Methadone vs. Buprenorphine: A Review of Current Treatments for Opioid Addiction

According to the United Nations Office on Drugs and Crime, recreational opioid abuse addiction poses serious social and medical concerns throughout the world. Globally, opioid addiction contributes to excessive morbidity, mortality, and economic costs. The World Health Organization (WHO) and the United Nations Office on Drugs and Crime estimate that 15.6 million individuals abuse opioids, of which 11.1 million abuse heroin. *(1)*

WHO numbers indicate that there are nearly 12.6 million injection drug users (IDUs) worldwide, and the use of injected drugs has been documented in over one hundred and fifty countries. While the percentage of IDUs in any given population is usually low, these individuals represent the major point of entry for AIDS and other blood-borne diseases. The United Nations Programme on HIV/AIDS estimates that up to 80% of HIV infections in central Asia and Eastern Europe can be traced directly to injected drug use.(*1*)

The history of opioid abuse begins around 3400BC, when the Sumerians of Mesopotamia began cultivation of the poppy plant. The Sumerian word for the plant is roughly translated "joy plant", a reference to the physiological effects it produced. The Sumerians use of the euphoric poppy was passed on to the Assyrians, who passed it on to the Babylonians, who finally passed it on to the Egyptians. (2)

Around the year 1300BC, the Egyptians began cultivating the flowers in vast fields that supplied a rapidly growing opium trade. The Egyptians traded with the Phoenicians, and the Minoans who then brought the poppy to new markets in Greece, Carthage, and Europe. In 1100 BC, residents of the island of Cyprus crafted the first specialized tools for harvesting opium form the poppy plants, and were also known to smoke the substance. By 330 BC, Alexander the Great had introduced opium to the people of Persia and India, and by 400AD, Egyptian opium was introduced to China by Arabian traders. (*2*)

Hippocrates, the father of modern medicine, was familiar with opium, but rejected the mythical lore that had come to surround the euphoric effects of the drug. In perhaps the first medical reference concerning opioids, Hippocrates acknowledged opium's effectiveness as a narcotic, and proposed its use for treating internal disease, diseases of women, and epidemics.(2)

During the crusades, opium disappears from history as its use had become taboo to the early Christians. It wasn't until the 1500's that it re-appeared in the historical record when Portuguese traders began to smoke it, having discovered that doing so produced instantaneous euphoric effects. Around 1527, Opium began gaining popularity in medical literature, and was first medically prescribed in a pill form as remedy for pain. (2)

Widespread recreational use of opium began around the 1600's and spurred explosive growth of trade between the cultivation sites in Egypt and India and consumers in England and China. By 1700, the Chinese had adopted the practice of smoking opium from pipes, and soon after the drug was outlawed for recreational use by the Chinese emperor. (2)

In 1803 Friedrich Sertuerner purified the active ingredient in opium, and the resulting alkaloids became known as morphine. Medical physicians welcomed this new development,

believing a safe form of the drug had been found. It was the medical understanding at that time that morphine was a safe alternative, with good reliability and long lasting effects. Morphine was less than 20 years old, when E. Merck & Company began to commercially purify and manufacture the drug.(2)

The first direct published account of opium addiction dates to 1812, when Thomas De Quincey released his autobiographic account of opium addiction, titled, "Confessions of an English Opium-eater".(2)

In 1843, Dr. Alexander Wood, the Secretary of the Royal College of Physicians in Edinburgh, Scotland first injected morphine with a hypodermic syringe. He quickly discovered that by injecting the drug rather than smoking it, the effects were instantaneous and nearly three time more potent. In 1855, he published a paper detailing the use of a hypodermic syringe to administer opiates into painful joints for the treatment of neuralgia. Once the Civil War which broke out in the United States, Dr. Wood's discovery was put to use treating pain related to injuries sustained in battle. It was during and after the Civil War, that awareness of opioid addiction began to enter public awareness. (*3*)

About fifty years later, in 1895, Heinrich Dresser of the Bayer Company discovered that diluting morphine with acetyls produced a version of the drug with fewer side effects. Bayer began almost immediate production, and within three years had their new morphine formulation on the market, under the name heroin. (2)

The first historical notes related to using medication to treat opioid addiction surface in the early 1900's, when the Saint James Society in the United States began to supply free samples of heroin to morphine addicts through the mail. The hypothesis was that morphine addicts could

use the heroin to help them escape their addiction. By 1902, the subject could be found in various medical journals, and physicians were debating the use of heroin as a step-down cure for morphine addiction. (2)

