



**BEMIDJI**  
STATE UNIVERSITY

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# HONORS PROGRAM

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Megan M. Newberry

## Effectiveness of Methadone for Treatment of Heroin Use Disorder

Nursing, Chemical Dependency

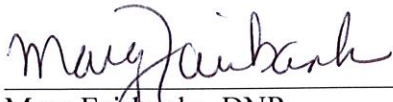
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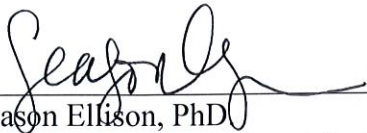
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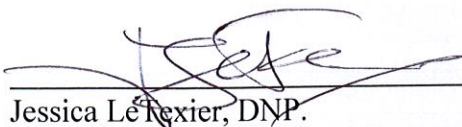
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### **Abstract**

Heroin use disorder in the United States has been at record high levels the last few years with the prevalence rate skyrocketing since 2011. Because of this increased prevalence rate, there is a need for effective treatment for these people. The current “gold standard” treatment is a harm reduction treatment with methadone to substitute for the use of heroin. Methadone suppresses the unpleasant adverse effects of withdrawal when detoxing from heroin. However, methadone treatment often leads to a secondary addiction to methadone itself. Because of this secondary addiction, there is a need for evaluation of methadone’s effectiveness as a treatment for addiction. This thesis defines the various types of treatment available for heroin use disorder and evaluates the effectiveness of these types of treatment.

### **Effectiveness of Methadone as a Treatment for Heroin Use Disorder**

Addiction is a complex disease process that has no cure-all. People who have an addiction may experience remission that remains throughout their life. However, some people may experience numerous relapses throughout their lives. Addiction can be an on-going, everlasting disease with both psychological and physiological impacts. This disease comes in various forms, severities, and through various illicit drugs or activities. However, heroin has recently experienced a surge in popularity, which indicates a need for an effective treatment. Currently, methadone is most common for treating heroin use disorder. Methadone suppresses the unpleasant adverse effects of withdrawal when detoxing from heroin, but often causes a secondary addiction to methadone itself. Because of this, there is a need to evaluate how effective methadone is for treating heroin use disorder. In this thesis I will define what heroin use disorder is, explore why finding an effective treatment is important, list the current treatment options available, and evaluate these treatment options through an analysis of current research.

### **Heroin Use Disorder**

#### **Definition**

According to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V), heroin use disorder can be defined as a problematic pattern of heroin use leading to clinically significant impairment or distress, as manifested by at least two of the following criteria, within a 12-month period:

1. Heroin taken in larger amounts or over a longer period than was intended
2. A persistent desire or unsuccessful efforts to cut down or control heroin use
3. Great deal of time spent in activities necessary to obtain the heroin, use the heroin, or recovering from its effects



4. Cravings or strong desire or urge to use heroin
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
6. Continued heroin use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of heroin
7. Important social, occupational, or recreational activities given up or reduced because of heroin use
8. Recurrent heroin use in situations in which it is physically hazardous
9. Continued heroin use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been the cause or exacerbated by the substance
10. Tolerance as defined by either a need for markedly increased amounts of heroin to achieve intoxication or desired effects, or a markedly diminished effect with continued use of the same amount of heroin
11. Withdrawal as manifested by either the characteristic withdrawal syndrome, or heroin taken to relieve or avoid withdrawal symptoms (APA, 2013).

These eleven diagnostic criteria are categorized by severity. The three rankings of severity are mild, moderate, and severe. Mild is the presence of two to three of the diagnostic criteria. Moderate is the presence of four to five of the diagnostic criteria, and severe is the presence of six or more of the criteria (APA, 2013). The diagnosis of heroin use disorder, as well as the severity of the disorder, helps initiate therapy by gauging where the patient currently is and then track progression throughout treatment.

### **Heroin and the Body**

During heroin use there are several biochemical reactions within the body. In the first few hours there is warm flushing of the skin, dry mouth, a heavy feeling in the extremities, possible nausea and/or vomiting, decreased cardiac output, bradycardia, decreased respiratory rate, and drowsiness (Liska, 2009). There are also biochemical reactions in the brain. Once it enters the brain, the heroin converts into morphine and binds to mu-opioid receptors. By binding to these receptor sites, heroine stimulates the release of dopamine, the pleasure neurotransmitter (NIDA, 2014). Heroin's effect on the brain stem is what causes the changes in cardiac and respiratory systems and leads to decreased cardiac output, bradycardia, and a decreased respiratory rate. Heroin can also effect the limbic system of the brain, which regulates emotions (Liska, 2009).

Long term use of heroin includes all of the previously listed short-term effects, in addition to lasting effects such as imbalances in the brain due to an increase in the stimulation of dopamine (Liska, 2009). The decrease or inability to regulate behavior is due to long term dopamine effects on the limbic system. Deterioration of white matter in the brain is another possible lasting effect and can lead to impaired decision making, inability to regulate behavior, and decreased responses to painful situations or stimuli. Other long term effects also include tolerance and dependence (Liska, 2009).

**Withdrawal.** Long term effects of heroin use often lead to withdrawal during times of abstinence. Symptoms of withdrawal can increase in severity depending on the number of hours since heroin was last used (AAC, 2016). At zero to eight hours following abstinence from heroin, no symptoms of withdrawal occur. At eight to twelve hours, uncontrolled yawning, running nose, tearing eyes, and diaphoresis (sweating) occur. At twelve to sixteen hours, withdrawal symptoms include restless sleep and awakening unrefreshed and miserable (AAC, 2016). At sixteen to forty-eight hours following heroin abstinence, a person can experience loss of appetite,

nausea and/or vomiting, diarrhea, irritability, and full body chills. The most significant symptoms of withdrawal occur at forty-eight to seventy-two hours following abstinence from heroin. These severe symptoms include all of the previously stated symptoms as well as muscle twitching, severe sneezing, general body weakness, depression, intestinal spasms, back pain, chills/flushing, spontaneous ejaculation (in men)/organisms (in women), decreased white blood cell count, and acid-base imbalances (Liska, 2009). These symptoms are often extremely unpleasant and can deter people from abstaining from heroin use. Techniques to overcome this barrier will be explained later in more detail.

### **Current Statistics**

Since 2011 the prevalence of heroin use has skyrocketed, which has led to increased rates of overdose, dependence, and death due to heroin use. The Substance Abuse and Mental Health Services Administration (SAMSHA) states that numbers have grown from 5% of persons reporting use within the last 30 days in January of 2011 to over 30% in December of 2014 (SAMSHA, 2015). Those currently affected by heroin use number at roughly 20.5 million people in the United States (SAMSHA, 2015). These numbers show the recent surge of popularity in heroin use.

With the increased rates of heroin use there are also increased rates of heroin-related overdose leading to death. As of 2015, 12,990 of the 52,404 overdose-related deaths in the United States were due to heroin use, which is approximately 24% (SAMSHA, 2015). These statistics show heroin as the second leading cause of overdose, with opioids being the leading cause at 38% of overdoses. However, since 2013 heroin overdoses have been climbing whereas opioid overdoses have begun to decrease (Rollins, 2016). These statistics show that addressing heroin use and overdoses due to heroin use are a new priority. Because of the drastic increases in

popularity and overdose rates of heroin, the response by the Center for Disease Control (CDC) details three different strategies to manage the current heroin epidemic. The three strategies are prevention of persons starting heroin, education on the reversal agent, Naloxone, for heroin overdose, and the reduction of heroin use through access to medication-assisted treatment (MAT) (Rollins, 2016). The CDC's plan to use MAT to initiate treatment for heroin use disorder leads to the need to find which MAT will be the most effective for treatment. An extension of this strategy beyond initiating treatment is needed for it to be effective.

### **Treatment Options for Heroin Use Disorder**

After initiating MAT there are several options available for heroin use disorder. One option is to continue the use of MAT and another option is to utilize cognitive behavioral therapy. This section explains the various types of treatment available for heroin use disorder including the different types of MAT and cognitive behavioral therapy. Each treatment is defined and explained in detail, as well as any associated risks or adverse effects.

