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Expanding access to Medication Assisted Treatment: The U.S. government's response to the current heroin epidemic

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Abstract

The rates of heroin addiction and opiate overdoses have skyrocketed in America in the last decade. The government's response is to expand the availability of Medication Assisted Treatment (MAT). Because social workers can be expected to be a significant component of the workforce in providing MAT, MAT is relevant to social workers. Many social workers who are working in the area of addictions do not hold favorable views of MAT. This paper considers their objections and evaluates the validity of the basis for these objections. The rationale for the government's approach is provided and validity of the rationale for the MAT approach is evaluated. The "pros" and "cons" of methadone and buprenorphine are reviewed. The paper distinguishes, beneficial treatment for the individual from the long term impact of a change in policy on the society.

Key Words: Medication Assisted Treatment, Methadone, Buprenorphine, Opiate Epidemic, Opiates, heroin

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The Present Epidemic

The rate of illicit drug use has risen precipitously in the US over the last decade. Seventy-five percent of these new cases have been addicted through prescription drugs such as OxyContin (Cicero, Ellis, Surratt, & Kurtz, 2014). When prescription drugs such as OxyContin become too expensive, many patients switch to cheaper street heroin. In addition to opiate addiction rates increasing, overdoses have also quadrupled from 1999 to 2010. Prescription opiate drug overdoses in 2010 (at 16651 cases) far exceeded overdoses from street heroin (at 3036 cases) (Volkow, Frieden, Hyde, & Che, 2014).

Along with the increase in the numbers addicted to opiates, the demographics of those who become addicted to opiates have changed. Heroin addiction is no longer restricted to urban areas (Cicero et al., 2014). While all demographic groups experienced an increase in heroin use, the highest increases occurred for females, persons initiating use between ages 18-25, persons initiating use after age 26, persons earning between $20,000 and $49,999 annually, non-Hispanic whites, and those with private insurance (CDC, 2015).

A major component of the government's response to the epidemic is the promotion of medication assisted treatment (MAT). Medication assisted treatment includes being maintained on methadone or buprenorphine. Tom Frieden, from the CDC, and Nora Volkow, from the National Institute of Drug Abuse, have promoted the expansion of methadone and buprenorphine (Volkow et al., 2014). Michael Botticelli, Director of the White House's Office of National Drug Control Policy, is also a strong advocate and spoke at the April 2015 convention of persons

who operate opioid treatment clinics (American Association for the Treatment of Opioid Dependence, AATOD) in Atlanta, Georgia. Presently, Drug Courts which fail to offer MAT options are not eligible for federal funding (Grim & Cherkis, 2015; Knopf, 2015; see also Substance Abuse and Mental Health Services Administration (SAMSHA), 2015b). SAMSHA (2012, p. 9), the government agency that regulates MAT, is on record as encouraging the change in perception of opioid agonist maintenance. We are to call methadone maintenance, "Medication Assisted Treatment". According to SAMSHA (2012) "The terms 'substitution treatment' should be avoided because it incorrectly implies that long-acting opioid medication act like heroin and other short-acting opioids", p. 9.

SAMSHA's New Rules

Methadone programs have been operating since the mid-1950s in New York State. Under the Narcotic Treatment Act of 1974, methadone maintenance clinics became legal in the United States, although states vary in state regulations. What is new is that SAMSHA has effectively rewritten the rules on how methadone maintenance clinics are run. Whereas the law of 1974 limited methadone to those who had been addicted for a year, the SAMSHA (2012, Tip 43; 2015, p. 22) guidelines allow for those who are not physically dependent on opiates to receive methadone. While initially the goal was to wean patients off, SAMSHA (2012, p. 117) advises directors of clinics that when a patient requests a dosage reduction that they should "educate" the patients on the importance of staying on their Medication Assisted Treatment. There is no duration limit on MAT. Moreover, there is no longer a limit on dosage. Given that stress is a reliable precipitant to relapse in drug abusers, SAMSHA discusses increasing dosage during stressful times (see page 77, in SAMSHA's *Tip 43, Medication-Assisted Treatment*). Similar recommendations for not limiting treatment to those who are physically dependent for a

year, no dosage limit, and discouraging discontinuation of buprenorphine are also are found in SAMSHA's recommendations for buprenorphine treatment (SAMSHA, 2004).