OPIOID ADDICTION

The efforts of the Saint James Society were ahead of their time, but without a modern understanding of opioid addiction their efforts produced very limited results. Opioid addiction is a physiological condition involving not only formed habits, but also physical and chemical changes in the brain. Regular opioid use causes an individual to develop tolerance for its euphoric effects, while at the same time becoming sensitized to desire the drug. Tolerance and desire sensitization is the result of long-term changes to the mesolimbic dopaminergic pathways, responsible for producing pleasure and desire. These changes occur due to repeated activation of the central μ opioid receptors, and subsequent down-regulation of receptor expression. Reduced receptor expression requires the user to take higher and higher doses to achieve the same effects. (4)

OPIOID TREATMENT

Effective treatment plans for opioid dependence usually require both psychosocial therapy and pharmacological detoxification or a maintenance program. (4) The primary goal of detoxification or a maintenance program is to replace the short acting illicit opioid with a longer acting and more controllable substitute. Sufficient doses of the substitute should assist in the elimination of the drug-seeking behavior, and better allow the patient to take advantage of psychosocial therapy and rehabilitation.(5) Various studies have substantiated the beneficial

outcomes of controlled opioid treatment programs, and found such treatment reduces the use of heroin, prescription opioids, and other non-opioid drugs.(*6*)

There are several different strategies for pharmacologically treating opioid addiction, including opioid maintenance, opioid detoxification with various opioid agonists, using adrenergic agonists, and symptomatic based treatment plans. By far, the most common is a tapered approach, in which the illicit drug is replaced by a calculated equivalency of another opioid agonist. The dose of the replacement agonist is then gradually reduced until the patient can function without the medication. The two most common medications used methadone and buprenorphine. (4)

METHADONE

Methadone is a full μ opioid agonist, (7) and currently the most widely used medication for the treatment of opioid dependence. The pharmacological action of methadone is achieved when the R-methadone isomer binds to and activates μ opioid receptors in the central and peripheral nervous system. Methadone's action is unopposed, allowing for strong dosedependent activation. Activation of the μ opioid receptors by any opioid produces desirable analgesic and euphoric effects. (6)

Methadone is a lipid soluble synthetic opioid with excellent oral bioavailability and high mucosal absorption. It is excreted in saliva, breast milk, amniotic fluid, and umbilical cord plasma. Other attractive features of methadone include its long half-life, low cost, and availability in oral, parenteral, and suppository preparations. (*6*)

BUPRENORPHINE

While methadone is the most common agent for treating opioid withdrawal, the use of buprenorphine rather than methadone is starting to gain popularity. Introduced in 2002, and now with various studies and trials have demonstrating its effectiveness, buprenorphine is quickly becoming an attractive alternative for use in opioid maintenance or detoxification programs. (8)

While methadone is a full μ receptor agonist, buprenorphine is a partial μ receptor agonist, and a full kappa receptor antagonist. This medication is unique in that while expressing a higher affinity for the μ receptor than methadone and many other opioids, buprenorphine displays a low intrinsic activity. Due to the high affinity, buprenorphine can unseat other opioids from the μ receptors while still causing a lesser degree of activation. Additionally, other full agonists with a weaker affinity cannot unseat buprenorphine, and are essentially blocked from producing a significant effect. (9)

When compared with methadone and other opioids, buprenorphine has a very slow rate of disassociation from the mu receptor, (10) resulting in effects lasting up to three days.(5) This slow disassociation allows for extended suppression of withdrawal symptoms, and protection against additional full agonists and their effects. Because of the extended effects, buprenorphine can be dosed much less frequently than traditional opioids, with some practitioners advocating doses every other day. (11)

Selecting a superior medication for the treatment for opioid dependence requires that multiple issues all be considered at the same time. The medication must effectively reduce the symptoms of withdrawal, while at the same time preventing concurrent use of other illicit substances. Additionally, practitioners need consider the factors that may cause a patient to discontinue treatment, as well as the overall safety of the chosen medication.

