A QUALITATIVE STUDY OF PATIENT PERCEPTIONS OF AND EXPERIENCES WITH LONG-ACTING INJECTABLES AND SUBLINGUAL BUPRENORPHINE

BY

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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>CBT</td>
<td>Cognitive behavior therapy</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma aminobutyric acid</td>
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<tr>
<td>IAR</td>
<td>Initial Administration Route</td>
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<tr>
<td>IOP</td>
<td>Intensive Outpatient Program</td>
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<td>LAI</td>
<td>Long-acting Injectable</td>
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<td>MAT</td>
<td>Medication-Assisted treatment</td>
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<td>MOR</td>
<td>µ-Opioid Receptor</td>
</tr>
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<td>OUD</td>
<td>Opioid use disorder</td>
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<td>SL</td>
<td>Sublingual buprenorphine</td>
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<tr>
<td>SUD</td>
<td>Substance use disorder</td>
</tr>
<tr>
<td>WFBPBM</td>
<td>Wake Forest Baptist Psychiatry and Behavioral Medicine</td>
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ABSTRACT

Research on opioid use disorder (OUD) and possible treatments has made strides in recent decades. Three options are currently on the market for treatment of OUD. These include methadone, naltrexone, and buprenorphine. Each of these treatments has a different method of action and offers unique benefits. Looking specifically at buprenorphine, there are multiple treatment options, including sublingual buprenorphine (SL) and a long-acting injectable (LAI) medication. Even with the research on treatments, there is limited data that compares the multiple forms of buprenorphine, and even less so done from the perspective of the patients. Through one-on-one semi-structured interviews, we have highlighted the individual experiences of each patient. Using the interview transcriptions, we have conducted a thematic analysis to determine key themes and their contribution to patient preferences for the injection or SL buprenorphine. The seven themes identified were: prior heroin use, adverse effects and sex differences, preferences, cravings, family factors, prior treatment, and a desire to stop buprenorphine. These themes highlight similarities in patient experiences. Though some contributed directly to medication preference, others were just commonalities between patients. The unique perspective given by subjects allows for more information to be given to other patients interested in the LAI.
CHAPTER 1: INTRODUCTION

Opioids are responsible for the majority of overdose deaths, and in 2016 all overdose deaths surpassed those due to any armed conflict since World War II, including the Vietnam War and Korean War (Phillips, 2017). Opioid deaths also surpassed heroin and cocaine combined (Manchikanti et al., 2012, p.9). This data highlights the vast issue related to opioid use in recent decades. Opioid use disorder (OUD) is defined as, “signs and symptoms of compulsive behavior related to the self-administration of opioid substances” (Lagisetty et al., 2017). It is often referred to as opioid addiction, and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) uses a series of 11 criteria to categorize and classify OUD (Hartney, 2019). Some of these include: taking in large amounts or for longer than intended, craving the use of opioids, or using in hazardous situations (American Psychiatric Association, 2013). The widespread problem with opioid use began in the late 1990s, when prescribers, who were unaware of the addictive potential of opioids, began overprescribing the medications to their patients (Leshner, 2019). This caused a surge in opioid misuse and addiction that continues today.

Fortunately, there are treatments available for people with OUD. These can include behavioral treatments and medications. Behavioral treatments consist of group therapy, 12-step programs, and inpatient rehab facilities. The structure of each treatment facility may differ in the type of behavioral therapies offered, and are often used in conjunction with medication to promote abstinence (McHugh, Hearon and Otto, 2010). The three currently approved medications to treat OUD include methadone, buprenorphine, and naltrexone. Methadone started as a treatment specifically for heroin in the 1960s, and by the 1970s became a treatment for a wide array of opioids (Institute of Medicine, 1995). It is usually
administered as a liquid and must only be given by a healthcare provider. Buprenorphine administration ranges from implants to sublingual tablets and films, and a monthly injection (Jonan, Kaye & Urman, 2018). It became a popular treatment for patients as they can self-administer buprenorphine, versus relying on a provider for each dose. Naltrexone can treat both OUD and alcohol use disorder (AUD), and comes in a pill or monthly injection (Buddy, 2020). Each of these three treatments provides a different method to treat OUD. Even with a surge in research on OUD since the 1990s, there is little data on patient perspectives of these medications, and qualitative research can be used to address this limitation.

Because there are limited qualitative studies on OUD treatments, this method can offer a unique perspective. Qualitative research is the “development of concepts which help us to understand social phenomena in natural (rather than experimental) settings, giving due emphasis to the meanings, experiences, and views of the participants” (Pope & Mays, 1995). The non-numerical data can allow for a detailed description into patient experiences and perspectives, while answering more broad questions that can be further refined throughout the duration of the study (Rahman, 2016; Fossey et al., 2002). Once researchers determine the purpose of the study, data can be collected through interviews, focus groups or observation (Austin & Sutton, 2014). After collection of data, thematic analysis can be used to determine key themes and better understand the participants’ perceptions (Austin & Sutton, 2014). The strengths in methodology of qualitative research include the deeper examination of issues and flexibility in how it is conducted (e.g. interview questions) (Anderson, 2010). Qualitative research can be interpretive or critical in nature, and each paradigm has specific methods that can be used (Fossey et al., 2002). Interpretive research
includes ethnography or phenomenology, while critical research consists of participatory action research (Fossey et al., 2002). Qualitative methods can benefit participants by promoting self-expression, enhanced self-understanding, and the sense of helping others (Opsal et al., 2015). Looking specifically at research on OUD, getting qualitative data can provide a deeper investigation into the lives of patients. The flexibility offered with qualitative research allows patients to use their unique voices to communicate their opinions on OUD treatment methods, and provide more information that is necessary for patients interested in these medications. Receiving opinions on the medications from patients in similar situations will allow those interested in the LAI to personally associate with the subjects. Looking into OUD and the treatment options from the perspective of qualitative research, will provide further understanding of the patient’s opinions on their treatments, and address a limitation in research on OUD treatments.

I. Opioids and Opioid Use Disorder

Opioid Pharmacology

The recent opioid epidemic has led to a plethora of research on the topic of opioid use and addiction. However, opiates themselves have been around for centuries, dating back to the 4th century B.C. (Lucyk and Nelson, 2017). Opiates originate from the narcotic opium, that is extracted from the opium poppy plant (Lucyk and Nelson, 2017). Three of the 20 naturally occurring opiates include morphine, codeine, and thebaine (Lucyk and Nelson, 2017). These opiates are then used to make semisynthetic opioids, which are a combination of the naturally occurring opiates and synthetic materials (Lucyk and Nelson, 2017). Opioids bind with one of the opioid receptors. There are four classes of opioid receptors: Mu, Kappa, Delta, and opioid receptor like-1 (Al-Hasani & Bruchas,
Al-Hasani & Bruchas (2011) mention that µ-opioid receptors (MOR) are one of the most common opioid receptor types, and one of their functions includes pain regulation. Pain perception can be regulated in areas that include the periaqueductal grey, cingulate cortex, insula, and thalamus (Volkow, Benveniste, & McLellan, 2018). Opioids attach to opioid receptors to block pain signals. By activating opioid receptors, they prevent communication with neurons that perceive pain, and prevent pain signals from reaching the brain (Al-Hasani and Bruchas, 2011; NAABT, 2008). They do this by preventing the release of neurotransmitters from the presynaptic cell (He et al., 2018).

When opioids bind to opioid receptors on the presynaptic neuron, they prevent the ion channels from opening and Ca2+ (calcium) from entering the cell (Al-Hasani and Bruchas, 2011). Ca2+ normally allows the release of neurotransmitters, but without it, no communication to the postsynaptic cell occurs (He et al., 2018; Al-Hasani and Bruchas, 2011). Opioids can also bind to MOR on the postsynaptic cell and cause K+ (potassium) channels to open and release, leading to a decrease in positive charge, which prevents action potential firing or further communication to the brain (Tsantoulas & McMahon, 2014). Overall, opioids can change brain chemistry by blocking pain signals, but can also lead to drug tolerance and dependence (Kosten & George, 2002). The MOR subtype is associated with the negative, reward, and pleasured effects of opioids (Lucyk and Nelson, 2017; Volkow, Benveniste, & McLellan, 2018).