Relevance of MAT for Social Workers

Social workers will be part of the professional work force employed in methadone clinics and the professionals providing social services for persons receiving buprenorphine. Social workers currently comprise a sizable portion of the Substance Abuse treatment workforce (Roman, Johnson, Ducharme, & Knudsen, 2006). Moreover, NASW offers a specialty credential in the addictions. Most addiction treatment in the U.S. continues to be dominated by the AA points of view (Fletcher, 2012) and in a national sample of treatment providers, 45% reported being in 12 Step recovery (Rieckmann, Kovas, McFarland, & Abraham, 2011). A major tenant of Alcoholics Anonymous is the promotion of abstinence from mood and mind altering chemicals. In fact, many social workers and counselors employed in the addictions field, especially those who are in AA supported recovery, do not approve of "Medication Assisted Treatment" (Bride, Abraham, Kintzle, & Roman, 2013; Fitzgerald & McCarty, 2009; Rieckmann et al., 2011). Thus, if the current substance abuse workforce is to be involved in MAT, many will need to reevaluate MAT.

The purpose of this paper is to consider the rationale for the shift in the federal government's policy regarding opiate drugs (viz., methadone and buprenorphine) and the validity of this rationale. We will examine whether methadone or buprenorphine maintenance results in compulsive acquisition of these substances. We will consider whether the expansion of MAT will result in an increase in the number of new opiate addicted persons. The paper ends with reflections upon the current shifts in SAMSHA's policies and shifts in the public perceptions of various drugs which have previously been viewed with opprobrium.

A Little Background: the Physiology of Opiate Drugs

In explaining and evaluating the changes in the government's policies regarding the treatment of drug addiction, a frank look at the physiological consequences of these substances is required. The effects differ, depending both on the drugs and whether, and how, they are combined. To help the reader navigate these passages, this section of the paper (the next five paragraphs), offers background information on the body's opiate receptors and the drugs that occupy them. Those familiar with this material can skip directly to the section headed: "What is Medication Assisted Treatment."

There are 3 types of opiate receptors in the body: mu receptors, delta receptors, and kappa receptors. The natural chemicals that bind are, respectively: endorphins, enkephalins, and dynorphin. Dynorphin, a natural chemical in the body, will counter the effects of activation of mu receptor and generally produces effects opposing the activity at a mu-receptor (Bruijnzeel, 2009).

Opiate receptors are wide spread throughout the body. They are found in the spinal cord and in many brain areas as well as on white blood cells and in the neurons in the digestive track. Opiate drugs come in two forms: agonists drugs that act like an endorphin and antagonist drugs that block the action of pharmaceutical agonists and natural endorphins. Opiates, which include opium, heroin, morphine, methadone, fentanyl, OxyContin, and buprenorphine, exert agonist (turn on effects) activity at the mu-type receptor (Lűscher, 2012). The predictable effect of opiate agonist drugs include: a diminution in pain, diminution in distress/anxiety, minor immune cell suppression, itchiness in the skin (attributable to histamine release from a type of white blood cell), constipation, pupil contraction, decreased libido and compromised sexual functioning, suppression of periods, dry mouth, sweating, euphoria/positive mood, an

enhancement in motivated behavior at low dose but sleep induction at high doses, and blurred vision (SAMSHA, 2012, p. 34; Seewald, 2013; Shipton, 2005). Opiates can induce nausea and vomiting but tolerance to these effects builds rapidly (Shipton, 2005). Tolerance also develops to the sexual function side effects and effects on menstruation (Joseph, 1994; Joseph, Stanclilff, & Langrod, 2000).