BPURENORPHINE/NALOXONE

In an effort to increase safety and help prevent diversion and abuse, buprenorphine is often combined with naloxone in a sublingual tablet or film. Naloxone is an opioid antagonist that causes no activation of any opioid receptors. When taken alone without any opioid agonists present, naloxone shows no pharmacological or physiological effects. In the presence of an opioid agonist, however naloxone will prevent and/or reverses the μ receptor activation. This reversal of opioid effects occurs very quickly, and in instances of dependence, such reversal will precipitate symptoms of a complete withdrawal. (*12*)

Naloxone is not known to cause tolerance, physical, and or psychosocial dependence of any kind. While the current mechanism of action is undetermined, evidence from in vitro research indicates that naloxone competes for μ , kappa, and sigma opioid receptors in the central nervous system. (13)

The buprenorphine/naloxone sublingual formulation prevents diversion due to differences in mucosal absorption. While buprenorphine is easily absorbed through the mucus membranes of the mouth, naloxone is not. Naloxone is ten to twenty times less effective when administered sublingually, than when administered by injection. Because of this discrepancy, when the combination drug is taken sublingually as prescribed, the patient receives the correct dose of buprenorphine but very little naloxone, and experiences no antagonistic effects. If one were to attempt to abuse this combination drug by dissolving the tablet or film and injecting parentally, the naloxone would be fully absorbed and induce an unpleasant withdrawal event.(*5*)

EFFECITIVENESS

There is a large body of research suggesting that no significant difference in efficacy between the methadone and buprenorphine. A comprehensive study of 140 patients revealed that between methadone and buprenorphine groups, the medication used for pharmacological treatment was not a significant predictor of outcome.(14) A 17 week randomized single center trial showed no significant difference in the rate of positive drug screens, and a six week trial concluded that buprenorphine was not an inferior treatment. A twenty-four week parallel group trial also found no difference in the reduction of illicit drug use between methadone and buprenorphine groups. (12)

Because buprenorphine is a partial μ agonist rather than a full μ agonist, there is valid concern that it may not be effective in patients who have been sensitized to high doses of illicit opioids over a long period of time. In these cases, even high doses of buprenorphine may not achieve the level of Mu-receptor activation needed to be therapeutically effective. (15)

REDUCTION OF WITHDRAWAL

Opioid replacement therapy works by reducing or eliminating the negative symptoms of withdrawal, and there does not appear to be a consensus as to which medication is better for this purpose. In 2008 a study, found both methadone and buprenorphine effective at reducing withdrawal symptoms, with only non-significant differences favoring methadone over buprenorphine. (*14*) In another study conducted in 2010, significantly more patients reported withdrawal discomfort with methadone, than buprenorphine. (*8*) The fact that buprenorphine may not reduce withdrawal symptoms in long term and heavy users may be due to the medication's limited μ receptor activation. (*15*)

CONCOMITANT DRUG USE

The primary reason for treatment with an opioid maintenance program is to reduce the dependence on illicit drugs. It is common that multiple illicit drugs are used in combination, thus any treatment mediation must be able to reduce the use of all substances. Some research suggest that while not at the level of statistical significances, the rate of positive tests for benzodiazepines cocaine, and cannabis were somewhat lower among buprenorphine treatment groups.(*14*) This has been contradicted by newer research which has found significantly greater rates of concomitant drug use among participants treated with buprenorphine.(*16*)

RETENTION

Opioid treatment is only effective as long as the patient continues receiving care, and low patient retention rates are a chronic issue. There is no clear picture of which medication results in fewer dropouts. Overall completion of treatment appears to be significantly higher in methadone, rather than buprenorphine treatment groups. Higher retention rates also seem to be significantly correlated with higher medication doses, in both medication conditions, however this effect is more pronounced in buprenorphine groups.(*16*) A study of incarcerated heroin users displayed opposite though non-significant results, finding higher retention rates in their buprenorphine group.(*8*)

There is a strong possibility that lower retention rate suggested in buprenorphine groups are due to over cautious dosing. As with most new medications with a short track record, practitioners tend to use a slower rate of induction and more conservative dosing when initiating buprenorphine treatment. It is very likely that more aggressive dosing and faster initiation will reduce the difference in retention rates seen between the two medications.(*5*) This idea is

supported by findings that retention rates were correlated with perceived symptom severity, but not the particular medication used.(*14*)

Medication safety is a serious concern when prescribing opioids, and both Methadone and buprenorphine can have serious and life threatening side effects. The risk of respiratory depression, accidental overdoses, and cardiac arrhythmias, and withdrawal due to sudden discontinuation are all serious concerns that require careful consideration. (6)

RESPIRATORY DEPRESSION

Almost all opioid overdose deaths are the result of sedation and respiratory depression. Excessive activation of μ opioid receptors induces a powerful sedative effect, to the point where the body's hypercapnoeic and hypoxic ventilatory drives are suppressed. Once this level is reached, the victim becomes unresponsive, loses the natural ventilatory drive, and expires due to hypoxia. (4)

