unstable Finances	-0.24	**0.043**	0.42	0.47	**<0.001**	0.23
Unstable Employment	-0.10	0.488	0.14	0.28	**0.005**	0.08
Custody Problems	-0.10	0.432	0.16	0.13	0.157	0.02
Social Stress	-0.14	0.238	0.24	0.43	**<0.001**	0.20
Non-Social Stress	-0.21	0.055	0.40	0.61	**<0.001**	0.33
Total Functional Risk Score	-0.18	0.105	0.33	0.52	**<0.001**	0.27

Time Since Last Visit

Multiple linear regression was used to examine the relationship between the length of time pregnant patients had between treatment visits and each of the functional risk scores, including the total risk score. The results identified that neither opioid use nor functional risk score were significant predictors of time since last visit in any of the regression models (see Table 38).

Table 38: Opioid use, functional risk score, and time since last visit.

Time Since Last Visit (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	0.13	0.373	0.01	0.06	0.577	0.00
Negative Contacts	0.12	0.401	0.01	0.10	0.401	0.01
Unstable Housing	0.15	0.281	0.01	-0.04	0.695	0.08
Criminal Justice System	0.14	0.304	0.01	0.10	0.355	0.01
Unstable Finances	0.14	0.341	0.01	0.05	0.651	0.00
Unstable Employment	0.15	0.282	0.01	0.01	0.962	0.00
Custody Problems	0.15	0.287	0.01	-0.06	0.577	0.12
Social Stress	0.14	0.306	0.01	0.10	0.374	0.01
Non-Social Stress	0.14	0.324	0.01	0.07	0.566	0.00
Total Functional Risk Score	0.14	0.309	0.01	0.05	0.656	0.00

Relationship Between Opioid Use, Functional Risk Score, and Medication Utilization

Multiple linear regression was used to examine the relationship between medication utilization and each of the functional risk scores, including the total risk score. The results identified opioid use as a significant predictor of medication utilization in all regression models. Functional risk score was significant only with negative contacts (β = 0.28, p < 0.001, $_pr^2$ = 0.08), criminal justice involvement (β = -0.02, p = 0.021, $_pr^2$ = 0.04), and total risk entered into the model (β = 0.20, p = 0.019, $_pr^2$ = 0.04; see Table 39). These findings show that as opioid use increased, pregnant patients were less likely to utilize their buprenorphine as MT for their OUD.

Table 39: Opioid use, functional risk score, and medication utilization.

Medication Utilization (% buprenorphine +) (Sum)	Opioid Use			Functional Risk Score		
	β	p	$_pr^2$	β	p	$_pr^2$
Negative Social Supports	-0.57	**<0.001**	0.27	0.08	0.244	0.01
Negative Contacts	-0.59	**<0.001**	0.30	0.28	**<0.001**	0.08
Unstable Housing	-0.55	**<0.001**	0.26	0.05	0.506	0.00
Criminal Justice System	-0.04	**0.001**	0.08	-0.02	**0.021**	0.04
Unstable Finances	-0.55	**<0.001**	0.25	0.00	1.000	0.00
Unstable Employment	-0.55	**<0.001**	0.38	0.10	0.192	0.01
Custody Problems	-0.55	**<0.001**	0.26	0.05	0.508	0.00
Social Stress	-0.56	**<0.001**	0.27	0.13	0.126	0.02
Non-Social Stress	-0.57	**<0.001**	0.27	0.17	0.065	0.03
Total Functional Risk Score	-0.56	**<0.001**	0.28	0.20	**0.019**	0.04

Relationship Between Opioid Use, Functional Risk Score, and Treatment Retention

Logistic regression was performed to examine the relationship between treatment retention and each of the functional risk scores, including the total risk score. These

results show that neither opioid use nor functional risk had a significant impact on pregnant patients and their ability to be retained in treatment (see Table 40).

Table 40: Opioid use, functional risk score, and retention.

Retention (Sum)	Opioid Use			Functional Risk Score		
	B	p	OR	B	p	OR
Negative Social Supports	-1.24	.796	.289	-1.57	**.032**	.207
Negative Contacts	-2.85	.546	.058	-.464	.355	.629
Unstable Housing	-4.04	.371	.018	-.213	.581	.808
Criminal Justice System	-3.29	.489	.037	-.911	.086	.402
Finances	-3.67	.434	.025	-.241	.770	.786
Unstable Employment	-4.03	.389	.018	-.445	.221	.641
Custody Problems	-3.78	.402	.023	.249	.459	1.283
Social Stress	-3.86	.403	.021	-.394	.334	.674
Non-Social Stress	-3.45	.456	.032	-.433	.445	.648
Total Functional Risk Score	-3.64	.432	.026	-.489	.308	.613

Aim 2 Results

The second aim of this study was to determine if functional risk score was a better predictor of treatment success than opioid use in a sample of pregnant patients with OUD enrolled in treatment. The study findings showed that among the pregnant population included in this study, opioid use was a significant predictor of medication utilization only (see Table 41). In contrast, functional risk score was significant in five of the nine regression models, and these include, maintenance visits, no-show visits, rescheduled visits, number of other encounters, and total time in care (see Table 41). There were no significant differences with both opioid use and functional risk on random maintenance visits, number of care interruptions, time since last visit, or treatment retention.