### **Harm Reduction**

The symptoms of withdrawal can be unpleasant and often deter people from abstaining from heroin use. Withdrawal can become life-threatening if a person suddenly stops (AAC, 2016). When a person uses an opioid to replace heroin, suppression of withdrawal symptoms occurs. Heroin reacts with the opioid receptors in the brain. By using an opioid or synthetic opioid to replace the heroin, the opioid receptors remain engaged which release the neurotransmitter dopamine. This process prevents the symptoms of withdrawal from appearing. This replacement puts a person on a drug that can be better controlled and closely monitored, which can slowly wean the person off of the illicit drug. This idea of using a less harmful drug to replace the illicit drug is MAT, or harm reduction. As the name suggests, it involves reducing the

harm done to the person until detoxification from heroin or other forms of treatment can be initiated and total abstinence can be achieved.

Harm reduction efforts for heroin detoxification include five main types. These types include methadone maintenance treatment (MMT), buprenorphine, diamorphine, Levo-alpha-acetyl-methadol (LAAM), and heroin-assisted treatment (HAT). These next sections will go into more detail about each one.

**Methadone Maintenance Treatment (MMT).** Methadone is a schedule II controlled substance, which means that a prescription is required from a medical professional for access. Methadone is an opioid agonist so it binds to the opiate receptor site in the central nervous system. Because it binds to the opiate receptor site, it is effective at suppressing symptoms of heroin or opiate withdrawal. Methadone has a half-life of 15-25 hours, meaning the amount of time it takes for half the substance to lose half of its pharmacologic or physiologic effect is 15-25 hours. This long half-life means that methadone only needs to be taken once a day (Deglin, 2017).

Methadone has several adverse side effects when it is used. Common side effects include confusion, sedation, dizziness, euphoria, hallucinations, headache, fatigue, energy loss, blurred vision, hypotension, bradycardia, QT interval prolongation, constipation, nausea, vomiting, urinary retention, sleep disturbances, difficulty sleeping, low sex drive, flushing, sweating, muscle pain, joint pain, physical dependence, psychological dependence, and tolerance. Many of the common side effects such as dizziness, nausea, vomiting, and sleep disturbances subside after a few weeks of use. Possible life-threatening reactions include respiratory depression, suicidal thoughts, and torsades de pointes (Deglin, 2017).

**Buprenorphine.** Buprenorphine is a schedule III controlled substance, which means it also requires a prescription in order to access it. Buprenorphine is an opioid analgesic so it also binds to the opiate receptor site in the central nervous system and causes generalized central nervous system depression. Thus, buprenorphine is able to suppress the withdrawal symptoms of heroin. Buprenorphine has a half-life of two to three hours when administered parenteral and 26 hours when used transdermal. Effects of buprenorphine can last up to seven days when used transdermal. This means a buprenorphine patch is needed only once per week (Deglin, 2017).

Similar to methadone, buprenorphine has numerous adverse side effects. Common side effects include confusion, dysphoria, hallucinations, sedation, dizziness, euphoria, floating feeling, headache, unusual dreams, blurred vision, diplopia, miosis, hyper/hypotension, palpitations, QT interval prolongation, nausea, constipation, dry mouth, ileus, vomiting, urinary retention, sweating, clammy feeling, erythema, pruritis, rash, physical dependence, psychological dependence, and tolerance. Possible life-threatening reactions include respiratory depression and hepatotoxicity (Deglin, 2017).

**Diamorphine.** Diamorphine is a type of synthetic opioid that usually used to manage pain due to cancer, but it is also effective in repressing the heroin withdrawal symptoms. Diamorphine is usually injected, and it is necessary for the injection to be given in a clinic. This medication also has a short half-life/duration which indicates the need for multiple injections in a single day (NIDA, 2014).

Similar to methadone and buprenorphine, diamorphine has several adverse side effects. Common side effects include dizziness, sedation, drowsiness, blurred vision, nausea, vomiting, constipation, dry mouth, sweating, confusion, urinary retention, palpitations, mood changes,

reduction of appetite, rash, and itching. Possible life-threatening reactions include respiratory depression (NIDA, 2014).

**Levo-alpha-acetyl-methadol (LAAM).** LAAM is also a schedule II controlled substance. It is another opioid analgesic, like buprenorphine, which means it binds to the opiate receptor site and suppresses the withdrawal symptoms of heroin. LAAM has a half-life of 6 hours and the effects of this drug can last up to 2-6 days (Liska, 2009).

LAAM has several side effects similar to the other types of MAT. Common side effects include analgesia, sedation, pupillary constriction, nausea, vomiting, tolerance and physical dependence (NIDA, 2014). Possible life-threatening side effects include respiratory depression, significant QT interval prolongations, and severe arrhythmias (Liska, 2009).

**Heroin-Assisted Treatment (HAT).** HAT requires a person to go into a heroin clinic to be injected with specific and decreasing amounts of heroin by trained professionals. This type of treatment was originally set up for people to safely use heroin or other types of illicit drugs and prevent possible complications such as spread of hepatitis B or HIV through the sharing of contaminated needles. This therapy set-up also has the safety measure of reversal agents on scene along with trained professionals in case of possible overdose. This therapy works by helping addicts slowly decrease their heroin use until they can stop completely without any withdrawal symptoms. Adverse side effects are identical to the other harm reduction methods previously mentioned.

### **Cognitive Behavioral Therapy**

Other than using MAT, there is a therapy option that involves talking with a trained professional. The most common talk therapy used for heroin use disorder is cognitive behavioral therapy (CBT) (Van Wormer, 2013). CBT is based on the understanding that maladaptive

thinking can cause and maintain problem behaviors. The strategy behind this therapy is to change the way one thinks about certain situations, which can lead to behavior change. CBT emphasizes mindfulness and acceptance instead of negative thoughts and sensations. CBT helps bring about positivity in replace of negativity, and helps a person focus on their strengths (Van Wormer, 2013).

Cognitive behavioral therapy has four tenets that play a powerful role in the initiation, maintenance, and recovery of a patient with heroin use disorder. The first of these tenets is reinforcement, or the process of shaping behavior by controlling the consequences of the behavior. Response to either positive or negative stimuli is followed by the response being strengthened or weakened respectively. A person dependent on heroin uses it to feel relief or euphoria. Euphoria feels good, which is positive reinforcement, making the person want to use the drug again to achieve this same feeling. The use of CBT reinforcement helps a person find healthier alternatives to give receive this positive reinforcement (Van Wormer, 2013).

The second tenet is modeling, which is when a person learns through observing what others do and seeing the costs or benefits. Setting an example for the client or having a previous client as a mentor are a few ways to effectively use modeling. The third tenet is conditioned responding, which is when a person is in the situation or environment which made them want to use heroin. Recovery strategies to counteract these urges involve identifying possible triggers and coming up with alternative strategies to resist them (Van Wormer, 2013).

The final tenet is cognitive factors. Cognitive factors include the belief that one cannot cope with a particular situation without using heroin. The person lacks a belief in his or her own self-efficacy or power to create change. The best way for cognitive factors to have a positive influence on CBT is to help instill positive self-efficacy. This positive self-efficacy is the part of



the therapy that relies on focusing on a person's strengths rather than their weaknesses (Van Wormer, 2013).

### **Discussion of Treatment Options**

Now that the various treatment options have been explained, each will be evaluated to determine their effectiveness in treating heroin use disorder through analysis of previous research. The most common measures of effectiveness in this research are retention rates, patient satisfaction in treatment, and the treatment of psychological factors as well as physiological ones.

#### **Harm Reduction**

Harm reduction particularly heroin-assisted treatment, can be a controversial form of treatment. The next few sections will evaluate the effectiveness of each different types of harm reduction explained above. This section will highlight how these treatments are effective as well as some of their short-comings.