Because methadone is a full μ opioid agonist, it displays unopposed action on the central nervous system in the same manner as heroin. Even though it is a prescribed medication, the risk of methadone overdose is still very real, and not unlike that of illicit opioids. (4)

While buprenorphine is still an opioid, its chemical attributes significantly mitigate some of the risks seen with methadone. Because of being a partial, rather than a full μ receptor agonist, buprenorphine exhibits a ceiling effect at moderate and high levels. (*17*) Unlike methadone and other full μ receptor agonists that display a linear relationship between dose and effect, there is a limit to the degree of μ receptor activation buprenorphine can achieve. Once this limit is reached, additional medication causes little or no increase in the opioid agonist

effects of sedation and respiratory depression. The levels of sedation and respiratory depression reach a plateau, which is usually under the threshold required to cause adverse effects. (1)

While it is physiologically difficult to overdose on buprenorphine alone, it is no impossible; especially when used in combination with other sedatives. When this does occurs, the favorable attributes of high receptor affinity and long disassociating time become problematic. Significantly more naloxone is required to reverse buprenorphine induced respiratory depression, than would be needed for other opioids. Because of the long disassociation time, naloxone may need to be administered continuously over several hours, rather than in the traditional one time dose. (*15*)

ACCEDENTAL OVERDOSE

Even when used correctly, methadone exhibits a dangerous disparity between the onset time of analgesia, and respiratory depression. Respiratory depression peaks later, and persists for longer than the analgesic effect. This disparity has contributed to overdoses, even by medical professionals, when additional medication is given or taken because the original dose did not achieve the desired level of analgesia. This issue in particular, is most common during initiation, and initial titration of the drug. (*18*)

CARDIAC EFFECTS

New information is suggesting that methadone may increase a patient's risk of adverse cardiac arrhythmias. Along with opioid receptor stimulation, methadone can also blocks Ikr potassium channels in the heart, *(19)* and cause prolonged QT intervals. QT prolongation was

found to be dose dependent, and was significantly correlated with a prolongation rate of 0.140 ms/mg methadone.(20) The prolonged QT intervals often trigger runs of Torsade de Pointes, a life threatening (21) polymorphic ventricular arrhythmia.(22)

Unlike methadone, buprenorphine does not interfere with the Ikr potassium channels, and no evidence suggests that it can cause QT prolongation. *(23)* It has been successfully used as an alternative to methadone in cases of methadone induced Torsade de Points. One such case study describes a 56 year old male in a methadone maintenance program was found to have reoccurring unexplained syncopal episodes. ECG examination revealed repetitive short runs of Torsade de Pointes, sinus bradycardia, and prolonged QT intervals. The patient was transitioned to a buprenorphine regimen, and no longer displayed QT pathology or ventricular arrhythmias. *(19)*

Strong evidence suggesting that buprenorphine has a lower cardiac risk profile is limited, and is still mostly derived from case studies. What evidence does exist, however suggests that buprenorphine should be strongly considered for patients who have documented ventricular arrhythmias. (23)

SUDDEN DISCONTINUATION

Sudden discontinuation of both methadone and buprenorphine can precipitate serious withdrawal symptoms. In cases where the treatment medication is suddenly no longer available, patients often return to illicit opioids to avoid withdrawal. When buprenorphine is abruptly discontinued, the withdrawal effects are much less severe and of shorter duration that those of methadone. 1 It is theorized that buprenorphine's slow disassociation time is responsible for the lower levels of physical dependence and withdrawal symptoms. (*10*)

PREGNANCY

A serious question that until recently until recently received very limited attention is that of how to treat opioid addiction in pregnant women. The current agreement is that while buprenorphine and methadone both extend their effects to the developing fetus, the alternative of allowing the mother to remain untreated and abusing illicit substances poses far greater risks. (24)

Opioid addiction in pregnancy affects not only the mother, but the fetus or neonate as well. Several different studies have shown that the on average seventeen percent of pregnant mothers receiving buprenorphine treatment test positive for other illicit opioids at time of delivery. This rate of positive tests is similar to that of mothers in treatment programs using methadone. While not conclusive, this similarity suggests that both methadone and buprenorphine based treatment programs have similar efficacy in terms of preventing illicit opioid use in pregnancy. (25)