These study findings provide evidence that functional outcomes are predicting how pregnant patients utilize treatment. In aim 2, it isn't surprising that opioid use is predicting

medication utilization. Measuring buprenorphine levels via UDS shows whether a patient in treatment is utilizing their medication. In contrast to Aim 1 where both opioid use and functional risk predicted treatment retention in the total sample, neither opioid use nor functional risk predicted treatment retention in the pregnant sample (see Table 41). The results from this study clearly outline that functional risk scores are better predictors of a pregnant patient's ability to seek, engage, and remain in treatment when compared to solely relying on UDS as measures of treatment success. These findings highlight how important it is to evaluate functional outcomes while in treatment for OUD.

In summary, when evaluating the impact of opioid use and functional outcomes on treatment utilization measures for pregnant patients enrolled in treatment, findings conclude that functional outcomes are predicting how pregnant patients utilize treatment as well as if not better than opioid use alone. This is especially true for pregnant patients who face more legal implications and stigmatization as a result of their drug use. Pregnant women with OUD have the desire to seek treatment and results from this study show that functionally women who are pregnant functionally do better in treatment. These measures cannot be captured via traditional UDS and thus it is imperative to ensure that women who are pregnant get the care they need for themselves and their babies. Findings from this study conclude that a pregnant women's ability to function while in treatment was a better predictor of treatment utilization than opioid use. These findings also suggest that evaluating functional outcomes is an important tool when gauging a pregnant women's ability to be successful in treatment.

Table 41: Aim 2 results.

Treatment Utilization Variables	Opioid Use	Functional Risk Score
Number of random maintenance visits	---	**---**
Number of maintenance visits		*
Number of "no-show" visits		*
Number of rescheduled visits		*
Number of other encounters		*
Number of care interruptions	**---**	**---**
Total time in care		*
Time since the last visit	**---**	**---**
Medication utilization	*	
Treatment retention	**N/A**	**N/A**

CHAPTER 5

DISCUSSION

This chapter highlights study findings, implications for practice, limitations, and questions for future research. The purpose of this study was to determine how opioid use and functional risk score predicts treatment utilization, medication utilization, and retention in patients in treatment for OUD. This was done in both the general population and a sample of pregnant women who received treatment for OUD. Medication treatment is the gold standard treatment for OUD (Mattick et al., 2009, 2014; Nielsen et al., 2016). Treatment with buprenorphine has been proven to be highly effective in enabling individuals to achieve substantial reduction in opioid use, while reducing the risk of overdose from opioid misuse (Shulman et al., 2019). Despite the strong evidence base, the barriers to treatment are high, and they include philosophical, regulatory, administrative, and clinical constraints (Aronowitz et al., 2022). Because the regulatory and administrative barriers to treatment are high, only about 11% of people with OUD receive the treatment they need for their OUD (Aronowitz et al., 2022; Han et al., 2021).

The opioid epidemic continues to evolve and impact all groups of people. Research has shown that the current opioid epidemic has produced important differences by sex, age, gender, and race (Barbosa-Leiker et al., 2020). Gender differences arise when looking at profiles of men and women with OUD, where women report more issues with drug, medical, psychological, family/social, and employment problems, while men have more problems with legal and alcohol-related issues (Back et al., 2010; Campbell et al., 2018). A cross-sectional study conducted by Winstanley et al. (2020) assessed concurrent alcohol and opioid use among syringe services and overdose prevention

programs found that among the population sampled (n = 1,142), the majority of clients were White (95.3%) and unemployed (60.5%); a little more than half were male (55.6%). The vast majority of clients in the study reported heroin use (91.6%), with (61.3%) who reported using prescription opioids and a little more than half reported alcohol use (53.5%) in the past 3 months (Winstanley et al., 2020). Our study revealed consistent findings in that males in the study reported having unstable finances (t = 2.2, p = 0.030), and increased challenges with employment (t = 3.1, p = 0.002) when compared to females in the study. Our current study also found that males had higher percentages of alcohol use compared to women in this sample (17.1% vs. 11%, $t = 2.7$, $p < 0.001$). This study also found that males in the study sample had higher attendance rates at maintenance visits (81.6 vs. 61.0; $t = 3.9$, $p < 0.001$), spent longer time in care *(*0.9 vs. 0.8*;* $t = 3.2$, $p = 0.001$), and had longer periods of time in between visits (0.3 vs. 0.2; $t = 2.8$, $p = 0.005$), when compared to females in the sample.