**Methadone Maintenance Treatment (MMT).** MMT is the current gold standard for heroin use disorder treatment and the most frequently used MAT. However, methadone treatment is questionable with regards to how effective is is for treating heroin use when patients replace their dependency on heroin with dependency on a different drug, although retention rates as described by several studies is fairly high. The meta-analysis conducted by Bell (2014) on previous research studies evaluates methadone and several other medications as treatment options. Findings from this study show that methadone has a long-term retention rate, reduces the risk of death, and subjectively improves quality of life. Methadone also has a stronger appeal to heroin users than other drug-free approaches. However, methadone has been problematic

because of the “one-drug-fits-all” approach. Bell’s research shows that for some people, methadone is not as effective as heroin-assisted treatment. Many participants cycle in and out of treatment, but Bell’s research shows that methadone is effective at replacing heroin, which is the goal of harm reduction.

A similar meta-analysis of previous research carried out by Gracia-Portilla, et al. (2014) confirmed some findings found in the study done by Bell. One of the supported findings is methadone’s high retention rates. Studies evaluated by Gracia-Portilla showed methadone has retention rates ranging from 84% at twelve months, and 70% at 18 month, 2 year, and 6 year follow-ups. Gracia-Portilla also found in several studies that there is a significant reduction in the use of the illicit drugs. This information is identified through self-reporting and/or urine drug screens and shows that methadone is effective at reducing heroin use. Garcia-Portilla’s meta-analysis shows a significant reduction in criminal activity through studies of incarcerated populations, the probability of arrest, illegally acquired incomes, and the frequency of crimes (Gracia-Portilla, 2014). Garcia-Portilla’s study shows that methadone can be effective at making overall improvements in a person’s life, not just in reducing heroin use.

A treatment barrier lies in the difficulty of a patient setting aside their personal life, work, and family in order to enter rehabilitation for treatment. In the case of this treatment barrier, out-patient treatment may be more effective. A study conducted by Carrieri et al. (2014) looked at the use of methadone in a primary care setting for treatment of heroin use disorder. This research agrees with Bell (2014) and Garcia-Portilla’s (2014) conclusions that methadone treatment has high retention rates. This study included a control group and an experimental group totaling 221 people: 155 in primary care and 66 in specialized care. The study evaluated the retention rates and abstinence rates, from illicit drugs, over a 12 month period following the start of treatment to

compare how effective methadone can be for outpatients in addition to inpatients. The primary outcome is that abstinence from illicit drug use at 12 months was 83% for those in primary care, 50% for those in specialized care, an overall 73% retention rate. Outcomes from this study show primary care is an effective way to retain participants and is more effective than in an inpatient setting. Abstinence from illicit drug use for primary and specialized care is 55% and 33%, respectively. Carrieri's study also shows that methadone is somewhat effective in reducing heroin use rate for those in treatment. Carrieri's study supports methadone treatment as a feasible option for an out-patient care setting as well as for an inpatient care setting (Carrieri, 2014).

A study done by Roux et al. (2012) evaluates the effectiveness of in-patient versus out-patient therapy. Roux's study supports Carrieri's (2014) findings. Roux's study included 195 participants, split between in-patient and out-patient groups to obtain retention rates and therefore gauge effectiveness. The results of this study showed no significant difference between inpatient and outpatient groups. However, the article does note that when using MMT, the possibility of an overdose is significantly higher at the initiation of therapy and close observation is the recommended when starting therapy. Even with the need for initial close observation, outpatient therapy is a viable option. This consideration is important for people who cannot step away from their lives to enter inpatient treatment. Outpatient therapy may also be effective for people who have relapse tendencies following inpatient treatment due to abstinence difficulties when no longer an inpatient.

Shifting focus from retention rates and inpatient versus outpatient effectiveness, Trujols (2013) conducted a study to look at patient valued assessment on the outcome of MMT. Trujols surveyed patient satisfaction from both the provider as well as the patient's perspective. Trujols assessed how satisfied both provider and patient were with the treatment as well as how provider

felt the patient was satisfied with treatment. Trujols found that clinicians reported patient satisfaction outcomes higher than the patients reported satisfaction outcomes. This discrepancy also appears in studies conducted by Pulford et al. (2009) and De Maeyer et al. (2009) as quoted in Trujols findings. Whether this satisfaction was due to the clinician initiating the therapy or satisfaction due to the therapy option available to the patient was not specified, but this finding does show a need for further research in this area. Regardless, these results show that patients are not necessarily satisfied with their treatment. When evaluating by patient satisfaction, methadone is an effective form of treatment.

The use of functional magnetic resonance imaging (fMRI) on MMT patients is a relatively new area of study and lacks the amount of research compared to fMRI studies on heroin or other illicit drug users. FMRI is currently the mainstay of neuroimaging in cognitive neuroscience and is the most informative tool available for gaining insight into brain function. A study carried out by Wang et al. (2011) evaluates how addictive drugs, such as nicotine, alcohol, cocaine, marijuana, and heroin have cue-reactivity paradigms, which stimulates the dynamic neural activations in the prefrontal cortex. On similar terms, when a person who previously suffered from these various addictions were showed images associated with the use of their drug of choice, there is significant activity in various parts of their brain that appears on the fMRI. A study of 14 men, all formerly suffering from heroin use disorder and whom currently use MMT looked at whether specific areas of their brain still react in the fMRI. Each participant was shown 24 images of heroin related stimuli which included injection, preparation, or paraphernalia and 24 images of household items. Each of the 48 images were shown for 2 seconds and the fMRI was observed. Following this, patients were asked to rate their craving to use heroin on a scale of 0 (not at all) to 10 (extremely high). Results of the fMRIs confirmed activation of PFC,

mesocorticolimbic, and visuospatial-attention regions in response to visual drug-related stimuli in former heroin users. These findings signify that even though participants report no changes in craving for using heroin, these parts of the brain are still activated. However, subjective craving scores before and after the session did not statistically differ in wanting to use heroin. However, this study by Wang does show that the brain's memory for heroin is still present regardless of the patient's report of no cravings. This study suggests that although methadone masks the wish to use heroin, it does not cure the brain's memory and response to triggers of previous heroin use (Wang, 2011).

Each of these sources confirms that methadone has a high retention rate and decreases illicit drug use and criminal behavior. Furthermore, methadone is proven to greatly suppress heroin withdrawal symptoms. This suppression could be the cause for the high retention rate. Methadone also works well as an outpatient therapy option, which is best for patients who need to present at work and with their families. Even with all of these benefits, there are still risks associated with this treatment. As described in the previous section, methadone has numerous adverse side effects and potentially life-threatening effects as well.

**Buprenorphine.** Buprenorphine is less popular and less widely used when compared to methadone. According to meta-analysis research done by Bell (2014), buprenorphine is less effective at suppressing withdrawal symptoms and requires higher doses to be as effective as smaller doses of methadone. Since the buprenorphine does a poor job of suppressing withdrawal, it gives less positive reinforcement, which leads to lower retention rates as participants are not highly motivated to keep up with treatment. Bell's analysis did not state if these studies adjusted buprenorphine doses to a higher amount in order to evaluate if those higher doses gave more positive reinforcement. Furthermore, Bell's research found a lower retention rate of patients

compared to methadone and many people switched from buprenorphine to methadone in order to better suppress withdrawal symptoms. However, Bell did find that buprenorphine does not have significant risks from cycling the drug when going in and out of treatment when compared to methadone. Further research is needed to determine the effectiveness of short-term relapse prevention in patients during times of high risk. Buprenorphine could be effective for the maintenance of abstinence (Bell, 2014).