MATERNAL OUTCOMES

As of 2012, the single largest and most comprehensive study assessing the differences between methadone and buprenorphine treatment plans in pregnancy is the Maternal Opioid Treatment: Human Experimental Research study (MOTHER). This study found no significant difference between methadone and buprenorphine based treatment programs, in terms of weight gain, obstetrical visits, incidence of caesarean section, abnormal presentation, use or need of analgesia, positive tests for illicit substances, or medical complications with delivery. (25)

The incidence of preterm labor was found to be nearly eight times higher in the methadone condition. While significant, researchers are cautious to draw any conclusions regarding preterm labor stating than additional research is needed. Significantly higher rates of non-serious maternal events, such as high or low blood pressure or pulse rate were observed in the methadone condition, however when the rate of each individual adverse measure was compared with its counterpart in the buprenorphine condition, there was no significance.(25)

FETAL OUTCOMES

Sadly, opioid addiction affects not only the mother, but also the developing fetus as well. Due to their water soluble nature, most opioids cross the placenta and enter fetal circulation. Standard fetal assessment is usually accomplished via non-invasive Non-Stress Testing (NST) and use of the Biophysical Profile (BPP). Lower levels of reactivity of the Fetal Heart Rate (FHR) and less fetal movement strongly predict lack of fetal growth, low oxygen saturation, and sub-optimal outcomes. (*25*)

Several studies have indicated that fetuses exposed to buprenorphine had higher levels of FHR variability and fetal movement than those exposed to methadone. It was also found that in the third trimester, those exposed to buprenorphine displayed higher levels of motor activity over longer periods of time then their methadone counterparts.(*26*) Significant reduction in FHR reactivity and movement was post methadone administration, while those fetuses exposed to buprenorphine showed no significant deviation from baseline. (*27*) While more research is still needed, current evidence suggests that buprenorphine poses no greater risk then methadone, and may actually cause less suppression of FHR reactivity. (*25*)

NEONATAL OUTCOMES- NAS

Continued exposure to opioids in-utero cause a fetus to display physiological opioid addiction similar to that seen in adults. At birth, the newborn is no longer connected to the maternal circulation, and thus is no longer exposed. Unfortunately, sudden loss of the opioids in the fetal circulation leads to a condition physiologically similar to acute withdrawal in adults, known as Neonatal Abstinence Syndrome (NAS).(7)

NAS is a serious condition that can be dangerous or deadly to the newborn if not treated appropriately. Treatment modalities for NAS usually involve supportive treatment and a morphine step-down regimen adjusted to symptom severity. Untreated, the newborn will suffer from varying degrees of poor growth, gastrointestinal distress, hypersensitivity of the central nervous system, increased irritability, dysfunction of the autonomic, seizures, and potentially death.(*7*)

In populations of neonates who are chronically exposed to opioids in utero, the incidence of NAS ranges from twenty-one to ninety-four percent. The time to onset, severity, and duration of symptoms depend on the type of opioids used, and if the mother breastfeeds. Due to the serious nature and high incidence of NAS, it is important to determine how the medication used for opioid replacement in pregnant women influences newborn outcomes. (7)

A double-blinded study of 175 pregnant women suffering from opioid addiction treated with either methadone or buprenorphine found no significant difference in the percent of neonates treated diagnosed with NAS. Although there was no difference in incidence, the study also found that neonates in the methadone group required nearly ten times more morphine to treat their symptoms, and required longer duration of treatment. It was also found that neonates in the methadone group had a younger gestational age at birth, and required lengthier hospital

stays. Neonates in the methadone group had more severe NAS symptoms than did the buprenorphine group, (p=.04) but because the authors used a p value of .01, the difference was reported as non-significant. No significant difference in APGAR, abnormalities during birth, Cesarean section, or percent of mothers requiring analgesia during delivery were found. (7)

Along with showing that buprenorphine use during pregnancy correlates with milder NAS symptoms, less morphine required for treatment, and shorter hospital stays, it also demonstrated no adverse effects. All measures that showed a significant difference indicated that buprenorphine had either a positive effect or no effect on neonatal outcomes. Jones reported no measure where the buprenorphine group displayed an undesirable outcome. (7)

A retrospective study published in 2011 by Isemann et al. also examined data regarding NAS in neonates born to mothers receiving opioid maintenance therapy at the University Hospital in Cincinnati, Ohio between 2002 and 2007. In the 128 records that were examined, the researchers found that NAS severity was correlated to the maternal dose of methadone, indicating that the amount of opioid reaching the neonate was correlated the level of opioids in the mother.(*24*)