Literature shows that women face more barriers in accessing substance use treatment services (Apsley et al., 2023; Green, 2006). This issue is more prominent in women with addictive disorders and includes barriers such as higher reports of stigma, burdens of work, home care, childcare, and other family responsibilities, and fear that authorities will remove their children from their care (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*). Our findings are consistent with the literature with females in this study reporting more custody problems ($t = -6.2$, $p = <0.001$) than males in the study. Women face unique challenges in relation to their OUD. Significant mental health concerns for women, which include co-occurring psychiatric disorders, make it crucial to identify gaps to target solutions that consider women's risks

and needs as they relate to OUD (Barbosa-Leiker et al., 2020). A study by Campbell et al. (2018) found that more women than men (79.3% vs. 58.1%; $p<0.001$) reported psychiatric history, including anxiety/panic disorder (59.8% vs. 38.9%; $p<0.001$) while receiving treatment for their OUD. Another study by Rosic et al., (2021), explored the association between trauma, PTSD, and treatment outcomes in a sample of patients (N = 674) receiving MT for OUD. The study found that 11% of participants met past-month criteria for PTSD ($n = 72$) and 48% reported history of traumatic events with no current PTSD ($n = 323$). Participants with PTSD were more likely to be female (odds ratio 2.13, 95% CI 1.20–3.76) and less likely to be employed (odds ratio 0.31, 95% CI 0.16–0.61) or married (odds ratio 0.51, 95% CI 0.26–0.90) than those with no trauma history. Our study findings were similar with slightly over half of women in the sample (55.8%) reported symptoms of anxiety and slightly over one third of the sample (36.5%) reporting a history of PTSD or trauma (PTSD_trauma) related to their treatment for OUD. With OUD, co-occurring psychiatric disorders such as anxiety, and trauma or PTSD that are prevalent among patients, especially women with OUD (Barbosa-Leiker et al., 2020; Campbell et al., 2018; Rosic et al., 2017). Consideration of PTSD and trauma symptoms in relation to how these impact an individual's treatment for OUD is warranted.

Opioid use in pregnancy has escalated dramatically in recent years, paralleling the epidemic observed in the general population. The increase in opioids has resulted in babies born dependent on opioids, otherwise known as NAS, due to the mother's opioid use during pregnancy (ACOG/*Opioid use and opioid use disorder in pregnancy*; Patrick et al., 2015; Tolia et al., 2015). Research shows that the use of tobacco, alcohol, or illicit drugs or misuse of prescription drugs by pregnant women can have severe health

consequences for mother and child (Patrick et al., 2012, 2017). The use of MT with buprenorphine during pregnancy is a recommended best practice for the care of pregnant women with OUDs (SAMHSA.gov/*Evidence-based, whole-person care for pregnant people who have opioid use disorder*). Despite the evidence that treatment with buprenorphine results in improved fetal and maternal outcomes (ACOG/*Opioid use and opioid use disorder in pregnancy*; Jones, Martin, et al., 2008; Minozzi et al., 2013; SAMHSA.gov/*Evidence-based, whole-person care for pregnant people who have opioid use disorder*), many pregnant women with OUD choose not to disclose or seek care for their OUD (Terplan et al., 2015). Women have a number of reasons to not disclose substance use in pregnancy, including legal ramifications, child custody issues, and stigma (ACOG/*Opioid use and opioid use disorder in pregnancy*). The fear of consequences can actually discourage women from seeking prenatal care, placing both mother and fetus at higher risk of complications (Jones, Martin, et al., 2008; Lester et al., 2004; Stone, 2015). In many states, pregnant and parenting women can be reported to child protective services if found positive for opioids during treatment (SAMHSA.gov/*Clinical guidance for treating pregnant and parenting women with opioid use disorder and their infants*).

Results of this study show that among the female population in this study, slightly over half (53.2%) of the women reported being pregnant during their time in treatment. Findings also show that pregnant women in the sample had higher numbers of custody problems when compared to their non-pregnant counterparts (t = -4.5, p = <0.001). These findings are consistent with the literature in that pregnant women do in fact struggle with more child custody issues when compared to non-pregnant women in treatment. Despite

all of the deterrents and barriers that pregnant patients with OUD face. it could be speculated that pregnant women are often no retained in treatment due to these restrictive measures however, finding from this study show that there was a significant relationship between pregnancy and treatment retention ($\chi^2 = 26.6$, $p = 0.000$), this is telling us that pregnant women do want to do better for both themselves and their families.