**Opioids for Pain Treatment**

Opioids can be used to treat acute or chronic pain, which can both be associated with other diseases, disorders and cancers. Acute pain is a short-term effect of surgery, or trauma (Nicholson, 2003). For acute pain, physical measures should be taken first and anti-
inflammatory drugs used prior to prescribing opioids (Donroe, 2016). Chronic pain is often more difficult to treat, which is highlighted in the Nicholson (2003) article on Responsible Prescribing Opioids for the Management of Chronic Pain. He states that the nature of chronic pain can make it more difficult, as it can be neuropathic, nociceptive, or both (Nicholson, 2003). This pain can be debilitating and often affects daily life functions. However, due to the issues with opioid dependence and tolerance, healthcare providers are reluctant to prescribe opioids to patients, even with the millions of Americans that use opioids for chronic pain (Jamison and Mao, 2015). Sherry, Sabety, & Maestas (2018) used the Ambulatory Medical Care Survey to determine why opioids were prescribed by physicians, and found that 28.5% of opioids were prescribed without a formal pain diagnosis. According to the Center for Disease Control’s Guidelines for Prescribing Opioids for Chronic Pain, when prescribing for chronic pain, the lowest dosage of opioids should be given and slowly increased if needed, as higher doses can promote dependence. They further state that for acute pain, no more than the amount necessary should ever be prescribed (Centers for Disease Control, 2019).

**Opioid Abuse**

A rise in sales by 300% (since 1999) can highlight the increase in popularity and availability of opioids (Mack, Jones, & Paulozzi, 2013). Opioids may cause other effects such as euphoric feelings, which may contribute to the misuse of opioids (Wise & Bozarth, 1985). Opioid dependence can occur within a few weeks, however as is the case with most addictions, each individual’s susceptibility is different. Some possible factors that may increase vulnerability are:
Current or past substance-use disorders or psychiatric comorbidities, and/or a family history of these disorders are clinically relevant warning signs. Brain development is also a vulnerability factor, and adolescents are at particularly high risk because of the enhanced neuroplasticity of their brains, which allows them to learn more rapidly but also leads them to condition to drugs more rapidly (Volkow, Benviente, & McLellan, 2018, p.460).

When using opioids for pain treatment, there can be increased risks for developing opioid abuse. As stated earlier, the DSM-5 has a series of 11 criteria to categorize OUD. According to the DSM-5, mild OUD is categorized by having 2-3 of the 11 criteria, moderate OUD involves having 4-5 of the symptoms, and severe is ≥ 6 of the symptoms (American Psychiatric Association, 2013). Figure 1 depicts all of the 11 criteria for OUD (American Psychiatric Association, 2013; Gustin, Nichols, & Martin, 2015).
A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period of time than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused by or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continuous opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that’s likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
   a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect
   b. A markedly diminished effect with continued use of the same amount of an opioid
11. Withdrawal, as manifested by either of the following:
   a. The characteristic opioid withdrawal syndrome
   b. The same—or a closely related—substance is taken to relieve or avoid withdrawal symptoms

*Figure 1: DSM-5 Criteria for OUD. Mild OUD- 2-3 Criteria, moderate 4-5, severe ≥ 6. From: Gustin, Nichols & Martin (2015).*
The dose of medication and the duration of treatment must be carefully monitored by physicians, or may lead to misuse and addiction (Volkow, Benviente, & McLellan, 2018). There are some common signs of abuse seen with people using opioids, which can include: the inability to control opioid use, uncontrollable cravings, and isolation from family or friends (American Psychiatric Association, 2013).

The euphoric effects of opioids in the reward pathway may contribute to tolerance and OUD. In normal reward processing, dopaminergic neurons located in the Nucleus Accumbens (reward processing) release the neurotransmitter dopamine, but during addiction, dopamine levels increase and cause the euphoric effects (Horsfall and Sprague, 2016). This occurs when GABA is inhibited, which is usually responsible for dopamine reduction (Fields & Margolis, 2016). When the opioids activate receptors on GABA inhibitory neurons, they decrease the amount of GABA, and more dopamine is released into the synapse, heightening the euphoric effects of the opioids (Horsfall and Sprague, 2016). These effects can eventually lead to opioid tolerance and dependence (Horsfall and Sprague, 2016).

**Tolerance**

Opioid tolerance occurs when people adapt to taking opioids get used to the effects, and a higher dose is required to produce the same result (Lavand-homme, 2017). The DSM-5 states a diminished effect may occur with consistent use of an opioid (American Psychiatric Association, 2013). These diminished effects that may require an increased dose include, analgesia or pain relief, pleasure, and calmness (Volkow, Benveniste, & McLellan (2018). Research on tolerance suggests that it can be either innate or acquired. “Innate Tolerance is predisposition to exhibit drug sensitivity. Acquired
tolerance is attributed to learning, either behavioral or conditioned” (Dumas & Pollack, 2008, p. 538). There is some controversy over tolerance, with some doctors suggesting it is due to progression of disease or worsening pain, and not a change in effect by the medication (McQuay, 1999). Other studies suggest that tolerance is due to a decrease in the number of MOR available (Kieffer & Evans, 2002). Still others suggest a desensitization of opioid receptors, which occurs when the opioids are taken repeatedly (Case-Lo, 2017). Potency, route of administration, and latency of onset can all lead to tolerance (Volkow, Benveniste & McLellan, 2018). The increased dose required to produce the pain relieving effects can potentially lead to dependence (Volkow, Benveniste, McLellan, 2018). If this develops it becomes more difficult to discontinue the drug and may cause withdrawal when the drug is ceased.

**Drug Scheduling and Commonly Abused Opioids**

Different opioids have different abuse potential. Because of this, opioids and other controlled substances are divided into different schedules. Schedule I drugs have the highest potential for abuse and are not currently prescribed by doctors in the US (DEA, 2019). This class of drugs includes heroin as the only opioid, but also includes marijuana, LSD (lysergic acid diethylamide) and ecstasy (methylendioxymethamphetamine) (DEA, 2019). Schedule II substances still have a high likelihood of abuse, but less so than schedule I substances. Schedule II opioids include OxyContin, Vicodin, fentanyl, hydromorphone, methadone & meperidine (DEA, 2019). Schedule III-V have less abuse potential and include buprenorphine, commonly prescribed to treat OUD, and other combination drugs (DEA, 2019). Table1 highlights many of the classes of drugs and the
corresponding schedule category. Opioids are distributed among all schedules based on abuse potential or pertinence to medicine.