Garcia-Portilla et al.'s (2014) meta-analysis research supports Bell's findings that smaller numbers of patients with short durations of treatment use buprenorphine. This study shows that buprenorphine is not as popular or as well-known as methadone. Effectiveness, or lack thereof, could be contributed to buprenorphine being relatively unknown. Garcia-Portilla found various results for retention rates among buprenorphine use. Various studies show that rates range from 60% to almost 90%. Due to contradictory information between Bell and Garcia-Portilla, it is difficult to draw conclusions about whether methadone or buprenorphine is more effective for reducing heroin use in terms of retention rates. However, Garcia-Portilla found greater significant reduction in percentage of opioid and heroin in negative urine tests when compared to those using methadone. This information shows that buprenorphine can be more effective than methadone at reducing heroin use and more effective at weaning down the use of opioids needed to suppress withdrawal symptoms. However, no clear conclusion can be drawn about the cause for less opioid or heroin that is found in urine tests (Garcia-Portilla, 2014).

A meta-analysis study done by Fareed et al. (2010) compiled previous studies and evaluated the effectiveness of buprenorphine as a treatment for heroin use disorder. One article that Fareed presented, research done by Fudala et al. found that buprenorphine is safe and helpful in the reduction of heroin cravings in heroin-dependent persons. No details were given on dosage

that was used to show effectiveness of treatment, however. Fudala's results were confirmed by a study done by Greenwald et al., Comer et al., and Ling et al. which showed that high-dose buprenorphine attenuated drug-seeking behavior and self-reported heroin craving. This study showed that buprenorphine can be effective form of treatment in terms of suppressing withdrawal symptoms (Fareed, 2010).

While different sources have slightly varied results and information about the effectiveness of buprenorphine, the vast majority of sources conclude that with higher doses, buprenorphine is effective in suppressing symptoms of withdrawal. Buprenorphine is also effective if a person is cycling in and out of treatment as it does not cause many serious adverse side effects. However, as pointed out in the research done by Fareed et al. (2010), there is a need for more direct research to compare the effectiveness of methadone and buprenorphine.

**Diamorphine.** Diamorphine is a much less commonly used type of MAT. Research compiled by Bell (2014) shows that diamorphine is often used for people who have "failed" methadone treatment. Bell found that the two hypotheses of why diamorphine may work for those who methadone treatment did not work is some tolerate methadone poorly. As mentioned previously, methadone can have numerous side effects and some patients do not tolerate these effects well. A person may not have significant side effects present when using diamorphine compared to when they are using methadone. The other hypothesis is that some individuals seek a more reinforcing treatment plan than methadone. Diamorphine requires injections twice a day to equal one oral dose of methadone. These injections are required to be administered by trained professionals, which requires a patient to attend a clinic multiple times per day. The fact that diamorphine requires injections twice a day can be a deterrent for some patients because of the

time and travel commitment (Bell, 2014). This research shows that determining effectiveness of diamorphine depends largely on the patient and their specific needs surrounding treatment.

Diamorphine does not have the high retention rate that other treatment options do. A study, quoted by Bell, of 2000 patients showed that 70% of patients left diamorphine treatment by 6 years meaning it has only a 30% retention rate. Of the 70% of patients that left diamorphine treatment, 60% transferred to methadone treatment and the other 40% switched to drug-free treatment. This study shows that diamorphine treatment can serve as a transitional step in treatment for those who cannot originally tolerate methadone (Bell, 2014). Perhaps diamorphine is most effective during the initial stage of treatment until a patient can withstand the side effects associated with methadone. Additional research is necessary to draw more definitive conclusions about the effectiveness of diamorphine.

**Levo-alpha-acetyl-methadol (LAAM).** Garcia-Portilla et al. (2014) performed a meta-analysis study evaluating the effectiveness of LAAM as a treatment option for heroin use disorder. Results from this meta-analysis showed that LAAM has a longer active half-life, which gives patients a longer interval between needing a secondary dose. The longer half-life would theoretically suggest a higher retention rate than methadone. However, studies have shown a small treatment difference favoring methadone (Garcia-Portilla, 2014). The study did not specify the reasons for this difference.

As mentioned in a previous section, LAAM has some possible severe adverse cardiovascular reactions such as significant QT interval prolongation and severe arrhythmias. Due to the possibility of severe adverse reactions, many physicians prefer a MAT with less significant adverse reactions such as methadone or buprenorphine. Any persons with heroin use disorder as well as cardiac issues are not recommended for the use of LAAM. The relative lack



of knowledge about LAAM as well as its low retention rates and severe adverse reactions make LAAM not very effective as a form of treatment for heroin use disorder despite its long half-life.

**Heroin-Assisted Treatment (HAT).** In Garcia-Portilla et al.'s (2014) meta-analysis, they evaluate the use of HAT as a treatment for heroin use disorder. Studies show that retention rates are higher among HAT when compared to methadone. Studies showed that rates at 12 months are 90.4% and 55.7% at 4 years. Another benefit of HAT is that assisting with injection of heroin use limits the use of street drugs, reduces illegal activities, possibly improves health, and reduces mortality (Garcia-Portilla, 2014). However, HAT is an extremely controversial form of treatment, and some people view this form of harm reduction treatment as one that makes illicit drug use seem acceptable by the government. Because of negative views about this form of treatment, it often leads to a stigma about the treatment and those that use it. This stigma can lead to negative reinforcement, which makes the treatment unsuccessful (Van Wormer, 2013). Overall, effectiveness of this treatment is difficult to determine due both to the lack of research currently on the topic and the fact that the person is still using heroin, which makes an assessment of decreased heroin use an impossible point for evaluation.

### **Cognitive Behavioral Therapy**

Another type of treatment option for heroin use disorder is cognitive behavioral therapy. CBT is the most widely used form of talk therapy and shown to be an effective form of treatment. A research study by Chen et al. (2015) evaluated the effectiveness of therapeutic treatment compared to MMT. The study consisted of 705 participants, 553 in MMT and 152 in therapeutic treatment. This study compared effectiveness by evaluating incidence of heroin use within the last 30 days and major depressive disorder, dysthymic disorder, and suicide attempts throughout the lifetime. Results of this study show an increase in the amount of heroin use within

the last 30 day among those using MMT compared to those going through therapy. Chen et al.'s study showed that MMT has a statistically significant higher prevalence of major depressive disorder compared to that of therapeutic communities when measured one month after initiation of treatment. This study shows that therapy treatment is effective in decreasing rates of depression among participants when compared to MMT. However, the study yielded no difference between occurrence of lifetime prevalence of suicide attempts and dysthymic disorder. Results from Chen et al. study contributes to the idea that CBT could be more effective in treating certain psychological aspects associated with heroin use disorder when compared to MMT (Chen, 2015).

However, Chen's study did point out that in a review of previous studies as well as their own, heroin users that used therapeutic treatment compared to MMT had a significantly greater number of previous treatments and a longer history of heroin use than those in MMT. This study presents no further information to why this occurs. Results suggest that MMT is more effective at initiating and maintaining a person in treatment and preventing relapse of heroin use during treatment.

### **Combination of Therapies**

Following evaluation of the two different categories of treatment, harm reduction and talk therapy (specifically CBT), each of these therapies were found to be effective in different ways and neither is very effective in an entirely holistic way. Perhaps there is a possibility of combining multiple types of therapies simultaneously to generate a more holistic and effective treatment.

A research study done by Pan et al. (2015) evaluated the efficacy of cognitive behavioral therapy in conjunction with MMT versus just MMT, in terms of retention rates and opiate-

negative urine tests. This study consisted of 240 patients, 120 in CBT with MMT and 120 in just MMT for 26 weeks. Results concluded that the group with CBT in combination of MMT had higher proportions of opiate-negative urine tests at both 12 and 26 weeks. However, there was no significant variance in the retention rate between just MMT and CBT with MMT. This shows that CBT in conjunction with MMT can be effective in decreasing the need for MMT and opiate dependence compared to just MMT. However, this study did not show any difference in retention rates to determine effectiveness.