Pregnancy can be seen as a barrier or a motivator to seeking treatment thus, it is important to evaluate a women's perspective about her pregnancy. There are many aspects of pregnancy that serve as barriers; however, pregnancy can be seen as a motivator to adopt, or change, lifestyle behaviors to optimize their health and the health of their unborn child. Similar to the general population, treatment success is defined as having a negative UDS. For pregnant women, a positive UDS can result in punitive measures such as loss of custody of children, criminalization, and discharge from treatment (Barbosa-Leiker et al., 2020; Campbell et al., 2018; SAMHSA.gov/*Clinical guidance for treating pregnant and parenting women with opioid use disorder and their infants*; Stone, 2015). For these women, abstinence may not be attainable and thus a reduction of opioid use should be viewed as a positive attempt towards success in treatment. These women who are cutting down on their drug use are clinically doing well in treatment despite their positive UDS results.

Findings from our study show that among the pregnant sample, patients had fewer maintenance visits ($t = 5.0$, $p = <0.001$), rescheduled visits ($t = 4.1$, $p = <0.001$), were retained in care longer ($\chi^2 = 26.6$, $p = 0.000$) and on average were in care for longer lengths of time ($t = 5.1$, $p = <0.001$), than the non-pregnant population within the sample. Women who are mothers or pregnant are a particularly vulnerable group since they are

challenged by juggling substance dependence, pregnancy, and motherhood (Lamonica & Boeri, 2020). As providers, it is important to advocate for this often-marginalized group of patients, particularly in terms of working to improve availability of treatment and to ensure that pregnant women with OUD who seek prenatal care are not criminalized (ACOG/*Opioid use and opioid use disorder in pregnancy*).

The magnitude of the opioid crisis demands innovative ways to evaluate treatment success for individuals with OUD in MT. Many facilities regard unsupported assumptions and old-fashioned ways about what treatment and recovery "should look like." Among these views is the outdated policies and practices that require abstinence as the sole aim and only valid outcome of addiction treatment (Volkow, 2022). It is recognized that refraining from drugs or alcohol use poses the fewest health risks and is often necessary for sustained recovery (Volkow, 2022). However, there is no "one size fits all" approach to OUD treatment and thus different people need different treatment options. There are still many unknowns about the different trajectories that recovery may take, however healthcare and society must move beyond this dichotomous, moralistic view of drug use and abstinence, while attempting to extinguish the judgmental attitudes and practice that come with it (Volkow, 2022).

Similar to other medical conditions (diabetes, hypertension, etc.), addiction should be viewed as a chronic relapsing condition, that requires life-long treatment and management. A large part of successful treatment outcomes is measured by medication utilization, as MT is the most effective way to assist individuals in treating OUD. Literature shows that successful treatment outcomes are highly correlated with adherence to a good medication regime with buprenorphine. (Madras et al., 2020; Shulman et al.,

2019; Wakeman et al., 2020). This study found that (94.9%) of individuals tested positive for the presence of buprenorphine in their urine. Although UDS can provide encouraging results of medication utilization, a positive UDS can signify a return to drug use. A return to use is often viewed as a setback in recovery or treatment failure. In some cases, return to use can lead to program discharge for individuals who are positive for opioid use while in treatment (Volkow, 2022). Temporary returns to drug use during treatment are part of the recovery process and thus should be regarded as such. For many individuals with OUD, decreasing or temporarily returning to use may be viewed as a positive attempt to get better during their treatment course. Many patients have difficulty achieving abstinence, which can discourage seeking treatment, potentially leading to devastating health outcomes.

A secondary analysis conducted by Falk et al. (2019) compared two reduction-drinking outcomes as proposed by the WHO, with total abstinence and no heavy drinking outcomes in a randomized, placebo-controlled clinical trial of medications for treating alcohol dependence. The study data obtained from 3 different treatment facilities and was conducted to evaluate the outcomes measures of the WHO 1- and 2-level reductions in risk levels compared to total abstinence and no drinking outcomes (Falk et al., 2019). Study findings showed that both the WHO level reduction measures differentiated medication effects in a similar manner to US Food and Drug Administration- recognized outcomes of abstinence but were achieved by more patients in the study. The results of this study are focused on the outcomes and show that a reduction in drinking (assessed by risk level) align with patients' goals more strongly when compared to using abstinence alone as a sole measure. This study is already recognized as a meaningful clinical

outcome in treatment, research and medication development for alcohol addiction. Clinical endpoints other than abstinence, such as a reduction in opioid use should also be considered for OUD (Falk et al., 2019).