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Abuse Potential</th>
<th>Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schedule I</td>
<td>Most potential for abuse, not used medicinally</td>
<td>Heroin, LSD, marijuana, Ecstasy</td>
</tr>
<tr>
<td>Schedule II</td>
<td>High abuse potential, some medical qualities</td>
<td>Vicodin, Methadone, OxyContin, Adderall</td>
</tr>
<tr>
<td>Schedule III</td>
<td>Moderate potential for abuse, accepted medicinal qualities, Prescription required</td>
<td>Ketamine, Testosterone, Buprenorphine,</td>
</tr>
<tr>
<td>Schedule IV</td>
<td>Low abuse potential, prescription required</td>
<td>Xanax, Valium</td>
</tr>
<tr>
<td>Schedule V</td>
<td>Lowest potential for abuse</td>
<td>Robitussin, Lyrica</td>
</tr>
</tbody>
</table>

*Table 1: Drug Scheduling is used in the United States to highlight the potential for abuse and clinical relevance of each drug.*

Fentanyl has been around since the 1960s, and as a treatment it comes in six common forms including a patch, tablet, and liquid (Stanley, 2014; Crane, 2019). However, it has become a common illicit substance in recent years, which is partially due to its mixing with other opioids and street drugs like heroin (Kuczyńska, 2018). This can lead to a greater likelihood of overdose as fentanyl, which is more potent than heroin and morphine, may result in people taking more than expected (NIDA, 2019). It is fairly inexpensive and easy to find the materials to make fentanyl in clandestine laboratories, which are used to produce illicit substances (Pichini et al., 2018; Cunningham, 2007). Figure 2 shows how potent fentanyl is compared to heroin, and why this can result in overdose. The dangers associated with fentanyl are the potential for misuse and abuse, especially with street fentanyl (Stanley, 2014).
Heroin originates from morphine, which is one of the opiates from the opium poppy plant. It is a schedule I drug due to its high abuse potential, and is not currently prescribed for pain (Drug Enforcement Agency, 2019). It is often injected directly in the blood stream, which leads to a more rapid high (Hines et al., 2020). While there are other routes of administration, injection is the most common and considered the most dangerous. The study by Hines et al. (2020) looked at the length of time between first opioid administration and use disorder or heroin abuse. They found that based on the type of usage, only 1% of people who injected heroin did not eventually progress to using heroin daily (Hines et al, 2020). That is compared to snorting heroin (9%) and chasing heroin (12%) (Hines et al, 2020). Chasing heroin, or often referred to as “chasing the dragon,” involves inhaling or

Figure 2: Fentanyl is more potent than morphine and heroin. More people are overdosing because heroin is being laced with fentanyl as it is easier and cheaper to make than heroin. A 300 mg dose of heroin is equivalent to a lethal 3 milligram fentanyl dose. From Bond, 2016.
smoking the fumes produced by melting the substance (Hendricks et al., 2001). The Hines et al. (2020) study, found that “participants whose IAR was through injection (compared to those who initiated through chasing or snorting) were more than four times as likely to use daily within a month of initiation” (p.6). The study by Michael Gossop et al. (2004) was interested in how routes of administration changed for heroin users. Routes of administration can effect likelihood of overdose, showing that about 30% of injectors overdosed, versus 2% of people who take heroin by chasing (Gossop et al., 2004). This study did not find many changes in routes of heroin administration, as about 75% of users used the same route a year later (Gossop et al., 2004).

II. Opioid Withdrawal and Treatments
Withdrawal and Detoxification

Withdrawal is a decrease in the availability of MOR (Volkow & Blanco, 2020). It occurs when a dependent person stops taking opioids (Shah, 2019). Some common symptoms of withdrawal are nausea, vomiting, diarrhea, fever, and sweating (Patterson, 2019). Opioid replacement is now a popular alternative, rather than completely stopping opioids. This occurs when patients going through withdrawal, take other opioids such as methadone or buprenorphine. They have a long half-life and can increase the likelihood of abstinence (Burma, Kwok, and Trang, 2017). These are often used long-term as maintenance treatments in combination with behavioral therapies, which is known as medication assisted treatment or MAT (Sofuoglu et al., 2019).

Detoxification and maintenance therapies can both be used as treatments for OUD. Detoxification involves entirely removing the drug from one’s system and kick starts the treatment for OUD, while withdrawal is the effect caused by no longer consuming the drug
Other forms of treatment should be used following detoxification in order to prevent immediate relapse (Rosenthal & Goradia, 2017).

**Therapy**

Behavioral therapies have served as common practice for substance use treatments for many years. Different methods of therapy can be used depending on each patient’s situation. Some of the behavioral therapies for OUD include cognitive behavior therapy (CBT), narcotics anonymous (NA), 12-step programs, and residential and hospital based treatments. CBT allows for multiple methods that can be tailored to patients, whether one-on-one or group sessions (McHugh, Hearon and Otto, 2010). NA and 12-step programs may offer free options with assisting patients in staying clean, and may often be attended following completion of treatment to sustain recovery (Kelly et al., 2011). Inpatient residential treatments can allow for intensive treatment to kick start recovery (Schuman-Oliver et al., 2014). Even though a wide variety of behavioral therapies exist and are common practice for substance use, they are not considered highly effective for OUD when delivered independently (Sofuoglu et al., 2019). There is limited use of independent behavioral interventions, and more are being used in conjunction with medical treatments (Sofuoglu et al., 2019).

CBT is often used as a method of treatment for all SUD. It can involve multiple interventions, including one-on-one sessions and group or couples’ therapy (McHugh, Hearon, and Otto, 2010). The benefit of CBT for SUD is the structure that can come from regularly scheduled therapy and group sessions (McHugh, Hearon and Otto, 2010). Each clinic may structure their therapy differently, using a combination of group and individual therapies, and the length of treatment may also vary accordingly.
Another method of therapy is a 12-step program or facilitation. This is often done as part of NA’s treatment platform, which has free sessions designed to help people stay clean in a group setting (Kelly et al., 2011). The 12-step program involves a series of stages that offers assistance in recovery, starting by admitting the problem or power the addiction has over daily life, and ending with a spiritual awakening (NIDA, 2018).

Residential and hospital-based treatments are often inpatient forms of rehabilitation, and are done with close observation and intensive treatment (Nunes et al., 2018). This often starts with detoxification from the opioid, and can provide counseling and other services to assist with recovery (Schuman-Oliver et al., 2014). Hospital based treatment is done if additional care for illness or injury in needed in conjunction with opioid treatment (D’Onofrio, et al., 2015).

There is mixed evidence supporting the use of behavioral interventions for OUD, and many of these behavioral treatments are often used in conjunction with medication (D’Onofrio, et al., 2015). Currently, research shows there are three MAT’s for the treatment of OUD that are approved by the United States Food and Drug Administration (Volkow et al., 2014). These treatments include the opioid antagonist naltrexone, the full opioid agonist methadone, and buprenorphine, which is a high-affinity partial agonist at mu-opioid receptors (Volkow et al., 2014; Elkins, 2018).

Methadone

Methadone is an opioid that works as an analgesic to treat pain, but has commonly been used as a treatment for people with moderate to severe OUD (Brown et al., 2004). This works by preventing the occurrence of withdrawal symptoms (McCance-Katz, 2018). It is a full mu-opioid receptor agonist, which means it can fully activate the receptor, and
has a long half-life compared to other opioids (Anderson and Kearney, 2000). It can be offered as a short or long-term treatment. As a short-term treatment, it is offered from days to weeks and used to diminish withdrawal symptoms (McCance-Katz, 2018). Patients using methadone have shown a decrease in heroin use, and an overall decrease in diseases associated with use and needle sharing (Anderson and Kearney, 2000). Figure 3 shows a comparison of research by 6 articles: Yancovitz et al., (1991); Vanichseni et al., (1991); Schwarz et al., (2006); Kinlock et al., (2007); Gruber et al., (2008) and Dolan et al, (2003). Each of these compared patients who were treated with methadone versus control, and all found that the control patients were more likely to use opioids than those treated with methadone (NIDA, 2018).

![Figure 3: Opioid Use with or Without Methadone Treatment](image)

*Figure 3: Opioid Use with or Without Methadone Treatment, Shows the comparison between multiple articles for patients who underwent methadone treatment compared to controls. In all cases The control group tested more positively for opioids versus the methadone treatment group. From NIDA, 2018.*
Naltrexone

Naltrexone was manufactured in 1965, and is a MOR antagonist (Kleber, 1985). This means that it blocks the receptors to prevent opioids from activating them. With naltrexone, patients have to be off opioids, and in many cases withdrawal is started with methadone prior to use of naltrexone. Of the three treatments, naltrexone is the only medication also approved for treatment of AUD. Naltrexone blocks the effects caused by taking opioids or drinking alcohol (Juergens, 2019). While on naltrexone, the opioid receptors are blocked by the antagonist, and when an opioid is taken there will be no euphoric effects (Samokhvalov et al., 2013). It is available in injectable and oral formulations. In a study by Gonzalez & Brogden (1988), naltrexone reduced cravings for heroin, and 23%-62% of patient stayed in treatment after naltrexone.