Results from Pan et al.'s (2015) study were supported in a study conducted by Schwartz et al. (2011) that looked at effective use of MMT when combined with CBT (standard therapy), versus only MMT (interim therapy), versus only CBT (restored therapy). A randomized controlled trial was conducted by comparing these treatment options at 4 and 12 months. This study included 230 participants; 99 in interim, 104 in standard, and 27 in restored therapy. The outcomes of this study compared each of the different types of therapy at baseline, 4 months, and 12 months. Results included a comparison of retention rates, average number of days of heroin use within the last 30 days, and opiate-positive tests in original treatment programs. Results of this study showed that the MMT only treatment was 3.5 times more likely to have people enrolled in treatment with a 91.9% retention rate at 4 months and a 60.6% retention rate at 12 months. The MMT only treatment also had a decrease in average heroin use within the last 30 days from 29.2 to 4.4 times at 12 months. MMT only treatment had a positive opiate urine test of 97% at baseline which dropped to 46% at 12 months. However, the article did note that the average methadone dose for the interim group was significantly greater at both 4 and 12 month evaluations compared to that of the other two groups. MMT in combination had the results of retention rate of 80.8% at 4 months and 54.8% at 12 months. These rates are only slightly lower

than that of MMT only. Combination therapies also had decreased average heroin use with in last 30 days from 29.1 to 6.2 at 12 months, and positive opiate urine tests of 98% at baseline to 48% at 12 months. Lastly, the results for the CBT only treatment had retention rates of 88.9% at 4 months and 37.0% at 12 months, decreased average heroin use within the last 30 days from 29.1 to 6.9 at 12 months, and a positive opiate urine test of 96% at baseline to 0.51% at 12 months (Schwartz, 2011).

Schwartz et al.'s study showed that only MMT and MMT with therapy have the highest retention rates, which is supported by other studies. Restored therapy had the lowest retention rate at 37%, showing that it was not an effective therapy compared to standard and interim when evaluating retention rates. Each type of therapy had a significant decline in reported heroin use within the last 30 days, showing that each of the treatment modalities is effective in decreasing heroin use. The last focus of effectiveness, negative urine tests for opioids, shows that therapy with only emergency MMT has the lowest percentage of people testing positive for opioids. No significant difference in the amount of opioid negative urine tests shows that both approaches are equally effective at decreasing the need for methadone or other form of opioid treatment for maintaining abstinence from heroin (Schwartz, 2011).

Overall, Schwartz et al.'s study shows only slight improvements in statistics for comparing effectiveness for the combination of therapies compared to only using MMT. However, these studies were conducted over a 12 month period, so looking at long-term maintenance or treatment is not possible. Further research in this area would be beneficial because more statistical analysis comparing which specific types of talk therapies used in standard treatment are most effective to combine MMT. Further statistics about standard dosing

of MMT between each of the different categories is also needed to compare trends (Schwartz, 2011).

### **Conclusion**

Overall, there are several types of therapy that can be effectively used to treat heroin use disorder. Amongst harm reduction therapy the main types are methadone, buprenorphine, diamorphine, LAAM, and HAT. According to current research, the most effective approach to harm reduction therapy is replacing heroin with methadone, closely followed by buprenorphine. Because of conflicting results in existing research, it is difficult to determine if buprenorphine is more effective than methadone, but what does exist shows that methadone is the more well-known form of treatment. Methadone is effective in terms of retention rates, for inpatient and outpatient therapy, exceptional at suppressing cravings to use heroin, and helpful to decrease heroin use and criminal activity. However, more research about how patient satisfaction is perceived for methadone and buprenorphine treatments is needed.

The other main form of treatment for heroin use disorder, CBT, is marginally effective. CBT is a type of talk therapy and it decreases prevalence of depression in those who use heroin when compared to those patients in just MMT. However, CBT does not have the retention rate MMT does and research has shown many relapses associated with the use of only talk therapy as treatment. However, in research comparing MMT and CBT with combination therapies, the effectiveness increases. Research shows that retention rates are similar between combination therapies and MMT only, as well as having a decrease in the amount of heroin use within the last 30 days. A combination of therapies also shows a decrease in dosage of methadone needed compared to that of MMT only treatment, which shows effectiveness at decreasing methadone usage as well as heroin usage in the combination of this type of therapy.

To address the current resurgence of heroin use across the United States, there is a need for effective treatment. While there are treatment barriers and more research on long term studies is needed, the most effective form of treatment for those with heroin use disorder is following the initiation of treatment with either methadone or buprenorphine, and combining these therapies with CBT.

### **Appendix A: Thesis Proposal**

#### **An Evaluation of the Effectiveness of Methadone as a Treatment for Heroin Use Disorder**

##### **Background**

Heroin is an extremely addictive illicit drug that currently affects 1.3% of the United States which is roughly 4.15 million people (NIDA, 2014). Numbers have grown from 5% of person reporting use within the last 30 days in January of 2011 to over 30% in December of 2014 (NIDA, 2014) showing a current resurgent of popularity. Symptoms of withdrawal when attempting to detox and recover from this addiction include: nausea, abdominal pain, sweating, shaking, nervousness, agitation, depression, muscle spasms, and cravings for drugs. These symptoms can be extremely unpleasant, which often deter people suffering from heroin use disorders from detoxing and abstaining from heroin use. Withdrawal from heroin can also be considered life-threatening and ceasing heroin use cold-turkey can be deadly, which is why the use of a synthetic narcotic or opioid is usually used in order to slowly wean a person off their physical dependence. (American Addiction Centers, 2016). The most common opioid that is used for this is methadone which became a legal form of treatment in the United States in 1947 (National Drug, 2006). The use of this opiate to reduce harmful effects of another drug, such as using methadone in substitution of heroin, is referred to as harm reduction (Harm Reduction, 2015).

In theory, the methadone maintenance treatment (MMT) is to slowly take the withdrawal of heroin from a condition of extreme discomfort resulting and bring them to a more bearable state. Slowly the amounts of methadone needed to match the high or counter act the withdrawal caused by heroin is decreased and they are weaned off the methadone resulting in complete abstinence from any drug (Bell, 2014). However, frequently those who use methadone to recover

from heroin use disorder replace one addiction with another addiction as they do not wean themselves off the methadone.

### **Purpose and Research Question**

Methadone is a harm reduction effort to reduce heroin use by replacing it with an opioid. Opiates action in the brain cause them to become addictive as well which can lead to a physical dependence. Harm reduction efforts focus on treating the physiological aspects on the body from heroin use instead of the psychological aspects that originally lead to the addiction in the first place. When you focus only on the physiological aspects of addiction and ignore the psychological, you only end up trading one addiction for another. This leads to the question: is methadone an effective form of treatment for heroin addiction.

### **Literature Review**

Research by Bell (2014) was a meta-analysis of effectiveness of methadone, diamorphine, and buprenorphine, three forms of opioids used in the area of harm reduction to help treat heroin use disorder. In the article, Bell discussed how methadone shows a lot of success in number of clients who participate and stay in treatment using methadone, also called retention rate. The limitations to research done about methadone is that there is no definitive to gauging success of the treatment (Bell, 2014). The evaluation of diamorphine includes benefits being there are clear objectives, adequate doses and monitoring response for evaluation of this form of treatment whereas methadone does not. However, diamorphine does not have the retention rate that methadone has (Bell, 2014). The last opioid drug evaluated in this article was buprenorphine. Buprenorphine has the benefits of decreased adverse reactions in the body as well as low mortality rate compared to other opioids used for harm reduction. However,



buprenorphine is less effective at suppressing heroin withdrawal symptoms compared to other opioids used for treatment options (Bell, 2014).

Garcia-Portilla et al. (2014) completed a meta-analysis of previous multifactorial experimental studies on the long term outcomes of different opioids used in treatment of heroin addiction including methadone, buprenorphine/naloxone, heroin-assisted treatment (HAT), and Levo-alpha-acetyl-methadol (LAAM). This analysis is similar to the research done by Bell and looks at the benefits and limitations of each of the types of opioid treatments. Garcia-Portilla's research into methadone and buprenorphine yielded similar results to those of Bell. Garcia-Portilla found buprenorphine had high retention rates in patients and clients had decreased adverse reactions due to use of buprenorphine (Garcia-Portilla, 2014). Garcia-Portilla broadens analysis done by Bell by also looking at HAT in that physiological dependence is greatly decreased, but this form of treatment has a higher relative risk for illicit drug use during treatment. LAAM was developed with a longer half-life of the opioid hoping that it would increase the retention rate of patients. Studies evaluated by Garcia-Portilla yielded results that LAAM has similar retention rates to that of methadone (Garcia-Portilla, 2014).