Concerns regarding current program policies and standards that regard complete abstinence as treatment success are unrealistic and unobtainable. In this study, (7.8%) of the population tested positive for opioids These results show that an individual's ability to decrease opioid use is possible however, even a one-time lapse can trigger unnecessary guilt, shame, and hopelessness for individuals seeking treatment for OUD. These feelings could potentially make it more likely for those slips to become more frequent and serious relapses (Volkow, 2022). Current policies that enforce complete abstinence create a culture that penalize individuals. Even a slip (or one time use) can produce a positive urine sample, which can then trigger the judgment and punitive policies of their treatment program or the law as well as trigger the personal sense that they have failed again and there is no hope to be successful in recovery (Volkow, 2022). The cycle of shaming, blaming, and punishing individuals who are trying hard to achieve treatment success must be acknowledged as part of the reality of the disorder for many who struggle with it.

Treatment success measures for individuals in MT for OUD has been incorrectly defined (Gustin et al., 2015; Jarlenski et al., 2017). There is little evidence that has identified alternate measures, other that UDS alone to identify treatment success for individuals in treatment (Sobel et al., 2021). Often, it is speculated that a person who has a positive urine screen and is not abstinent from opioid use 100% of the time is not complying with treatment. Despite requirements by oversight agencies, available guidelines, and widespread epidemic rates of overdose and death, many practitioners do

not use a standardized approach for the risk assessment for substance misuse or addiction either at the time of the initial evaluation, or at follow-up visits (Ducharme & Moore, 2019). Thus, these individuals are labeled as non-compliant and often face discharge from treatment programs (Ducharme & Moore, 2019).

Results from this study highlight the need to examine other factors of treatment success, such as how an individual functions in their daily lives and their ability to be retained in treatment. This study found that (70.4%) of individuals were able to remain actively engaged in treatment despite the numerous barriers they face while in care. Functional outcomes such as having supportive contacts, maintaining stability with their employment, finances, and housing, help to tailor interventions for an individual to be successful in treatment. Despite recommendations that support non-abstinent approaches to the treatment of OUD, there remains a clear gap in research examining alternative ways in which we can measure treatment success for individuals enrolled in MT.

Implications

Opioid treatment and policy standards vary from state to state with a lack of individualized standards that misses key opportunities to engage patients at risk of the serious consequences of OUD (Madras et al., 2020). The lack of standardized treatment which makes it increasingly difficult for providers to measure treatment success for individuals actively enrolled in medication treatment programs (Madras et al., 2020; Reed et al., 2023). Although the objective of this study was not to define treatment success, we know that measuring the presence or absence of opioids via UDS does not provide the full picture of how an individual utilizes treatment. Professional guidelines make clear that urine drug testing is not an adequate assessment of whether an individual

is clinically doing well in treatment (ACOG/*Opioid use and opioid use disorder in pregnancy*). Positive results of a urine drug test do not establish a diagnosis of addiction or serve as a gauge of treatment compliance. It is important to understand that someone who is unable to achieve abstinence 100% of the time may not be failing treatment. Any reduction in opioid use, should be viewed as a positive movement in treatment. Findings from this study support looking at different ways of viewing treatment success as functional outcomes better predicted treatment utilization.

Incorporating functional outcomes, help to frame how individuals with OUD utilize treatment from a harm reduction standpoint. Functional outcomes/risk score provide a less penalizing approach to the traditional measurement via UDS. Positive UDSs do not necessarily reflect how well someone is or is not doing in treatment, rather these results are used as evidence that a return to use signifies treatment failure. The goals of MT should be highly individualized, and treatment success should be defined from the perspective of the individual receiving care. The findings from this study further validate that an individual's ability to function, as evidenced by support, contacts, finances, employment, etc. play a major role in their ability to be successful while in treatment. Both men and women have very different and unique challenges when it comes to treatment for OUD. Functional outcomes such as those that have been proposed in this study are typically not included in the measurement of treatment success. Future research is needed to fully understand how functional outcomes can inform treatment success for individuals in treatment for OUD.

Implications for Policy

More than 106,000 persons in the U.S. died from drug-involved overdose in 2021, including illicit drugs and prescription opioids (NIDA.NIH.gov/*Drug overdose death rates*) and these numbers are rising. These alarming statistics should prompt the need for comprehensive, people-centered policies to provide equitable OUD treatment for people with OUD. Effective programs and medications to treat OUD exist yet only about 11% of people with OUD receive treatment (Volkow, 2022). Most treatment programs enforce achieving and sustaining abstinence from opioid or other drug use as a singular goal (NIDA.NIH.gov/*Principles of drug addiction treatment*). Additionally, the system is punitive to those who do not achieve abstinence, as exemplified by the widespread practice of involuntary treatment discharge for those who return to use (Paquette et al., 2022). The current study found that opioid use, not functional risk, better predicted care interruptions. This finding is likely due to patients being discharged from treatment due to positive opioid use screens as this often is viewed as treatment failure and often required by payors.