Buprenorphine

Buprenorphine is a semisynthetic opioid developed from thebaine, which is one of the opiates from the opium poppy plant, Papaver somniferum. It is a partial MOR agonist, meaning it does not fully activate the receptor, but has a high binding affinity and can unbind other opioids such as morphine (Cisewski et al., 2019). Because it is a partial agonist, there is a decreased chance of overdose, which is shown below in Figure 4. It also has a slow method of action and a low ceiling effect, which causes dose related effects such as respiratory depression, sedation, and intoxication to plateau when this ceiling is reached (32mg) (Walsh et al, 1994). Buprenorphine can be used in the same way as methadone, either for long-term or short-term use. Short-term use helps with withdrawal symptoms but relapse often occurs if not continued long-term (McCance-Katz, 2018). Research by
Donroe et al. (2016) suggests no significant difference in using buprenorphine versus methadone for detoxification.

![Diagram showing the comparison between Heroin and Buprenorphine](image)

**Figure 4: Buprenorphine is a partial agonist at MORs and does not fully activate the receptor as a full agonist such as heroin does. From Drugbank, 2005.**

Since 2002, when buprenorphine was first marketed as a treatment for OUD, multiple forms of the medication have come on the market (Drug Enforcement Agency, 2019). The most popular versions come in sublingual formulations (SL), as either tablets or films. These medications are taken sublingually because buprenorphine cannot be absorbed in the digestive lining (Gowing et al, 2017). Buprenorphine tablets or films can either be administered as buprenorphine alone, or in combination products that contain buprenorphine and naloxone (Thomas et al., 2014). Naloxone, an opioid receptor antagonist, is added to these combination buprenorphine products to decrease their diversion and abuse potential (Thomas et al., 2014). Naloxone can cause opioid withdrawal in patients who attempt to snort or inject their combination SL buprenorphine/naloxone medications (Thomas et al., 2014). However, if the medication is taken correctly, the buprenorphine component is absorbed while minimal absorption of naloxone occurs
(Thomas et al., 2014). The two brand names for combination SL buprenorphine and naloxone are Suboxone and Zubsolv (Heo & Scott, 2018). In this document, the SL films and tablets will be referred to together as sublingual buprenorphine (SL).

Other buprenorphine products used in the US for the treatment of OUD, include a long-acting subdermal implant and a subcutaneous long-acting injectable (LAI), sold in the US under the brand name Sublocade (Rosenthal & Goradia, 2017; Lorman, 2018). The buprenorphine implant can last up to six months and works by slowly releasing buprenorphine when implanted subdermally (Smith et al., 2017). The LAI is a treatment method for moderate to severe OUD that is administered every 28 days (Rosenthal & Goradia, 2017). It is injected in liquid form in the lower abdomen and becomes solidified, slowly releasing buprenorphine over the course of the month (Ling, Shoptaw, & Goodman-Meza, 2019). According to previous research, the theoretical benefit of using these long-acting buprenorphine formulations, is a decrease in the possibility of diversion or misuse in comparison to the SL formulations (Rosenthal & Goradia, 2017). Because the medication is taken less frequently than the other formulations, there is an ease of use associated with the injection. The LAI comes in 300mg and 100mg formulations, and the recommended dosing for the LAI is 300 mg for the first two months followed by 100mg for each additional month (Indivior, n.d.). Each patient may differ in response to the injection and some may start on 100mg or stay on 300mg for the entire duration (Indivior, n.d.). Figure 5 shows a comparison of the number of opioid free weeks for LAI patients (brand name Sublocade) who took a 300mg dose followed by a 100 mg dose, or two 300mg doses, compared to control (Indivior, n.d).
MAT Comparison

Buprenorphine, naltrexone, and methadone are all effective treatment methods for OUD, however each have their own specific benefits. Not much research has been done to compare the effectiveness of all three together. As it has come to market in the past few decades, buprenorphine has started to overwhelm the market share for OUD treatments (Grand View Research, 2019). According to Grand View Research (2019), “Buprenorphine’s SL tablets are the most widely prescribed drugs for OUD, and buprenorphine was the largest revenue generating segment in 2018.” Figure 6 shows the majority of the market share going to buprenorphine.

Figure 5: The number of Opioid Free weeks for patients taking 300/100mg vs 300/300 mg injections compared to control. All participants underwent Individualized Drug Counseling. There was no significant difference between the number of opioid free weeks for both sets of Sublocade patients, however both groups lasted significantly longer than the control group without the use of illicit opioid substances. From Indivior, 2018.
Figure 6: The 2018 Global Opioid market share was majority given to buprenorphine. Buprenorphine treatments have gained popularity on recent years, with sublingual tablets and films being the most popular products. From: Grand View Research, 2019.

A study done by Bart (2012), compared these medications and looked specifically at retention rates. For a 24-week retention rate, the authors found retention of “84%, 59%, and 21% for methadone 50mg, buprenorphine 5mg, and naltrexone 50mg, respectively, despite suboptimal doses of methadone and buprenorphine” (Bart, 2012, p.9). This study found that between buprenorphine and oral naltrexone, naltrexone was inferior (Bart, 2012). The study highlighted the percentage of patients that stayed on their MAT after 24 weeks, and patient preference for the specific treatments (Bart, 2012). Comparing the effectiveness for oral naltrexone to buprenorphine, an article by Velander (2018), found that patients on naltrexone at 6 months were equally likely to relapse than those on placebo. Relapse rates on naltrexone or placebo were three times higher than rates for buprenorphine maintenance (Velander, 2018). While side effects may not contribute to the effectiveness
of medications, it is important to note the variability in potential effects. The side effects of these medications also differ slightly. Some side effects for buprenorphine include, sedation/drowsiness and constipation, while side effects for methadone include sweating, insomnia, constipation and decreased libido (Lange et al., 1990; Kreek, 1973). Lastly, the side effects for naltrexone include, nausea, headache, vomiting, and loss of energy (Gonzalez & Brogden, 1988). More research must be done to directly compare these treatments to give those with addiction the most appropriate treatment option.

III. Qualitative Research

There has been debate about the legitimacy of qualitative research, as it often does not follow the form of the scientific method (Sale and Thielke, 2018). According to Pathak, Jena, and Kalra (2013), “[The] qualitative method is used to understand people's beliefs, experiences, attitudes, behavior, and interactions. It generates non-numerical data (p.192).” However, qualitative data offers the ability to ask open ended questions, while also having to consider a wide range of possibilities for flawed data based on how the studies are performed or data is collected (Ranney et al., 2015). It is more flexible than quantitative data and offers participants the ability to speak in their own words and not be categorized, which allows for more meaningful responses (Anderson, 2010). For qualitative research related to topics in psychiatry, the interpretive and critical research paradigms are most commonly used to address these questions (Fossey et al., 2002). Each of these paradigms can offer different methods that can be used when conducting qualitative research.