Overdose. Opiates can suppress the activity of neurons in the breathing centers in the brain stem. Respiratory depression is responsible for drug overdose deaths of many addicts. In a survey of drug users, 64.6% indicated they had witnessed an overdose and 34.6% had experienced an overdose (Lagu, Anderson, & Stein, 2006). Naloxone is an opiate antagonist that will displace heroin, opium, buprenorphine, morphine, methadone from acting on the mu-receptor (O'Connor & Fiellin, 2000). Naloxone can rapidly reverse the respiratory depression induced by an opiate agonist. However, naloxone is gobbled up by the liver faster (with a half-life of 10-30 minutes) than are many opiate agonist drugs. Thus, even when respiratory depression is reversed by naloxone, after the naloxone is out of the body, considerable heroin may still be in the body where it will once again induce respiratory depression. It is important to continue to observe people who have exhibited respiratory depression for hours after their breathing improves (Schumacher, Basbaum, & Way, 2013). Naloxone can be delivered as a nasal spray. SAMSHA is recommending the widespread dissemination of "Opioid Overdose Toolkits" containing naloxone, and instructions (Volkow et al., 2014).

Drug withdrawal. When exposed to continuous opiates, the proteins involved in countering the impact of opiates on the cell are up-regulated. (Cells will attempt to maintain homeostasis.) An abrupt withdrawal of the mu-receptor agonist will yield an overactive cell. Symptoms of opiate drug withdrawal include: nausea, flu like aches, goose bumps, erections in

males, insomnia, lethargy, and increased blood pressure. Opiate withdrawal is not lethal in a healthy person, although it is uncomfortable (Lüscher, 2013; Redmond, Kosten, Reiser, 1983; Tetrault & O'Connor, 2011). Each particular withdrawal symptom is generated by a particular type of cell that has a receptor (a mu-receptor) for receiving a message from an opiate. For example, the cells in the Locus Coeruleus produce increased blood pressure and goose bumps (piloerection) associated with withdrawal, but not the flu like nausea (Mazel-Robison & Nestler, 2012; Nestler, 2004).

What Is Medication Assisted Treatment?

Medicated Assisted Treatment for opiate addiction includes methadone maintenance, buprenorphine maintenance, and maintenance on long-acting naltrexone. Explanations of these treatments are provided.

Methadone. Methadone is a synthetic drug which acts as an opioid agonist drug at mu-receptors throughout the body. It is administered orally in the form of a syrup. It was synthesized during World War II when Europe was looking for alternatives to the opium poppy for pain treatment. Its use as a MAT was pioneered by Vincent Dole and Marie Nyswander in New York state during the 1950-60s (Joseph et al. 2000; SAMSHA, 2012). Methadone has a longer duration of activity (24-36 hours) than heroin so that patients only need to dose once per day in order to forestall withdrawal symptoms in contrast to heroin which requires administration 3 times per day (Joseph et al., 2000; SAMSHA, 2012, p. 28). As a consequence, patients are able to sustain employment (SAMSHA, 2012, p. 17).

The side effect profile for methadone is common to all opiate drugs, although side effects are less severe with buprenorphine. Side effects include risk of respiratory depression, constipation with abdominal pain and bloating, sleep-disordered breathing, vomiting, sedation

(Webster, 2013). As with most opiates, methadone will decrease the body's production of estrogen and testosterone (Webster, 2013). Tolerance, over time, to the immune suppressant effects as well as the effects on sexual function does occur when the drug is administered on a reliable basis (Joseph, 1994).

In the last 20 years, data has emerged showing that outcomes in Methadone maintenance are much better when dosages are high (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Johnson et al., 2000; Joseph et al., 2000; Hartel et al., 1995). In the early days, those who ran methadone maintenance clinics often did not approve of maintaining patients on a drug (Joseph, 1994). Presently, federal regulations suggest no restriction on the duration of time in treatment, and federal guidelines prohibit a cap on the level of medication so that positive treatment outcomes (viz., retaining patients in treatment, avoiding relapse, preventing the emergence of withdrawal symptoms) can be ensured (SAMSHA, 2015).