Literature has addressed that there has been an increasing acceptance and need for non-abstinent outcomes as a metric for assessing treatment effectiveness for OUD (Volkow, 2022). The challenge is that universal abstinence goals are at odds with the objectives of many individuals with OUD (Paquette et al., 2022). Many individuals are often excluded from the process of determining the outcomes that define their ability to be successful in treatment. While there is a clear need to engage individuals to seek with OUD in MT, the goal of abstinence-based treatment is incompatible with the philosophies and views of the harm-reduction model. Low acceptance of non-abstinence goals among providers remains a significant barrier to treatment for individuals with

OUD (Rosenberg et al., 2020). Research suggests that empirical evidence supporting harm reduction is often insufficient to create policy change (Allen et al., 2015). As policymakers, community members, and treatment providers continue to reject scientific evidence supporting harm reduction, research examining more effective strategies for shifting public perception may be key to moving the field forward (Paquette et al., 2022).

In states that mandate reporting, policy makers, legislators, and physicians should work together to retract punitive legislation and identify and implement evidence-based strategies outside the legal system to address the needs of individuals who seek treatment for OUD. These partnerships will provide opportunities to develop, coordinate, and implement targeted strategies to prevent harm. Findings from this study show that a positive UDS does not provide the full picture of an individual's ability to be successful in treatment. Findings from this study showed that in the full sample, opioid use predicted treatment utilization in slightly approximately one third of the regression models while functional risk score was a predictor in more than half. These results show that functional outcomes better predicted how individuals utilize treatment. It is important to note in the models where opioid use was a better predictor, (number of care interruptions and time since last visit), this may be due to payor or program policy and discharge based on positive UDS.

There continue to be regulatory and delivery system barriers that hinder people from receiving needed care (Madras et al., 2020; Sharma et al., 2016). Harm reduction philosophies are essential to help reframe policy & practice standards for MT programs that solely utilize UDS to measure treatment success. The evolving and unstable nature of the opioid crisis demands a broader set of harm-reduction strategies that prioritizes health

and safety for individuals seeking treatment (Commonwealth Fund.org/*Substance use*). Current policies that use UDS solely to gauge treatment success are missing key opportunities in the treatment of individuals with OUD. An individual may be making positive attempts to achieve treatment success such as decreasing their opioid use and functionally doing better in treatment, but this positive attempt cannot be captured via UDS alone. It is important that all stakeholders realize the implications posed for patients who are considered to be non-compliant with treatment standards. Among the repercussions, with treatment discharge being likely, many patients also face bias and stigma which results in unfavorable outcomes. Understanding that a positive result can be a helpful indicator to the provider that necessary modifications should be made in the plan of care to help meet the needs of the patient. Identification of functional outcomes that influence an individual's ability to be successful in MT, as proposed in this study, will assist stakeholders in evaluating the factors that serve as motivators or barriers to improve treatment outcomes.

Implications for Nursing

Nurses represent the largest segment of the healthcare workforce and as such, bring a unique lens to the care of individuals with OUD. An integrative review conducted by Alexander et al., (2022) aimed to understand the impact of nursing on the health outcomes of people with OUD. After screening the articles (N = 773), a total of (n = 15) articles met inclusion and exclusion criteria and were included in the review. Among the articles selected, two themes emerged: 1. The effect of nurse-led care on patient outcomes, and 2. Nursing roles and environment of care. The studies emphasized the aspects of nursing care that promote patient-centeredness and patient satisfaction. There

was clear evidence that among the common themes, the importance of the registered nurse in providing quality care for people receiving medication treatment for OUD (Alexander et al., 2022).

Stigma surrounding OUD is pervasive throughout the healthcare system. Health professionals often express negative attitudes towards patients with OUD which can lead to poor patient outcomes. Stigma in healthcare settings affects healthcare-seeking behaviors and could result in patients concealing their OUD status or substance use history**.** A secondary analysis of qualitative data regarding experiences associated with stigma and its consequences found that participants reported various forms of poor treatment, believed to reflect views of people with SUD as morally culpable, intimidating, curious, untrustworthy, and less valuable than other patients, sometimes with tangible effects on the quality of healthcare (Garpenhag & Dahlman, 2021). These results implicate a need to investigate attitudes toward patients with OUD among healthcare professionals, as well as a need for interventions addressing knowledge deficits and issues tied to values and patient reception among healthcare staff.
OUD in pregnant and parenting individual's is a highly stigmatized health condition as expectations of this population may be incongruent with societal norms. For pregnant women in particular, nurse often play an important role in the screening for substance use disorders. The purpose of screening is to identify those women with potential OUD and provide them appropriate care in a nonjudgmental manner. As providers, it is important to advocate for this often-marginalized group of patients, particularly in terms of working to improve availability of treatment and to ensure that pregnant women with OUD, who seek prenatal care are not criminalized (ACOG/*Opioid use and opioid use disorder in*

pregnancy). Nurses must have prominent roles in developing local, state, and national policies and to serve as advocates for the care and treatment of individuals with OUD.