BREAST MILK

Neonates who were fed Maternal Breast Milk (MBM) required significantly shorter duration of NAS treatment, when compared to those who were fed with formula. A shorter length of hospital stay was also associated with neonates fed MBM. Out of all the infants in the study, five were re-admitted for NAS treatment. These five had all been receiving MBM prior to discharge, and at time of re-admission, MBM had either been discontinued, or severely restricted. (*24*)

The author suggests that these findings can be explained by the fact that methadone is expressed in maternal breast milk, in levels great enough to greatly reduce NAS symptoms. This idea is further corroborated by additional anecdotal evidence that cessation and quick weaning MBM has led to cases of rebound NAS symptoms. Although this study does not provide enough information to make comprehensive treatment decisions, it does suggest that expression of opioids in MBM is a factor for consideration. (24)

SIDE EFFECTS

Patients taking methadone may experience other less serious side effects such as changes in sexual function, reduction of psychomotor response time, and suppression of the immune system, depression, and social stigmatization. (28)

SEXUAL FUNCTION

A study investigating male sexual dysfunction between methadone and buprenorphine users found that participants in buprenorphine treatment groups were less likely to experience reductions in sexual function, than their counterparts treated with methadone. (15)

PSYCHOMOTOR

Impairment and sedation while driving or operating machinery is a significant concern with opioid use, and can adversely affect both mobility and livelihood. Preliminary research using a standardized battery of driving simulations suggests that buprenorphine has less impact on psychomotor responses than methadone. Patients taking buprenorphine performed significantly better both in cases of heightened stress and monotony. *(28)*

IMMUNE EFFECTS

Chronic opioid use, in particular that of heroin and morphine, has been linked to detrimental suppression to the immune system, and abnormal phases of cytokine stimulation and inhibition. Current research suggests that both buprenorphine and methadone exhibit the same ability to restore normal immune function, and stimulate cytokine production. Patients placed on either methadone or buprenorphine therapy actually exhibit cytokine levels higher that what would be expected in a normal healthy adult. In the future, this hyperactivity of the immune system could be supplemented with additional medication, in a multi-faceted approach to treating infectious diseases that are common among intervenes drug uses. *(29)*

DEPRESSION

Kappa receptor activation is linked to the negative effects experienced with opioid use. These effects include disphoria, anxiety, depression, and panic. By its kappa antagonistic activity, buprenorphine has been shown to restore patient's moods, and reduce the severity of depression. (29)

PERCEPTION

While not directly related to the pharmacology of either medication, public perception and name recognition may affect treatment outcomes. Interviews with patients enrolled in methadone maintenance programs indicate that many experienced stigmatizing experiences due to taking the medication. (*15*) Buprenorphine is relatively unknown to the general public compared to methadone, and thus its use may carry less of a stigma. These issues with public

perception may explain why significantly more heroine addicted inmates enrolled in a buprenorphine program, expressed their intention to enroll in a maintenance program on release than inmates who were given methadone.(8)

COSTS

No discussion of treatment options is complete without a review of the associated momentary costs. Unfortunately, projecting the monetary costs of two different treatment plans is inherently difficult, due to the high number of compounding factors. Using economic models and retrospective data from other studies, researchers in Australia predicted higher costs associated with buprenorphine, rather than methadone treatment plans. The higher costs result primarily from the higher cost of the medication, and the additional time used by the medical staff for monitoring the sublingual administration. (*5*)

While monetary costs are usually at the forefront of any economical discussion, the societal costs of not using all available treatment options may be far greater. By reducing illicit opioid use, there may also be a reduction in the amount of criminal activity associated with obtaining the drug, less use of the law enforcement and judicial systems, and reduced pressure on hospitals that would have to treat overdoses. The authors of the Australian study suggest that the long-term socioeconomic benefits far outweigh any short-term cost increases. (5)

MERCY VALUES

As healthcare continues to advance with new medications, treatment techniques, and sophisticated devices, the human aspect of care becomes deemphasized, and values such as mercy, service, hospitality, and justice are becoming increasingly overlooked. While making

better clinical decisions, particularly about what medication or treatment provides better results, it must not be forgotten that the primary focus must be on the person.

When decision making is focused on the values of justice and mercy, better outcomes and individualized results are possible. It is just for professionals to be aware of all options, and how different medications compare. It is also merciful for professionals to provide treatment options that provide the best outcomes. When persons with addictions receive treatment that best allows them to enter successful recovery, the service provided to the community is invaluable. By reducing the amount of illicit activity, especially in our cities, the general populous will feel more comfortable opening their doors to their neighbors in need.