Interpretive qualitative research seeks knowledge from participant perspectives and a subjective viewpoint (Ponelis, 2015; Fossey et al., 2002). Some of the methods used in interpretive research are ethnography and phenomenology (Fossey et al., 2002).
Ethnography is used to study cultures or a particular community that shares common beliefs, but it’s members have individual experiences (Fossey et al., 2002). It attempts to understand a social world using direct interactions with the subjects (Newton et al., 2000). In an ethnographic study by Newton et al. (2000), researchers attempt to develop rapport with subjects to improve the breadth of knowledge acquired through observation. A researcher observed mentally ill patients before and after discharge in attempt to study the effects of deinstitutionalization on patients (Newton et al., 2000). Phenomenology is specifically designed to study the experiences and lived events of subjects (Fossey et al., 2002). According to Neubauer, Witkop, and Varpio (2019), phenomenology can provide unexpected insight and deeper understanding of social phenomena. It asks questions based on understanding the meaning behind experiences (Errasti-Ibarondo et al., 2018). This method often examines common themes seen between subjects using open-ended interviews (Fossey et al., 2002). Interviews may be designed to make subjects feel more comfortable. Ranney et al. (2015) states, “An ideal qualitative interview will feel like an extended conversation for the participant – yet will yield data on each topic area outlined in the interview guide (p.3).” Interviews can be semi-structured, have an outline of questions, and can be set up as conversational or in-depth and more controlled (Jamshed, 2014). According to Ranney et al. (2015), a common approach to conducting interviews involves using an outline, with an introduction to explain the project, followed by main questions and probes. The probing questions usually follow the main questions and icebreaker questions, which help participants open up a bit more and be more comfortable with the interviewer (Ranney et al., 2015). The probing questions may help subjects better understand the questions or to elaborate further (Ranney et al., 2015).
Critical qualitative research is more focused on using the knowledge gained from research to affect change. It “enhances awareness of how our knowledge is constructed” (Higgs et al., 2008, p.157). One method of the critical paradigm is participatory action research. Using this method, subjects or participants may influence the research from beginning to end, and contribute to the study as equals to the researchers (Fossey et al., 2002). Because the focus is to directly enact change, it differs from other types of research, and as subjects serve as stakeholders in the study, this method is able to receive contributions directly from those it may impact (Baum, MacDougall, & Smith, 2006).

Qualitative research can be an important tool used to collect and analyze data in a unique way, and get results that can be based on opinion or attitudes (Fossey et al., 2002). Similarly, to quantitative research, there is an expected outcome or hypothesis, which can drive the set-up of the observational research or interviews (Ranney et al., 2015). This is also an important tool in comparing the experiences of multiple subjects or patients, and can be used to benefit quantitative research in the future. We used qualitative methods to conduct interviews with patients. The qualitative methods allowed us to get patient experiences with the LAI and SL buprenorphine.
CHAPTER 2: STUDY DESIGN

I. Introduction

OUD has been gaining a lot of publicity in recent years due to the opioid epidemic, and promising new treatments are being added to the market. One popular treatment is buprenorphine with multiple formulations, including SL buprenorphine, implants, and the LAI (Rosenthal & Goradia, 2017). The research described here, focuses largely on LAI and includes a qualitative exploration of patient experiences with the LAI compared to the SL forms of buprenorphine. As a relatively new treatment method, the scientific literature on LAI thus far has focused primarily on relapse rates or overdose. This has left knowledge gaps regarding patients’ experiences and preferences for one form of the medication over the other. Preliminary data related to LAI shows effectiveness of the medication compared to control. Ling et al. (2020) studied the long term effectiveness and satisfaction with the extended release injection and found “over 88% of patients reported medication satisfaction at the end of the study (p.4).” While the original research reports only the effectiveness of the LAI and the ease of use of a monthly injection, in-depth inquiry of patient experiences could provide a more comprehensive understanding while using qualitative data.

Importance

We collected qualitative data to get a deeper understanding of patient perspectives and compared the information gathered to each of the interviews conducted. This research is important because it provides a different level of information. As the LAI is a new treatment to Wake Forest Baptist Health Psychiatry and Behavioral Medicine (WFBPBM)
Many patients are interested in trying the injection for the first time. We hope by conducting this research, that we can share more information with patients interested in the LAI. Although not recommended as it may increase the risk of relapse, some patients opt to use the LAI to taper and eventually discontinue all buprenorphine medications (Weinstein et al., 2018). Results may differ for each patient based on factors such as emotional and financial stability and length of treatment (McCance-Katz, 2018). Other patients use it for the ease of only taking it once a month, or to eliminate opioids and medications from their household. Our research hopes to determine patient’s preferred form of buprenorphine, their experience on the injection, as well as if they would recommend it to other patients. All of the patients involved in the study at WFBPBM have started on SL buprenorphine prior to starting treatment with the injection. As stated before, the preliminary data states that SL buprenorphine and the LAI are found to be equally effective. We have noticed that patients have expressed differences between the LAI vs the SL buprenorphine, with cravings, pain, or the effectiveness of the either medication. There is limited data comparing the two, but one study by Haight et al. (2019) did find that the 300/300 mg and 300/100 mg injections may have lower plasma concentrations than the 24 mg SL form of buprenorphine. Because of this limited data and our interest in a direct comparison, our main goal was to find effective information to pass on to patients at the WFBPBM clinic, prior to switching to the LAI.

This research will focus specifically on patient perceptions and experiences with LAI for treatment of OUD, versus their experiences with using other formulations of buprenorphine. One-on-one semi-structured interviews will be administered to patients who are currently taking or have previously taken the LAI. Demographic data will also be
collected, along with patient thoughts on using the LAI versus SL buprenorphine to treat their OUD. Ultimately, the goal of this study is to determine if LAI works as an effective treatment based on the perspective of the patients, as well as to understand the reasons why some patients elected to switch from SL buprenorphine to the LAI. We hypothesize that overall, patients will prefer the LAI versus the SL buprenorphine formulations. However, we predict that these preferences will be due to varying reasons, which is why we have elected to perform qualitative interviews to observe and compare these results.

II. Methods

This research was conducted at WFBPBM clinic in Winston Salem, NC., which served as the sampling frame for this study. Participants were recruited directly from a population of 20 patients who attended regular group treatment visits and also received LAI at the WFBPBM clinic. A total of fifteen patients were recruited and consented, of which, nine patients were scheduled to complete a brief, in-person interview. During the consenting process, each patient became aware of the purpose of the research, and was informed that their personal information would not be shared with anyone outside of study staff. By providing signed consent, participants agreed to have their interviews recorded, transcribed, and analyzed. Each participant was assigned a random patient number ranging from 1-15, which was only given to study staff to ensure protection of privacy. Figure 7 highlights the study participation based on the number of patients consented and those who completed the study.
Following a semi-structured interview guide developed a priori, nine participants completed a one-time, one-on-one open-ended interview. The average interview lasted 40 minutes. Based on the focus of our research on preference for OUD treatments, we were able to develop a series of questions that served as a guide during interviews. Our methodological approach was similar to a phenomenological qualitative approach, as it was designed to use participant perspectives to understanding specific phenomena (Groenewald, 2004). These questions were designed to specifically address patient’s substance use and recovery while touching on specifics of the medications and any potential effects. Using semi-structured interviews, we started with more general questions to encourage openness with the interviewer, and followed the more specific questions with prompts to allow for clarity and deeper understanding (Rabionet, 2011). Prior to the interview, patients were given a brief synopsis of the project, that reiterated the purpose of
the interview. They were given time to ask any questions before the recording commenced. A series of demographic questions were also asked (Figure 8), before moving on to the main interview questions (Figure 9). Based on how brief or extensive participants were with their answers, further prompts may have been necessary, and other questions not listed may have been addressed based on situational differences. The questions were designed to invite open communication between the participant and the interviewer to provide a more conversational interview, and openness with sharing sensitive information.

<table>
<thead>
<tr>
<th>Demographic Questions</th>
</tr>
</thead>
</table>

**Gender**
- Male
- Female
- Other (please specify:)

**AGE?**

**Sexual Orientation**
- Heterosexual
- Homosexual
- Bisexual
- other (please specify): 
- prefer not to say

**Education**
- Less than high school diploma
- high school diploma or GED
- some college, no degree
- associate’s degree
- bachelor’s degree
- master’s degree
- professional degree
- doctorate

**What is your current employment status?**
- Full-time employment
• Part-time employment
• Unemployed
• Self-employed
• Home-maker
• Student
• Retired

**Number of people in Household? (including self):____**

**Which income group does your household fall under?**
• Less than $20,000
• $21,000 – $30,000
• $31,000 to $40,000
• $41,000 to $50,000
• $51,000 to $60,000
• Above $60,000

**Insurance**
Has your insurance changed recently?

*Figure 8: Demographic Information asked by each patient. The basis of these questions offered more information that was relevant in the course of the interview.*

**Interview Questions**

Over the next 45-60 minutes I’d like for us to share a conversation to help me better understand your experiences with different forms of buprenorphine, specifically long-acting injectables and sublingual films. Some of these questions may be a little sensitive and you do not have to answer any questions that cause you to feel uncomfortable. There are no right or wrong answers and everything you share with me will be kept strictly confidential; I am here to listen and to hear your story so that I might be able to understand and help others who have similar experiences to your own.