Research by Trujols et al. (2013) evaluates the importance of patient-valued and patient-centered care for those in MMT. The results of the study show a paradox of desynchrony indicating a lack of correlation between the different perspectives in outcome assessments. In other words, the study showed that patients were reporting a low level of satisfaction with the care that they were receiving. This was completely different from what the nurses/physicians reporting, which was a high level of satisfaction in treatment (Trujols, 2013).

The study conducted by Carrieri et al. (2014) looked at the use of methadone in a primary care setting for treatment of heroin use disorder. The study included a control group and an

experimental group totaling 221 people involved in the study. The study evaluated the retention rates, abstinence [from illicit drugs] rates, and adverse effects of those opioids for the experimental group participates over 12 months following initially entering treatment. The primary outcome was that abstinence from illicit drugs at 12 months was 83% for those that stayed in treatment. There were several adverse effects experienced by participants during the study including suicide attempts, fatigue/energy loss, difficulty sleeping, constipation, shortness of breath, muscle pain, tingling, poor appetite, wheezing, decreased sex drive, stomach pain, headaches, joint pain, weight loss, and blackouts (Carrieri, 2014). This research study agrees with Bell (2014) and Garcia-Portilla (2014) conclusions that methadone has high retention rates in patients, and has numerous adverse effects of methadone.

The study done by Roux et al. (2012) compares effectiveness of inpatient and outpatient treatment in terms of retention rates, quality of life, and satisfaction rates. The study included a study of 195 participants between the ages of 18 to 70 who met the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition (DSM-V) diagnosis of heroin use disorder. The study resulted with a 15% retention rate between both of the two study groups and differential success rates between in-patient and out-patient were inconclusive (Roux, 2012). Roux discussed how physicians and administrators of the study preferred to prescribe and administer the methadone to patients who were under much closer surveillance (in-patient care) due to risk for adverse effects from medication (Roux, 2012). This discussion maybe a possibility for improvement of harm reduction implementation.

Research done by Pan et al. (2015) looked at the outcome results from treatment for those undergoing cognitive behavioral therapy (CBT) in conjunction with MMT. They reviewed the rates of patients staying in therapy and reduction in rates of opiates and illicit drug use. The

initial results concluded with higher proportions of patients with negative urine tests for opiates within the first 12-26 weeks, and the use of CBT was effective in reducing opiate use and relapse. No significant improvement in retention rates were noted by combining MMT with CBT. (Pan, 2015). This research helps to evaluate how to simultaneously treat the psychological and physiological aspects of addiction to evaluate effectiveness of treatment of heroin use.

### **Methods**

The method of research that I will use is a synthesis of literature of various sources to analyze which form of treatment seems to be the best holistic treatment option for those with heroin use disorder. I will use information from various scholarly databases including CINHALL, Academic Search Premier, JSTOR, Cochrane, and PubMed to gather information from various studies done. These databases include journals about medical, biological, and psychological research that will be the most beneficial to my thesis. Key words that I will include are: methadone; heroin treatment; harm reduction, methadone maintenance treatment, psychological dependence, and holistic treatment.

I will examine primarily peer-reviewed journal articles written within the last 5 years. I will look at both meta-analysis articles relating to forms of treatment as well as experimental research studies done on people who experience heroin use disorder. I will include possible biases and limitations of the research done in each article to limit potential sources of error in my findings. Government supported websites that include information about various treatments and studies done will also be used to gather basic and background information about various forms of treatment. These websites can also give me additional perspectives, other than purely medical reasons, into the various forms of treatment options.

Once I gather information and articles, I will list articles in a Microsoft Excel Spreadsheet according to categories for my thesis that includes: study design, objective, author(s) and year, possible biases and limitations, number of subjects, sampling, setting, measures, and statistics, and results from for each article. I plan to review the information and evaluate what the evidence is for each article by category, identify the type of therapy and compare and contrast by category. I will be considering in terms of holistic healing, such as resolution of underlying causes leading to addiction, decreasing to ceasing forms of substance abuse or other addictions, and retention rates.

### **Expected Results and Outcomes**

Through my research I expect to find information on retention rate for abstinence of heroin, the long term effects and addiction rates to methadone. This will help me weigh the benefits of using methadone as a primary treatment option or identify other more effective treatment options.

### **Timeline:**

Task	Sept. 2016	Oct. 2016	Nov. 2016	Dec. 2016	Jan. 2017	Feb. 2017	March 2017	April 2017	May 2017
Collect Data/Research									
Analyze Information									
Writing									
Edit									
Finalize									
Submit									
Revision (if necessary)									

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- intervention trial. *BMC Public Health*, 12(1), 488-495. doi:10.1186/1471-2458-12-488.
- Trujols, J., Portella, M. J., Iraurgi, I., Campins, M. J., Siñol, N., & Cobos, J. L. (2013). Patient-reported outcome measures: Are they patient-generated, patient-centred or patient-valued?. *Journal Of Mental Health*, 22(6), 555-562. doi:10.3109/09638237.2012.734653.

### **Appendix B: Annotated Bibliography**

American Addiction Center (2016). Heroin withdrawal timeline, symptoms, and treatment.

Retrieved November 7, 2016, from: <http://americanaddictioncenters.org/withdrawal-timelines-treatments/heroin/>.

This website is supported by the American Addiction Center whose goal is to provide information to the public about addiction and available treatment options. The specific parts of the website that I focus on are the sections on heroin withdrawal symptoms and the sections that give a brief introduction to methadone maintenance treatment (MMT). The website explains the mild symptoms, moderate symptoms, and severe symptoms of withdrawal. I use this website to help explain the withdrawal symptoms associated with heroin use disorder. This background will help the reader understand how medication assisted treatment (MAT) can be beneficial. This information will strengthen my argument by provide the base that I will build my argument on. This website was a helpful place to start before expanding my research and is a government funded/ supported site so is generally nonbiased. There is no financial or other kind of benefit.

American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders, 5<sup>th</sup> edition. American Psychiatric Association: Arlington, VA.

This book is the diagnostic manual for mental disorders and gives definitions for defining the various mental disorders. I will use this book to define what exactly heroin use disorder is, which will give the readers a good definition of what exactly heroin use disorder is and how it is diagnosed. In order for the reader to understand the treatment needed for this disorder, they will need to first know what the disease is. This is the best source for defining the disorder. This book is supported and written by the American

Psychiatric Association meaning it is fully funded and supported. This book is unbiased as its purpose is to give information and explain the various mental disorders.

Bell, J. (2014). Pharmacological maintenance treatments of opiate addictions. *British Journal Clinical Pharmacology*. 77(2). doi:10.1111/bcp.12051.

This article is a meta-analysis study of several types of medication assisted treatment (MAT) options including methadone, buprenorphine, and diamorphine. The article gives a brief synopsis of what each of the different medications are, a brief history of these medications, and a synopsis of research previously done to evaluate each of these MATs. This article, among a few others, will help me evaluate the benefits and drawbacks of the various types of medication used in harm reduction. I can use it to strengthen my argument about which of the MATs is most effective to treat heroin use disorder. It will also provide information to readers about these medications from other's research, which will build my argument. Initially, I found it helpful to outline my own thesis as the study was set up similar to how I wanted to set up my own research. Possible bias in this article includes receiving funding support from a pharmaceutical company within the previous three years as self-reported.

Carrieri, P. M., Michel, L., Lions, C., Cohen, J., Vray, M., Mora, M., & ... null, n. (2014).

Methadone induction in primary care for opioid dependence: A pragmatic randomized trial (ANRS Methaville). *PLoS ONE*, 9(11), 1-10. doi:10.1371/journal.pone.0112328.