In terms of dosage levels, SAMSHA suggests desirable target dosages should abolish craving and abolish withdrawal symptoms. However, if the patient is overly sedated, then the dosage should be reduced (SAMSHA, 2012, p. 70-82). Many drugs (e.g., antifungals, benzodiazepines, SSRIs, antibiotics) compete for the same metabolizing enzyme in the liver thereby decreasing the rate of elimination (Webster, 2013). Thus, particular drugs can increase the effectiveness of methadone so that lower doses suffice to achieve the targeted effect. Conversely, methadone can increase the effective dose of particular HIV medications (McCance-Katz, Sullivan, & Nallani, 2010).

The perception that methadone will not produce a euphoric "high" (Steiker, et al., 2013) and that it will preclude the capacity for getting high from heroin (Joseph et al., 2000) is sometimes encountered. According to Dole, Nyswander, & Kreek (1966), methadone is

supposed to be administered consistently at high enough dosage levels such that tolerance develops which will preclude euphoria if heroin is taken. This is referred to as a "blockade". In the 1966 article, Dole et al. presented data consistent with their hypothesis.

Buprenorphine. Buprenorphine is a derivative of the opium poppy (*Papaver somniferum*). Its backbone is similar to the shape of morphine and it has other "side chain" atoms attached. It will displace other opiate agonists (morphine, heroin) from the mu receptor, although it will be displaced by naloxone (Cowan, Friderichs, Straβburger, & Raffa, 2005; Walsh & Middleton, 2013).

Buprenorphine is available as a mono-preparation (Subutex) which comes in the form of a capsule. Experience suggests that some addicts will remove the capsule's contents and try to inject the contents with a hypodermic needle. To prevent this, the pharmaceutical house (Reckitt-Benckiser) has devised a way to limit injection use. Suboxone contains both naloxone and buprenorphine. Suboxone is delivered in a form that is placed under the tongue. Only the buprenorphine is absorbed from the mucus membrane in the mouth. If the tablet is crushed and injected, the naloxone effect predominates. Thus, the Suboxone preparation precludes high potency delivery. A new buccal preparation applied to the gums is also available from Reckitt-Benckiser (Phillips & Preston, 2013). Generic Suboxone pills became available in 2009 and Zubsolv is approved for use in office-based practice (Johanson, Arfken, di Menza, & Schuster, 2012).

Buprenorphine has been characterized as an antagonist at the opioid kappa receptor and as a partial agonist at the mu-opioid receptor. The characterization of buprenorphine as a partial mu-receptor agonist may provide a false impression that buprenorphine in contrast to heroin or morphine is not really an opiate. In fact, the characterization of a drug in this way is somewhat

misleading. According to Cowan et al. (2005, p. 18), "it seems inappropriate to describe buprenorphine with terms such as partial agonist or agonist-antagonist, which in any case are not very helpful since they are highly test-dependent." A drug can be a full activator in one type of tissue whereas it is a partial agonist in other areas of the brain, spinal cord, or other areas of the body.

A great deal is now known about how receptors for various neurotransmitters operate as well as where a particular drug binds to and influences a receptor. There are inhibitory proteins, called regulators of G protein signaling (RGS), which curtail the activity of an opiate drug or natural chemical at a particular mu receptor. Neurons at various locations differ in whether they have these RGS proteins associated with their mu receptors. Traynor (2012), who works on RGS proteins, argues that buprenorphine's partial agonist impact at the mu receptor may be because of its unique interaction with RGS. According to Traynor "depending on the level of RGS protein activity buprenorphine may be seen as a full or partial agonist" (p. 4). It should be noted that buprenorphine is a full agonist in terms of its impact on some measures of pain suppression (Cowan et al., 2005, p. 8).

There are several outcomes on which buprenorphine is a partial agonist. In contrast to other opioid agonists such as heroin or morphine, buprenorphine does exert less activity in the breathing centers in the brain stem. Thus, respiratory depression and death are less likely to occur with buprenorphine than with other opiate agonists (Dahan, 2005). However, when used in combination with alcohol, valium-type drugs (benzodiazepines), or antipsychotics, lethal overdoses have been reported (Kintz, 2001; McCance-Katz, Sullivan, & Nallani, 2010; Shipton, 2005).