Through increased knowledge of treatment options and their respective safety profiles, effectiveness, side effects, and impact on pregnant and nursing mothers, we can move forward toward creating a better future for all our fellow humans. Advancing this knowledge, and with it the health status of their patients, our healthcare professionals become better equipped to support the greater good of God's creation.

Works Cited

- Yokell, M., Zaller, N., & Rich, J. (2011). Buprenorphine and buprenorphine/naloxone diversion, misuse, and illicit use: An international review. *Current Drug Abuse Reviews*, 4(1), 28-41. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3154701/
- 2 WGBH/Frontline. (1998). *Opium throughout history*. Retrieved 14 Mar 2012 from http://www.pbs.org/wgbh/pages/frontline/shows/heroin/etc/history.html
- 3 Rosenblum, A., Marsch, L., & Portenoy, R. (2008). Opioids and the treatment of chronic pain: Controversies, current status, and future directions. *Experimental and Clinical Psychopharmacology*, *16*(5), 405-416. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2711509/
- 4 Lobmaier, P., Gossop, M., Waal, H., & Bramness, J. (2010). The pharmacological treatment of opioid addiction—a clinical perspective. 80(949), 654-659. doi: European Journal of Clinical Pharmacolgy
- 5 Doran, C. M. (2005). Buprenorphine, buprenorphine/naloxone and methadone maintenance: A cost-effectiveness analysis.*Expert Review of Pharmacoeconomics & Outcomes Research*, 5(5), 583-91. doi:http://dx.doi.org/10.1586/14737167.5.5.583
- 6 Brown, R., Kraus, C., Fleming, M., & Reddy, S. (2004). Methadone: applied pharmacology and use as adjunctive treatment in chronic pain. *Postgrad Mededical Journal*, 80(949), 654-659. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1743125/
- Jones, H., Kaltenbach, K., Heil, S., Stine, S., Coyle, M., Arria, A., . . . Fischer, G. (2010). Neonatal abstinence syndrome after methadone or buprenorphine exposure. The New England Journal of Medicine, 363(24), 2320-31. doi:http://dx.doi.org/10.1056/NEJMoa1005359 – (Jones, Kaltenbach, Heil, Stine, Coyle, Arria 2010
- 8 Awgu, E., Magura, S., & Rosenblum, A. (2010). Heroin-dependent inmates' experiences with buprenorphine or methadone maintenance. *Journal of Psychoactive Drugs*, 42(3),
- 9 Strain, E. C., Walsh, S. L., & Bigelow, G. E. (2002). Blockade of hydromorphone effects by buprenorphine/naloxone and buprenorphine. *Psychopharmacology*, 159(2), 161-6. doi:http://dx.doi.org/10.1007/s002130100920
- 10 Buprenorphine Hydrochloride Injection [package insert]. Hospira, Inc., Lake Forest, IL; June 2009. http://www.hospira.com/Images/EN-2088_32-5649_1.pdf. Accessed Feb 19, 2014