These authors of this article performed a multicenter trial study on the effectiveness of methadone treatment between primary care and specialized care centers. The goal of this study was to determine if methadone can be effective in a primary care setting as a effectively as specialized care center. The trial was of 221 clients, 155 in primary care



settings and 66 in specialized care centers over a 12 month period. Effectiveness was evaluated by abstinence during follow up, engagement in treatment, retention rates, and satisfaction with treatment. Results of the study were that drug abstinence included 55% in primary clinics and 33% of those in specialized care. Satisfaction in treatment was significantly higher in primary care setting compared to specialized care. Retention rates were similar and had no statistical significant difference between the two settings. The authors conclude that methadone was effective in primary care demonstrated by feasibility and acceptability to both physicians and patients. This research is helpful for my thesis because of the comparison of methadone is effective as outpatient in a primary care facility as well as a specialized care facility. This helps build a case for methadone as being a valid treatment option for outpatients and inpatients. These results makes methadone beneficial for all types of patients, regardless of their life's demands.

Chen, V.C.H., Wu, M.H., Lin, T.Y., Ho, Y.F., Wang, H.Y., & Gossop, M. (2015). Comparison of soci-demographic characteristics, substance, and depression among male heroin users attending therapeutic community and methadone maintenance treatment program in natou, taiwan. *Substance Abuse Treatment, Prevention, and Policy*. 10(41). doi:10.1186/s13011-0150037-y.

A study in Taiwan was conducted to compare the difference between therapeutic communities and methadone maintenance treatment (MMT) for treating heroin use disorder. This study compared the effectiveness of MMT through evaluating incidents of heroin use within the last 30 days, incidents of major depressive disorder, incidents of dysthymic disorder, and incidents of suicide attempts throughout the lifetime. Results of the study showed that MMT had statistically significant higher prevalence of major

depressive disorder compared to that of therapeutic communities when evaluated one month after initiating of treatment. However, the study yielded no difference between occurrence of lifetime prevalence of suicide attempts and dysthymic disorders. Results also noted an increase in the amount of heroin use within the last 30 day among those using MMT when compared to those going through cognitive- behavioral therapy. This article will help me evaluate cognitive behavior therapy when comparing therapy to the use of MMT. It will strengthen my position that therapy can improve quality of life in terms of decreasing incidence of depression. This research also shows that cognitive behavioral therapy can help decrease heroin use effectively.

Deglin, J. H., Mansell, H. G., Sanoski, C.A., & Vallerand, A.H. (2017). *Davis's Drug Guide for Nurses, 15th edition*. Retrieved from: <http://nursing.unboundmedicine.com/nursingcentral>.

This resource includes lots of background information about various types of medications used in medication assisted treatment (MAT). The drug guide includes information about what category the drug is in, what it is used for, how the drug works, time/action profile, possible drug-drug interactions, adverse/side effects, and possible contraindications or precautions when using the drug. This source is beneficial to provide more information about the different medications used for harm reduction, specifically methadone and buprenorphine. This will help me evaluate effectiveness through longer half-with the least drawbacks associated with them. This source is published as a resource for nurses to learn and reference medications making it a less biased source.

Fareed, A., Vayalapalli, S., Casarella, J., Amar, R., & Drexler, K. (2010). Heroin anticraving

medications: A systematic review. *The American Journal of Drug and Alcohol Abuse*. 36 (p. 332-341). doi: 10.3109/00952990.2010.505991.

This study was a meta-analysis study of previous research with the objective of exploring medication options that may curb heroin anticraving properties. Previous studies include randomized, controlled, as well as double-blind clinical trials, and nonrandomized and observational studies. This article evaluates prior studies about buprenorphine, haloperidol, memantine, naltrexone, probuphine, tetrodoxin, and rapamycin. I rely on the portion of this article that evaluates buprenorphine. I will use this article to look at the effectiveness of buprenorphine to treat heroin use disorder. Since this article looks specifically at buprenorphine instead of methadone, it is a good source for drawing more information specifically on buprenorphine. A need for a focused research on comparing methadone to buprenorphine is brought up in this article, which will be helpful for my conclusion section of my thesis because that is where I discuss the need for further research. The declaration of interest statement in the article states that the authors have no conflicts of interest, and are responsible for the content and writing of this article which shows that there is no issue of bias in the results of this article.

Garcia-Portilla, M.P., Bobes-Bascaran, M.T., Saiz, P.A., & Bobes, J. (2014). Long term outcomes of pharmacological treatments for opioid dependence: Does methadone still lead the pack? *British Journal of Clinical Pharmacology*. 77(2). doi:10.1111/bcp.12031.

The aim of this article is to update and summarize current scientific knowledge about long term outcomes of using medication assisted treatment (MAT) to treat heroin use disorder and determine if methadone is still the best option. The treatment options evaluated are methadone, buprenorphine, heroin-assisted treatment (HAT), and levo-

alpha-acetyl-methadol (LAAM). Similar to several other sources, this article is a meta-analysis of other research compiled into one document. The evaluations of treatment sections for methadone, buprenorphine, HAT, and LAAM by exploring the benefits and drawbacks of these types of MAT options will help me better evaluate treatment options. This article also directed me to other MATs to research when I first started to collect information at the beginning of my research process. No biases are indicated.

Liska, K. (2009). *Drugs and the human body with implications for society*. 8<sup>th</sup> Edition. Pearson Education, Inc.: Upper Saddle River, NJ.

Liska explores how drug (pharmaceutical and illicit) use interact in users bodies. In particular, sections on heroin withdrawal, society response to methadone clinics, and the use of levo-alpha-acetyl-methadol (LAAM) in treatment of heroin use disorder are useful. In fact, the section about heroin withdrawal has a very helpful chart that lays out signs of withdrawal according to hour since last heroin use. This chart is helpful to provide background and explain why using medication assisted treatment (MAT) can be beneficial. The section about society's response to methadone clinics is helpful to explain societal response on MAT options relating to success and usefulness of methadone as a treatment option. The last section about LAAM is helpful to evaluate LAAM. I originally used this book as the text for my Chemistry of Drugs class and to begin my Thesis proposal. The sections listed above were helpful in both evidence for my thesis as well as help direct me to the topic of my thesis, methadone.

National Institute on Drug Abuse (2014). Retrieved November 7, 2016, from:

<https://www.drugabuse.gov/drugs-abuse/>.

This website is a government funded and focuses on the research, information, and educating the public about various drugs and the abuse of these drugs. This website provides basic information about heroin, background information on diamorphine and levo-alpha-acetyl-methadol (LAAM). This website is helpful to gather statistics about prevalence rates of heroin use and direction to discuss which treatment options I should gather more information on at the beginning of my research process. I can use this information to explain why this topic is important and needs to be researched.

Furthermore, this website was helpful as I learned about diamorphine and LAAM. I used the information from this website on possible adverse or side effects related to these two possible treatment options. I will use this information for the background sections of diamorphine and LAAM.

Pan, S., Jiang, H., Du, J., Chen, H., Li, Z., Ling, W., & Zhao, M. (2015). Efficacy of cognitive behavioral therapy on opiate use and retention in methadone maintenance treatment in china: A randomized trial. *PLoS One*. 10(6). doi:10.1371/journal.pone.0127598.

This study tests whether cognitive behavioral therapy (CBT), in conjunction with methadone maintenance treatment (MMT), can improve treatment retention rates and reduce heroin/opiate use. This study included 240 patients, 120 in CBT with MMT and 120 in MMT for 26 weeks. Outcomes were evaluated by analyzing retention rates and opiate-negative urine tests at 12 and 26 weeks. Results included that the group with CBT in combination of MMT had higher proportion of opiate-negative urine tests at both 12 and 26 weeks. However, there was no significant variance in the retention rate between MMT and CBT with MMT. This study is helpful to evaluate a combination therapies help to treat heroin use disorder. The limitations of this study is that it was only

conducted for 26 weeks compared to other studies I have included that were conducted for at least 12 months or longer. Information will be hard to compare in terms of retention rate because the study is significantly shorter. This limitation supports the fact that more research about combination therapies is needed.