1. To get us started, tell me a little about yourself.
   a. Prompt: Tell me about your life growing/coming up.
   b. Prompt: Tell me about your family life when you were a child/teenager (who did you grow up with and how did you spend your time; what were your parents like?).
   c. Prompt: What about your current situation; what is life like at home?
2. Tell me about the factors that led up to your use of LAI/SLB.
   a. Prompt: What types of substance use have you been exposed to in your life? (define substances)
   b. Prompt: What personal experience do you have with substance/alcohol/tobacco/drug use? What was your drug of choice and what method of administration did you use?

3. I’d like to know more about your experiences with drug use and what caused it to become a part of your life.
   a. Prompt: Tell me how it all started.
   b. Prompt: How old were you and when did it develop into a dependency?
   c. Prompt: How and when did it start becoming a problem for you and others?
   d. Prompt: How have your family and friends reacted/responded to your use of drugs? How have they been helpful? How could they have been more helpful?
   e. Prompt: Tell me about use of substances among others in your family and those you spend time with.

4. Tell me about your experiences with LAI, what has it been like using it?
   a. Prompt: Tell me about the types you have used – injectables, sublingual – what do you think about them?
   b. Prompt: What led you to start taking it?
   c. Prompt: How has it been helpful?
   d. Prompt: How has it been challenging?
   e. Prompt: What might have made it more helpful to you?
   f. Prompt: What other substances have you also used while on LAI?

5. How have your cravings changed since using LAI? What are your short and long term plans with LAI?

6. I’d like for you to think about recovery from addiction – what does the road to recovery look like for you?
   a. Prompt: What would it be like to reach recovery?
   b. Prompt: What role does LAI have in helping you reach that goal?
   c. Prompt: What other supports and resources do you need to help you get there?

7. What advice do you have for others that are facing challenges with drug use?
   a. Prompt: In what ways might LAI be helpful for others?
   b. Prompt: If you could create your own intervention or program to help others reach recovery, what would it look like?
   c. Prompt: What information do you wish your family knew that could have helped you along the way?
   d. Prompt: What information/techniques/strategies do you wish your doctors/care team knew that could have helped you along the way?

Figure 9: The questions involved in the semi-structured interviews allowed for an in depth look into patient’s lives as well as their experiences with the LAI vs the SL buprenorphine. Based on each individual’s personal experience, additional questions may have been asked in order to clarify or elaborate specific points.
Following the completion of all interviews, recordings of interviews were replayed and transcribed by the interviewer. Transcriptions were reviewed by the principle investigator, who was not involved in the interview or the transcription process, in order to verify accuracy. Transcriptions were then analyzed by four members of the study team. They included the coordinator, interviewer, a member with expertise in qualitative research, and the principle investigator. The four members each collectively analyzed the transcriptions to compare codes, and 1-2 transcriptions were analyzed independently by each member of the study staff. The members collaborated and derived core themes representative of the collective data. The methodology included iterative thematic analysis, which was used to code key words, identify patterns and emergent themes, and compare and present findings. These themes could often be repeated words or concepts seen across interviews, or may be similar experiences related to the medications, or shared by multiple participants. For example, noticing multiple patients expressed using heroin, or had a preference for the LAI.

III. Results

Consistent with primarily quantitative evaluations describing high satisfaction with LAI, we hypothesized that the majority of patients we interviewed would have an overall positive view of the LAI. However, we expected to see differences in experiences between patients, which would provide more insight into the subjective preferences for LAI versus SL buprenorphine. The purpose of this research, highlighted earlier, was to develop a stronger context for understanding LAI, in order to inform clinical practice. Prior to the induction of this research, some patients at the WFBPBM clinic had already switched back to SL buprenorphine from side effects associated with the LAI. Guided by the intent to
better understand patients’ experiences, qualitative investigations like this one strive to abandon preconceived notions in order to let patient interviews speak for themselves. We hoped to gain more insight about the LAI and the related experiences, to provide a foundation for further inquiry in future studies. We consented a total of fifteen patients, and based on participation and scheduling of interviews we had nine patients participate in the interview process. These patient numbers include, 1-4, 8, 9, and 11-13, which will be used to distinguish each patient by experience (Table 2).

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Sex</th>
<th>Age</th>
<th>Prior Heroin Use</th>
<th>Cravings for buprenorphine</th>
<th>Prescribed opioids</th>
<th>Family drug use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>34</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>35</td>
<td>Y</td>
<td>Y</td>
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</tr>
<tr>
<td>4</td>
<td>F</td>
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<td>30</td>
<td>Y</td>
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</tr>
</tbody>
</table>

*Table 2: Patient Characteristics. Y/N are used in place of yes and no. The sections were left blank if the topic was not explicitly discussed in the interview.*

**Thematic Analysis**

When examining the transcriptions, emergent themes were identified within the data. We compared each of the interviews and looked for repeated words, phrases, or similar ideas, which were represented as “codes”. We determined if there were possible similarities between patients that caused them to have similar experiences, and also looked for marked differences between the interviews. As this research and the interview guides were structured to provide more information to patients interested in the LAI, emergent
themes are largely connected to the specific questions included in the interviews and draw a connection with patient preferences for the LAI or SL buprenorphine. The thematic analysis described here features similar experiences that may provide information related to use and acceptability of the medication. Because of the nature of qualitative data, much of the analysis and results have allowed us to note the existence of commonalities that we can further examine, however in many cases we cannot determine why the connection occurs without conducting further analysis and potentially quantifying some of the data. A total of seven themes emerged from the data and are described here, including: (1) prior heroin use, (2) adverse reactions may be related to sex differences, (3) preferences: LAI promoted freedom from the “slavery of” pill taking, (4) absence of cravings related to previous drug use experiences, (5) engagement in prior treatment, (6) family factors influence in drug use and recovery, and (7) patients desire to one day be “normal” and off of all medications.

**Prior Heroin Use**

Throughout the interview process we became aware of multiple patients who admitted to using heroin during their addiction. Of the nine patients, four patients (1,2,8,13) reported using heroin. Some patients expressed that using heroin drove them to enter recovery as it was the “wake up call” that they entered a new level of addiction. Patient 8 stated that when she first tried heroin, she regretted the day it happened, because things got worse. Patient 2 also used heroin, but for him it was the realization he needed in order to go into recovery. When asked the point when he realized his problem, patient 2 stated, “It was when I tried heroin...I tried it 3 times and realized how stupid it was.” Based on the four patients who have used heroin, all still had positive reactions to the LAI. There were
no differences compared to the rest of the subject’s preference for the LAI or SL buprenorphine.

**Adverse Reactions may be Related to Sex Differences**

Of the nine patients interviewed, three of them identified as women and six as men. When asked about reactions to the LAI, all of the women interviewed had an adverse reaction related to the injection. Patient 8 shared that she began breaking out in hives and started sweating, dry heaving, had a fever, and was shaking uncontrollably during the first few days on injection. She indicated that doctors diagnosed her with an allergic reaction to the preservative in the LAI. The patient also thought that the symptoms may be caused by the naloxone in the SL buprenorphine, and it caused withdrawal symptoms when the LAI was injected. Patient 3 also had negative reactions associated with the injection, and reported a burning sensation when getting the LAI, which she believed was due to the injection not being warmed prior. She also reported swelling in her lower extremities for 3 months while on the injection before eventually stopping the treatment and returning to SL buprenorphine. Patient 4 complained of inability to sleep, and rapid temperature changes (e.g., hot flashes), but said these only occurred in the last week of the monthly injection.