Limitations

There are several limitations to this research study. The study data was not a prospective evaluation of functional outcomes; rather, the data was a retrospective analysis of secondary data collected via an EHR. Coding of the EHR study data was performed by RAs, thus adding the element of human error such as data entry errors, omission of data, missed flagged phrases, and typographical or grammatical errors that would otherwise be pertinent to the data collection process. Despite the research and relevant literature that supports the study findings, the potential of error in the data analyses has the possibility to yield unreliable results. These results do not fully encapsulate the effect that functional outcomes have on an individual's success in treatment.

The limitations of EHR data also prohibit the ability of the researcher to ask specific questions as to how an individual functions while in treatment. The inability to ask questions is key as it is important to fully capture the individual's perspective of those measures that act as barriers or facilitators to their success while in treatment. Other limitations include the inability to eliminate study bias, which ultimately affects the reliability and validity of study results. There was also a significant lack of diversity among the individuals in this study, which presented findings that are generalizable and lack pertinent information to assist those who represent the vulnerable and underserved populations who experience health inequities and disparities in treatment.

Future application of theory

Through the application of Bronfenbrenner's social ecological systems theory, it is possible to imagine an approach to the opioid crisis that incorporates all facets of influence to an individual's recovery. Beginning at a macrolevel, leaders and government officials may address current policies and regulations regarding the issue (Carney, 2017). This level adheres to national or provincial characteristics including laws and regulations as well as the actions of leaders. More proximally, at the exo-level, the attitudes and beliefs of community members and leaders can be adjusted through media messages and the use of modeling (Carney, 2017). For example, mass media campaigns in the 1990s used advertisements and television shows to bring about change in the rates of drinking and driving, which lead to a prompt decrease. The mesosystem level includes organizations in which an individual is involved, such as school, the workplace, or even religious affiliations (Carney, 2017). Implementing treatment and prevention programs at this level will aim to target risk or affected populations. At a more personal level, the microsystem includes members of a person's family or close friend group. Families can positively influence individuals by providing support and healthy communication surrounding issues of drug use (Carney, 2017).

Questions for Future Research

Recommendations for future work would consider an opportunity for researchers to collect prospective data that addresses specific aspects of care that impact an individual's ability to function while in treatment for OUD. This can be achieved by developing specific questions that are focused on the functional outcomes identified in this study. The addition of functional outcomes to UDS is novel and provides an opportunity for a change in the culture of how OUD treatment should be addressed.

Much of the literature references that treatment for OUD should be individualized and is not a one-size-fits-all approach (Gustin et al., 2015; Madras et al., 2020). Harm-reduction strategies, such as evaluating measures that enhance or hinder an individual's ability to be successful in treatment allows for a more person-centered approach. Adding functional outcomes as a measurement of success will assist providers in gaining additional information that will help in determining a realistic treatment approach to a complex condition.

Questions remain as to what is the role of UDS in treatment programs that are guided by harm-reduction philosophies, in which abstinence is not required nor necessarily encouraged (Jakubowski & Fox, 2020; Sobel et al., 2021). The addition of functional outcomes will not replace UDS; rather it will enhance the quantitative findings to tailor treatment approaches that would otherwise result in discontinuation of care. Asking specific questions such as what individuals in MT consider a positive aspect or motivator of care, in addition to gathering information on barriers and motivators for treatment success are pivotal. Future research should focus on collection of prospective data regarding an individual's ability to function in MT, as these components influence their ability to not only stay in treatment but to ultimately live a better life that focuses on physical, social, and emotional aspects that influence their treatment status.

Conclusion

Measuring treatment success for individuals in MT for OUD is poorly defined (Gustin et al., 2015; Jarlenski et al., 2017). Traditionally, "success" in treatment is measured in terms of program retention (Askari et al., 2020; Timko et al., 2016), adherence to medication (Khan et al., 2021; Tkacz et al., 2014), and abstinence from

opioid and other drug use. Few alternate measures to identify treatment success in treatment have been found (Sobel et al., 2021). Furthermore, patients are excluded from the process of determining these outcomes that define their ability to be successful in treatment. Reliance on UDS as the primary measure of one's ability to be successful in treatment does not effectively capture progress in treatment. A shift away from focusing solely on UDS is necessary and essential to really understand who is and who is not progressing in treatment. A better understanding of treatment success will help identify who is not doing well in treatment so to best focus additional interventions and resources.