Rollins, J.A. (2016). Heroin addiction: Not a laughing matter. *Pediatric Nursing*. 42(3).

Rollins's article highlights statistical data about current prevalence rates of heroin use in the United States and discusses how these rates have escalated in recent years. I will use statistics and information to support my thesis because it explains why treatment for heroin use disorder is important in the current times and why it should be researched. The article also discusses the center of disease control (CDC) plan to respond to heroin use epidemic, which includes prevention of initiation of heroin use, education on the reversal to overdoses, and medication assisted treatment (MAT) as a harm reduction effort to stop people from heroin use. The purpose of my thesis is to address the third point of the CDC's plan. This article was written by a nurse, which indicates implications for practice by nurses. I was inspired by the passion shown about this topic in the article, if it did not make me slightly weary of the possible bias in the article.

Roux, P., Michel, L., Cohen, J., Mora, M., Morel, A., Aubertin, J., & ... Carrieri, P. M. (2012).

Methadone induction in primary care (ANRS-Methaville): a phase III randomized intervention trial. *BMC Public Health*, 12(1), 488-495. doi:10.1186/1471-2458-12-488.

The researchers compare the effectiveness of methadone as outpatient and inpatient treatment in terms of retention rates, quality of life, and satisfaction of treatment. 195 people between the ages of 18 and 70 participated in this study. Results showed a 15% retention rate between both of the two study groups and differential success rates between

inpatient and outpatient were inconclusive. These results show that outpatient treatment is a viable option and can be used in the primary care setting. The study warns against the possible dangers at the initiation of the therapy and how starting under strict observation by physician as initiation of therapy carries the highest risk for overdose and adverse reactions. Conclusions by the authors are both patients and physicians are satisfied with outpatient treatment. Information from this research is beneficial for the part of my thesis about evaluation treatment of methadone. This research also extends the research done Carreri et al. and will strengthen my argument.

Schwartz, R.P., Kelly, S.M., O'Grady, K.E., Gandhi, D., & Jaffe, J.H. (2011). Randomized trial of standard methadone treatment compared to initiating methadone without counseling: 12-month findings. *Addiction*. 107(p. 943-952). doi: 10.1111/j.1360-0443.2011.03700.x.

A study conducted by Schwartz et al. aimed to determine the effectiveness of 12-month trial of interim methadone, standard methadone treatment, and restored methadone treatment. This study was a randomized controlled trial conducted by comparing these treatment options at baseline, 4-months, and 12-months and evaluated the number days of heroin use within the last 30 days, opiate-positive tests, and retention in original treatment programs. 230 participants: 99 in interim, 104 in standard, and 27 in restored therapy were included in the study. I will use this research in the sections that compares the effectiveness of combination of therapies and effectiveness of methadone. Results are beneficial to my conclusion and stance that a combination of therapies is most effective as well as my position that more research in this area. The researchers indicated no biases.

Substance Abuse and Mental Health Services Administration. (2015). Substance Use Disorders.

Retrieved March 20, 2017, from: <http://www.samhsa.gov/disorders/substanceuse>.

The Substance Abuse and Mental Health Services Administration (SAMSHA) support is a database on the prevalence and definitions of various substance abuse and mental health issues within the United States. The purpose of this website is to provide information to the public. Each year SAMSHA publishes an annual report of prevalence rates and contributing factors on numerous substances in each region and state across the United States. I used the current statistics on this website for heroin use and overdose prevalence rates across the entire United States. This information will be beneficial as it builds ethos in my thesis and explains why this research is important and why treatment for heroin use disorder needs to be researched.

Trujols, J., Portella, M. J., Iraurgi, I., Campins, M. J., Siñol, N., & Cobos, J. L. (2013). Patient-reported outcome measures: Are they patient-generated, patient-centered or patient-valued?. *Journal of Mental Health, 22*(6), 555-562. doi:10.3109/09638237.2012.734653.

Trujols et al. does an evaluation of patient-satisfaction compared to physician-satisfaction in regards to how both the patient and physician view satisfaction regarding their methadone maintenance treatment (MMT). Results from this study showed a difference in reporting from physician's statement of patient satisfaction compared to what the patient reports what their satisfaction with the treatment option for therapy. This means patients are not as satisfied with MMT as the providers think their patients are. This should be a cause for concern. Implications for this study in my own research would be to evaluate patient satisfaction as a part of how effective methadone maintenance treatment is. I will include this information in the section that evaluates methadone as a treatment option. No biases indicated in this study.



Van Wormer, K., & Davis, D.R. (2013). *Addiction treatment: A strengths perspective*. 3<sup>rd</sup> Edition. Cengage Learning: Belmont, CA.

Van Wormer's book discusses various types of treatment options for various types of addictions. The sections of this book that I am using include cognitive-behavioral therapy, relapse prevention, and harm reduction. I will use the section on cognitive-behavioral therapy for the definition, background information for the section of my thesis about what cognitive behavioral therapy is, and how it is used in treating heroin use disorder. The section on harm reduction is used for the harm reduction section of my thesis and how harm reduction is used as treatment. The information from the relapse reduction section I will use for the evaluation of cognitive-behavioral therapy section in my thesis. I originally used this book as my text in my Chemical Dependency: Theories and Intervention class. This text gave excellent background on different kinds of therapies for different types of addiction and contributes to information and background in types of therapies for my thesis.

Wang, W., Li, Q., Wnag, Y., Tian, J., Yang, W., Li, W., Qin, W., Yuan, K., & Liu, J. (2011). Brain fMRI and craving response to heroin-related cue in patients on methadone maintenance treatment. *The American Journal of Drug and Alcohol Abuse*. 37, 123-130.

doi:10.3109/00952990.2010.543997.

The objective of this study is to investigate the subjective craving and brain response to heroin-related cues in former heroin addicts on long term methadone maintenance treatment. Extensive research has been done on function magnetic resonance imaging (fMRI) on nicotine, alcohol, cocaine, marijuana, and heroin, but hardly any to no research has been done for assessing how changes in fMRI in MMT patients. Results showed that

there is no statistical significance before and following procedure of exposing images associated with heroin use. This data was collected by self-reporting so there is a possibility of bias in information. However, in fMRIs they have confirmed activation of PFC, mesocorticolimbic, and visuospatial-attention regions in response to visual drug-related stimuli in former heroin users. This signifies that even though participants report no changes in craving for using heroin, these parts of the brain are still activated. This research is helpful in showing that even though the methadone maintenance treatment is treating patients for their response withdrawal, the brain's response to seeing the heroin use related images similar to during the time of patients using heroin. This shows that even though the body's response to heroin use disorder has changed, the brain's response has not changed.

White, W.L., Campbell, M.D., Shea, C., Hoffman, H.A., Crissman, B., & DuPont, R.L. (2013). Coparticipation in 12-step mutual aid groups and methadone maintenance treatment: A survey of 322 patients. *Journal of Groups in Addiction & Recovery*. 8(p. 294-308). doi: 10.1080/1556035X.2013.836872.

This study reports the levels of Narcotics Anonymous (NA) and/or Alcoholics Anonymous (AA) participation among 322 patients enrolled in methadone maintenance treatment (MMT). Survey results reveal high rates of past-year NA/AA participation (66%), high rates of self-reported helpfulness (77%), but much lower rates of participation in key 12-step program ingredients. 25% of NA/AA-involved patients reported a negative experience related to their MMT patient status. Treatment programs, including outpatient must address complex patterns of concurrent and sequential drug use presented by their patients. This research brings to light that most patients leave

outpatient leave on current doses of methadone without planned tapering and without medication support for the transition to recovery maintenance. Risk for relapse is great under these circumstances and needs to be addressed in current heroin use disorder treatment. I plan to use this in my thesis to support my point that MMT alone is not enough to help fully treat heroin use disorder and there should be a change to the standard of how treatment is carried out.

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