All of the women interviewed, despite the adverse effects, had positive reactions to the injection. They all agreed that the LAI worked well and was easier to manage than the SL buprenorphine. Out of the male patients, patient 11 was the only one that expressed side effects with stomach aches, headaches, and hot flashes for the entire month on the injection. However, he still described the LAI as “decent”. Further research is required to determine the frequency of the side effects seen in women, and if so, why these effects may be more common for women.
Preferences: LAI Promoted Freedom from the “Slavery of” Pill- Taking

Of the patients interviewed, all expressed a positive reaction to the LAI, and all but patient 8 had a preference for LAI over SL buprenorphine. This was due to a variety of factors, with some patients stating the benefits were the ease of not having to take it every day, or knowing they are not able to misuse an injection given by a provider. Some patients expressed the feeling that having a monthly injection breaks the obsession or cycle of medication use. When asked about his feeling towards the injection, patient 1 stated, “It has been a life saver, It’s breaking the chain of being a slave to a pill bottle or film bottle.” Similarly, patient 9 stated “[LAI is] great… It has changed my life in so many ways.” When patient 13 was asked to compare the LAI with SL buprenorphine he stated, “There’s really no comparison. The shot is way better. You don’t feel like up and down and you don’t feel like you need something, and it gets you out of the habit of taking something every day.” While the patients each had a different experience and different story to tell, overall the reaction to the LAI were positive, as we hypothesized. From their interviews emerged a theme of breaking free from being a “slave” to pills, which also was related to reductions in habit and obsessive behaviors. Patients 1, 2 3, 4, 9, and 13 each mentioned the injection offered them the opportunity to not take buprenorphine daily.

Even though most patients preferred the injection over the SL buprenorphine, some of the patients still had positive or neutral feelings towards the sublingual medications. For example, patient 4 stated, “It worked. I didn’t have any cravings so that was a plus, and it helped my pain too. For me I don’t think there was anything that I didn’t like about it, except for having to take something every day.” Patient 8 had mixed feelings stating, “Don’t get me wrong, it’s a life saver, but I’m a drug addict. For me, I’m about to replace
heroin with something else...I think it’s great, but I think it needs to be closely monitored.”

Patient 3 and 11 both had more negative opinions, stating they hated the taste of SL buprenorphine, with patient 3 stating she had to brush her teeth after each dose.

**Absence of Cravings Compared to Previous Drug Use Experiences**

During the interview process, patients were asked about any cravings they may have experienced on the SL buprenorphine. Of the patients, patient 2 and 8 both expressed having cravings. Patient 2 admitted to still having cravings and taking illicit substances while on the SL buprenorphine. Patient 8 stated, “I had cravings the first 30-45 days on Suboxone but after about 2 months all the cravings stopped. Suboxone has been great for me.” We also asked about any experience with cravings on the LAI. Patient 12 was the only patient that expressed having cravings on the injection. He stated, “I did have cravings, but I gave this a shot because I didn’t want to go back on the strips. Because it was my last resort. Either I was going to go do street drugs again because I might as well. To me the strips are drugs, and If I take the strips I might as well take drugs. That’s how I feel.” While only 3 patients reported any cravings for any form of buprenorphine, the cravings didn’t seem to effect the overall preference. Patient 2 was the only one of the three that stated the cravings led to relapse. Patient 8 had temporary cravings, and even with the cravings experienced by patient 12, he continued to use the LAI to completely come off buprenorphine. The majority of patients did not report any issues with cravings with LAI, but did comment on experiences with prior illicit drugs and treatment medications that had caused cravings (e.g., oral fixations and cravings to use SL buprenorphine). The lack of cravings reported among these patients using LAI is a positive indication for this treatment method.
Engagement in Prior Treatment

Throughout the interview process, we noticed a commonality between many of the patients, as they were treated previously at a different clinic prior to becoming a patient, or have undergone treatment at WFBPBM previously, before returning for a second time. All of the patients who previously underwent treatment did so for a variety of reasons. We hypothesize that in some cases patients were not able to commit fully to treatment, and the injection offered them that ability. Patient 8 had been through treatment at different facilities and come to WFBPBM previously. She had gone through a different intensive outpatient program (IOP) twice before. She stated her first treatment at another facility was “unethical” and she did not receive the counseling she needed. After attending WFBPBM the first time, she relapsed, but felt as though it was necessary to allow her to heal completely. Patient 4 was treated at a methadone clinic prior to treatment with WFBPBM. She decided to switch facilities after noticing the side effects of methadone were causing her to miss spending time with her family. Patient 1 had a more positive opinion of a previous rehab facility, crediting it with saving his life. The differences in previous treatment is interesting to note, however the experiences people have had all differ, so it cannot be concluded if this had an effect on patient experiences with the injection or SL buprenorphine.

Family Factors Influence Drug Use and Recovery

Interestingly, the interviews described the role of family factors as relevant to both the initiation and reinforcement of substance use, but also to help-seeking behavior and motivation to pursue recovery. Seven of the nine interview participants described a history of substance use within their families or close relationships, that prompted or helped
perpetuate substance use at some point during their lives. A majority of participants described first use of “drugs” during adolescence, often among friends, but later described the role of close family ties in reinforcing drug use (e.g., brother, sister, parent). Oppositely, multiple patients described similarities in situations leading to the realization that they should seek treatment for OUD, often describing pivotal moments in their family life indicating they had “hit rock bottom”. Family factors and relational ties were frequently cited as motivating factors for pursuing recovery, with one participant noting pregnancy and another describing her grandchildren as the reasons for finally “getting help”.

**Patients desire to one day be “normal” and off all medications**

Across interviews, patients routinely indicated a desire to one-day return to “normal”; to live a life free of medications and without the burden of needing regular treatment medications. Patient 9, as with many of the other patients, expressed his desired end goal was to be off all OUD treatments. However, these participants also acknowledged and valued the need for maintaining a stable treatment regimen for a prolonged period of time to ensure that they would not revert back to previous drug-seeking behaviors. Similar to the theme describing “preferences”, use of LAI appeared to be a step towards achieving normalcy, as the monthly injection removed some of the complications accompanying regular pill-taking along with temptation to misuse pills. Two patients (12, 13) have already used the LAI to taper off all medications. When describing his life off the LAI, patient 12 stated, “My son, he’s going to be 2 years old, and I’m ready to live my normal life, but I’ll always be an addict, a recovering addict. It is what it is. I’ve got a support system.”
<table>
<thead>
<tr>
<th>Theme</th>
<th>Quotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Prior heroin use</td>
<td>“I wish this day never happened, but someone was like, ‘Have you ever tried heroin?’… and we did that and then things just obviously, I mean of course, two addicts, things got worse.” (8)</td>
</tr>
<tr>
<td>(2) Adverse reactions may be related to sex differences</td>
<td>“The last week I can’t sleep, tossing and turning. Sometimes in freezing, burning up.” (4)</td>
</tr>
<tr>
<td>(3) Preferences: LAI Promotes Freedom from the “Slavery of” Pill-Taking</td>
<td>“[The LAI] was probably the best thing that happened because I hated being a strip slave, because I hated doing that.”(12)</td>
</tr>
<tr>
<td>(4) Absence of Cravings Compared to Previous Drug Use Experiences</td>
<td>I don’t know what it is about my body but I still took everything while I was on the SL buprenorphine.”(2)</td>
</tr>
<tr>
<td>(5) Engagement in Prior Treatment</td>
<td>“So first I started on Subutex at a methadone treatment facility…I wanted to get into a facility that wants you to get treatment. Cause the addiction is 80% mental and 20% physical. Abstinence doesn’t mean treatment. Just because you stop taking the drug doesn’t mean you’re clean and recovered.” (11)</td>
</tr>
<tr>
<td>(6) Family Factors Influence Drug Use and Recovery</td>
<td>“I had grandchildren and great grandchildren and I couldn’t keep doing what I was doing... I hid it really well. I did [get help] for myself. If I did it for the kids, it wouldn’t have stuck. I just got tired and had to change my life. I didn’t want to die and have my daughter bury me.” (3)</td>
</tr>
<tr>
<td>(7) Patients desire to one day be “normal” and off of all medications</td>
<td>My life goal is to eventually be off of Suboxone [SL], but at the same time I am aware that it’s okay if I need buprenorphine, and I feel as long as I am working treatment, that’s okay. I know what happens when I take that jump too quickly. I’ve given myself a year… and I wanted to be off of Suboxone. If that changes I am still okay with it, but as far as my end goal I would like to do recovery medically unassisted.”(8)</td>
</tr>
</tbody>
</table>