The magnitude of the opioid crisis demands novel, nonreformed ways to change the unsupported, outdated, and stigmatizing views of how treatment success is defined. Among these views is the traditional view that abstinence is the sole aim and only valid outcome of addiction treatment (Volkow, 2022). While refraining and abstaining from drugs or alcohol poses the fewest health risks and is often necessary for sustained recovery, different people may need different options (Volkow, 2022). Women with OUD have unique care needs (NIDA.NIH.gov/*Substance use in women/sex and gender differences in substance use*); UDSs can result in loss of custody of children, criminalization, or discharge from treatment. Treatment for OUD, especially for pregnant patients is critical as untreated OUD can have devastating consequential effects for both mother and child. Punitive laws targeted at individuals, especially pregnant patients with OUD are a significant deterrent to obtaining regular prenatal care and treatment for OUD. This study provides substantial evidence that redefining treatment success for individuals with OUD needs to be examined. The findings from this study provide evidence that

evaluating functional outcomes, in addition to UDS, can be an important piece to predicting treatment success for individuals with OUD in MT.

APPENDIX A

IRB APPROVAL LETTER

University of Massachusetts Amherst
108 Research Administration Bldg.
70 Butterfield Terrace
Amherst, MA 01003-9242

Research Compliance
Human Research Protection Office (HRPO)
Telephone: (413) 545-3428
FAX: (413) 577-1728

Certification of Human Subjects Approval

Date:	June 26, 2019
To:	Kristy Pereira, Nursing
Other Investigator:	Lisa Chiodo, Nursing
From:	Lynnette Leidy Sievert, Chair, UMASS IRB

Protocol Title: An Evaluation of Functional outcomes for Individuals with Opioid Use Disorder in Medication Treatment with a focus on pregnant women.
Protocol ID: 2019-5666
Review Type: EXPEDITED - NEW
Category: 5
Approval Date: 06/26/2019
No Continuing Review Required
UM Proposal #:

This study has been reviewed and approved by the University of Massachusetts Amherst IRB, Federal Wide Assurance # 00003909. Approval is granted with the understanding that investigator(s) are responsible for:

Consent forms - A copy of the approved consent form (with the IRB stamp) must be used for each participant (Please note: Online consent forms will not be stamped). Investigators must retain copies of signed consent forms for six (6) years after close of the grant, or three (3) years if unfunded.

Use only IRB-approved study materials (e.g., questionnaires, letters, advertisements, flyers, scripts, etc.) in your research.

Revisions - All changes to the study (e.g. protocol, recruitment materials, consent form, additional key personnel), must be submitted for approval in e-protocol before implementing the changes. New personnel must have completed CITI training.

Final Reports - Notify the IRB when your study is complete by submitting a Final Report Form in the electronic protocol system.

Serious Adverse Events and Unanticipated problems involving risks to participants or others - All such events must be reported in the electronic protocol system as soon as possible, but no later than five (5) working days.

Annual Check In - HRPO will conduct an annual check in to determine the study status.

Please contact the Human Research Protection Office if you have any further questions. Best wishes for a successful project.

APPENDIX B

AREF LETTER OF SUPPORT FOR DATA

Kristy Pereira
PhD Candidate
University of Massachusetts

May 22, 2019

RE: Letter of Support for Data

Dear Kristy,

This letter acknowledges that as Director of Research at the Addiction Research and Education Foundation (formerly the CleanSlate Addiction Treatment Centers), I am agreeing to provide the necessary data that will allow you to examine the study aims and hypothesis defined in your dissertation proposal. It is important that you understand that you will receive a de-identified data set and that you are only able to use the data set to answer the questions identified in your dissertation without additional consent.

This data transfer was vetted by the Vice Chancellor of Research at UMASS, Amherst. UMASS approved you receiving the data without obtaining a conflicts management plan. This information was forwarded to you in an e-mail by Jennifer Donais, MPA, CRA, on October 29, 2017. In her letter she indicated that she "presented the circumstances and analysis to the VCRE, who has confirmed for me that we can move forward with the students' access to the data without a conflicts management plan."

Once you have successfully defended your proposal and have obtained IRB approval, I will provide you the data set on an encrypted external drive. The data must stay on this drive. It is important that you do not save the data on the UMASS network.

Thank you,

Lisa Chiodo, PhD
Director of Research, Addiction Research and Education Foundation
Associate Professor, University of Massachusetts

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