- 11 Amass L., Kamien J.B., Mikulich S.K. Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans. Drug and Alcohol Dependence. 2001;61(2):173–181. [PubMed]
- 12 Orman, J., & Keating, G. (2009). Buprenorphine/naloxone: A review of its use in the treatment of opioid dependence. *Drugs*, 69(5), 577-607. Retrieved from http://libdb.mtaloy.edu:2206/docview/228067700/5EBA777174D54DE7PQ/1?accountid =12600
- 13 Naloxone Hydrochloride [package insert]. Hospira, Inc., Lake Forest, IL; January 2007. http://www.hospira.com/Images/EN-1367_32-5515_1.pdf. Accessed Feb 19, 2014.
- 14 Soyka, M., Zingg, C., Koller, G., & Kuefner, H. (2008). Retention rate and substance use in methadone and buprenorphine maintenance therapy and predictors of outcome: Results from a randomized study. *The International Journal of Neuropsychopharmacology*, *11*(5), 641-53. doi:http://dx.doi.org/10.1017/S146114570700836X
- 15 Bonhomme, Jean,M.D., M.P.H., Shim, Ruth S,M.D., M.P.H., Gooden, R., M.B.A., Tyus, D., M.S., & Rust, George,M.D., M.P.H. (2012). Opioid addiction and abuse in primary care practice: A comparison of methadone and buprenorphine as treatment options. *Journal of the National Medical Association*, 104(7), 342-50. Retrieved from http://search.proquest.com/docview/1073472522?accountid=12600
- 16 Hser, Y., Saxon, A. J., Huang, D., Hasson, A., Thomas, C., Hillhouse, M., . . . Ling, W. (2014). Treatment retention among patients randomized to buprenorphine/naloxone compared to methadone in a multi-site trial. *Addiction*, 109(1), 79-87. doi:http://dx.doi.org/10.1111/add.12333
- 17 Walsh SL, Preston K, Stitzer M, Cone E, Bigelow G. Clinical pharmacology of buprenorphine: ceiling effects at high doses. Clin Pharmacol Ther. 1994;55(5):569–80.
- 18 Dolphine® Hydrochloride CII [package insert]. ROXANE LABORATORIES, INC. Columbus, OH; October 2006. http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/006134s028lbl.pdf. Accessed Feb 19, 2014.
- 19 Esses, J. L., Rosman, J., Do, L. T., Schweitzer, P., & Hanon, S. (2008). Successful transition to buprenorphine in a patient with methadone-induced torsades de pointes. *Journal of Interventional Cardiac Electrophysiology*, 23(2), 117-9. doi:http://dx.doi.org/10.1007/s10840-008-9280-8
- 20 Heroin dependence; research on heroin dependence reported by scientists at university of copenhagen. (2007). *Mental Health Weekly Digest*, 122. Retrieved from http://search.proquest.com/docview/194515887?accountid=12600

- 21 Nordt, S. P., Zilberstein, J., & Gold, B. (2011). Methadone-induced torsade de pointes. *The American Journal of Emergency Medicine*, 29(4), 476.e1-2. doi:http://dx.doi.org/10.1016/j.ajem.2010.04.023
- 22 Latowsky, M. (2006). Methadone death, dosage and torsade de pointes: Risk-benefit policy implications. *Journal of Psychoactive Drugs*, 38(4), 513-9. Retrieved from http://search.proquest.com/docview/207972269?accountid=12600
- 23 Hanon, S., Seewald, R. M., Yang, F., Schweitzer, P., & Rosman, J. (2010). Ventricular arrhythmias in patients treated with methadone for opioid dependence. *Journal of Interventional Cardiac Electrophysiology*, 28(1), 19-22. doi:http://dx.doi.org/10.1007/s10840-009-9465-9
- 24 Isemann, B., Meinzen-Derr, J., & Akinbi, H. (2011). Maternal and neonatal factors impacting response to methadone therapy in infants treated for neonatal abstinence syndrome. *Journal of Perinatology*, 31, 25-29. Retrieved from http://libdb.mtaloy.edu:2206/docview/821494705/8DFA80008AE54922PQ/4?accountid= 12600
- 25 Jones, H., Finnegan, L., & Kaltenbach, K. (2012). Methadone and buprenorphine for the management of opioid dependence in pregnancy. *Drugs*, 72(6), 747-757.
- 26 Jansson, L. M., DiPietro, J. A., Velez, M., Elko, A., Williams, E., Milio, L., . . . Jones, H. C. O. E. (2011). Fetal neurobehavioral effects of exposure to methadone or buprenorphine. Neurotoxicology and Teratology, 33(2) doi:http://dx.doi.org/10.1016/j.ntt.2010.09.003
- 27 Salisbury, A. L., Coyle, M. G., O'Grady, K. E., Heil, S. H., Martin, P. R., Stine, S. M., . . Jones, H. E. (2012). Fetal assessment before and after dosing with buprenorphine or methadone. *Addiction*, 107, 36-44. doi:http://dx.doi.org/10.1111/j.1360-0443.2012.04037.x
- 28 Soyka, M., Horak, M., Dittert, S., & Kagerer, S. (2001). Less driving impairment on buprenorphine than methadone in drug-dependent patients? *The Journal of Neuropsychiatry and Clinical Neurosciences*, 13(4), 527-8. Retrieved from http://search.proquest.com/docview/195254330?accountid=12600
- 29 Neri, S., Bruno, C. M., Pulvirenti, D., Malaguarnera, M., Italiano, C., Mauceri, B., . . . Noto, R. (2005). Randomized clinical trial to compare the effects of methadone and buprenorphine on the immune system in drug abusers. *Psychopharmacology*, *179*(3), 700-4. doi:http://dx.doi.org/10.1007/s00213-005-2239-x