Table 3: Quotes that are representation of each of the seven themes. The numbers in parenthesis is the patient number associated with the quote.
CHAPTER 3: DISCUSSION

The qualitative study we conducted was done to address a limitation in research on opioids and OUD. We used this interview method to gain perspectives from the patients. By using their individual voices as data, we are able to get a unique perspective on the medication and how SL buprenorphine and the LAI have affected these patients’ lives. One benefit of this research is the flexibility of the study. While we did hypothesize that patients would have a preference for LAI and have different experiences, we did not anticipate what these specific themes would be. While only some may be directly related to the preference for the injection or SL buprenorphine, it is important to note some similarities between patients lived experiences. The lives and stories of the patients gave us an understanding of what led up to their drug use and recovery, versus only looking at their experience once on the medication. This study developed into comparing experiences of patients with OUD versus looking directly at the LAI. However, we are now able to share some of the patient experiences with other patients interested in starting the LAI for treatment.

I. Limitations

Our method of conducting interviews may have allowed for specific biases to come about. Patients were told during consent about the nature of the study, and that we were examining patient preference and opinions on the LAI. We interviewed patients at the WFBPBM clinic where they also receive their prescriptions and the injection. Because of this and specifically looking at patients who have been on the LAI, patients may have assumed that the interviewer wanted to primarily hear of positive reactions to the LAI, and therefore may have changed their opinion to be more positive. The interviewer assured
patients that their information would be confidential and not be shared with counselors or clinicians outside of study staff. However, because of the nature of the information and the research being conducted at the clinic, patients may have been uncomfortable and fabricated details of their substance use. Other possibilities of bias during interviews may have affected the results. This can include the interviewer being uncomfortable, having differences in opinion to the subject, and difficulty with remaining neutral (Mehra, 2002; Chenail, 2011). When the interviewer lets their specific opinions be known, whether subconsciously or consciously, it may affect the answers or direction of the interview (Chenail, 2011). To address the possibility of bias in future research, a critical qualitative research paradigm can be used. This paradigm works to use knowledge gained through research to make direct improvements and provide further understanding (Fossey et al., 2002). Specifically, participatory action research, could focus on the change and improvements that could be made through the research, and allows participants and researchers to both contribute to every aspect of the study (Baum, MacDougall, & Smith, 2006). The involvement of patients and their contributions to the research design and the outcome, will ultimately assist with patients interested in using the LAI. A potential benefit allows the information gathered using participatory action research to be given directly to their peers. As they also serve as contributors and their influence should eliminate any potential pressures felt by researchers. This will help to eliminate potential bias that could affect patient responses.

One limitation of our research is specifically the themes. The nature of qualitative data allows us to identify themes and commonalities between patients. Many of these themes became apparent while interviewing, noting common experiences that came about.
However, with the nature of the interviews, we are not always able to find the source of these similarities. It is offered as preliminary data to find potentially related information, but requires further investigation to pursue these specific themes and why they occur. The qualitative analysis allows for a potential focus of future quantitative data to further address these themes. For example, during the interviews with the patients who identified as women, we noted the adverse side effects. However, without further investigation into why women might experience these specific reactions, it is unknown why this commonality has occurred.

Another limitation of this research was the nature of the interviews. The open concept of these interviews allowed for patients to be more comfortable with the interviewer. While each interview was conducted by the same study team member to ensure consistency, each interview was unique and involved asking individually tailored questions based on the situation. This led to some questions or themes not being addressed with specific patients, which made it more difficult to undergo thematic analysis.

Lastly, the small sample size made the comparison of interviews more difficult. Because this research was conducted with patients at the WFBPBM clinic, who have previously taken or are currently taking the LAI, our sample size was limited. Out of the population of twenty patients, fifteen were consented. Of those fifteen, only nine were able to interview with the limited time constraint. Of those nine patients, four of them are no longer on the LAI, and one was no longer attending treatment. With only nine patients that underwent the entire interview process, some of the themes that we chose to further analyze, were only seen in a small sample of participants. In future research we hope to continue conducting interviews and to analyze more potential themes and comparisons.
II. Recommendations and Future Directions

In the future we hope to increase our participation in the study. By increasing our sample, we can further compare interviews and examine themes. This will allow us to determine if there are more common occurrences between a specific group of patients. Specifically increasing the patients to include an equal number of men and women, will allow us to further analyze any sex differences. Because of the limited population who have taken the LAI at the WFBPBM clinic, expanding the study to other psychiatry clinics may offer a wider variability in patients and a more diverse population.

In the future we also hope to quantify some of the data to further analyze specific themes. The qualitative data has allowed the us to discover the potential existence of themes, however focusing specifically on why the themes occurred will require further investigation and potential quantification. Looking specifically at patients who suggested they metabolize the medication faster and why women may be experiencing adverse effects, will allow us to further investigate these themes and the patients based on their experiences.
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Research Experience:

**Graduate Research Assistant**
“A qualitative study of patient perceptions of and experiences with long-acting injectables and sublingual buprenorphine”
Clinical research conducting interviews with patients with opioid use disorder
 Wake Forest University Master’s thesis-2020

Membership/Certifications:

**American Psychological Association**
01/2020-12/2020

**ASHI Training**
CPR/AED/First Aid/Oxygen- BLS
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Education:

**Master of Science in Neuroscience**
Wake Forest University, Winston-Salem, NC
Partial Tuition Scholarship $13244
2019-2020 Second year tuition scholarship $24000

**Bachelor of Science in Health Sciences**
University of South Florida, Tampa, FL
3.4 GPA

**University of North Florida**
Jacksonville, FL
Honors Program, Test Prep Scholarship $10000

**Associate in Arts Degree**
Brevard Community College, Melbourne, FL
3.4 GPA, Brevard Community College Dean’s List

Work Experience:
Rehabilitation Technician 02/2018–07/2018
First Choice Medical Group-Physical Therapy, Rockledge, FL
- Assist with patient exercises and therapy
- Provide proper heat or cold therapy packs for each individual patient
- Fill out patient forms to track overall progress in therapy

Recreation Aid 07/2017-04/2018
Patrick Air Force Base Fitness and Sports Center, Satellite, FL
- Maintain proper certifications and training for the safety of patrons and military personnel
- Greet patrons and gather information on military status for scatter plot data
- Check out, set up, and inform others of proper equipment use when necessary

Relevant Graduate Coursework:
- Neurodevelopment
- Neuroanatomy
- Neurophysiology and Neuropharmacology
- Career Planning in Biomedical Sciences
- Scientific Integrity and Professionalism
- Social psychology
- Sensory Neuroscience
- Memory Cognition and Aging
- Biological Research
- Quantitative Methods in Bioscience

Presentations:

Mariah Alexis; Megan Irby, PhD; Stephanie Weiss, MD, PhD; Tonya Fulton, Heather Douglas, MD

Mariah Alexis & Ashley Spring, PhD. Absorption of Ultraviolet Radiation from Squid Ink compared to Sunscreen. Undergraduate Research Exhibition, Eastern Florida State College, Melbourne, FL. April 25, 2018.