Another outcome on which buprenorphine appears to be a partial agonist is in the suppression of particular withdrawal symptoms. If those who are addicted to heroin and using very high doses substitute buprenorphine for heroin, then withdrawal symptoms will ensue (Preston, 2005). Transitioning a client from heroin to buprenorphine must be done carefully to avoid the discomfort of withdrawal.

Various mu-receptor agonist drugs can be compared with each other. With regard to withdrawal, buprenorphine withdrawal symptoms are minimal (McCance-Katz et al., 2010; Phillips & Preston, 2013), whereas methadone is associated with more severe and protracted withdrawal than heroin (Gossop & Strang, 1999). Burprenorphine is associated with lower levels of constipation than methadone (Shipton, 2005). Buprenorphine can be administered every other day while methadone requires daily dosing (Leal & January, 2013; Preston, 2005). Patients prefer buprenorphine to methadone (Phillips & Preston, 2013).

The DATA Waiver. Under the Drug Addiction Treatment Act of 2000 and a 2006 amendment, physicians who have received 8-hours of training are allowed to prescribe buprenorphine, a schedule III drug, for up to 30 patients during the first year of practice and then 100 patients per year after that. Treatment can be provided in the context of an outpatient primary practice office. This is referred to as the DATA waiver. If physicians are associated with an Opioid Treatment Program (OTP) certified by SAMSHA, physicians, who have DEA authority to prescribe methadone can also dispense buprenorphine for treatment of addiction in the context of the OTP. Presently, any physician may prescribe methadone (a schedule II drug) or buprenorphine (a schedule III drug) to treat pain without restrictions on numbers. A physician associated with an Opioid Treatment Program, can also prescribe methadone for patients seen in an office setting (Kropf, 2014; SAMSHA, 2012, p. 90). However, only an accredited Opioid

Treatment Dispenser, i.e., a DEA registered pharmacy, can fill a prescription for methadone (SAMSHA, 2012, p. 85). On-line, free continuing education and training is available through Providers' Clinical Support System sponsored by SAMSHA for physicians prescribing opiates for treatment of addition (Knopf, 2014).

Naltrexone. Naltrexone is an antagonist at the mu-type opiate receptor which exerts a longer duration than naloxone. While heroin, methadone, and buprenorphine will bind to an opiate receptor and induce a change in the neuron, naltrexone will bind to the mu receptor on the membrane of the neuron but will not have an impact on the neuron. Naltrexone is being used as a treatment for opiate addiction. Since the purpose of this paper is to consider the rationale for treatments disapproved of by those in Twelve Step Programs and there is little objection to naltrexone, it is beyond the scope of this paper to discuss naltrexone. However, it should be noted that the Cochrane collaboration concluded that naltrexone was, effectively, no better than placebo, largely because fewer than 20% of patients remain in treatment for longer than 6 months (Bart, 2013; Minozzi, et al., 2011). SAMSHA acknowledges the very poor compliance with naltrexone treatment (O'Connor & Fiellin, 2000; SAMSHA, 2012, p. 19). The side effects of naltrexone include anxiety, nervousness, insomnia, headache, joint/muscle pain, and tiredness (SAMSHA, 2012, p. 35). Additionally, naltrexone can only be started after a client has been other opiate abstinent for two weeks (SAMSHA, 2004, p. 6). While longer duration injectable formulations are now available, it is too early to evaluate the efficacy of longer duration preparations (Bart, 2013).

The Rationale for Treating Opiate Addiction with Another Opiate

The major rationale for medication assisted treatment largely rests on harm reduction arguments. Illicit opiate addiction creates a great deal of harm in American society. Injection

drug use does account for 1/3 of HIV cases in the United State and for many cases of infection with Hepatitis C. In fact, between 60-90% of those who have injected drugs are positive for hepatitis C virus (HCV) (SAMSHA, 2012, p. 7). Opiate use accounts for 1/3 of the money spent in the Criminal Justice System (SAMSHA, 2012). As discussed earlier, the number of opiate drug overdoses has risen sharply. Studies suggest that when MAT (methadone) programs provide adequate doses (about 100 mg/day), patients are retained in treatment (Mattick, Breen, Kimber, & Davoli, 2009); involvement in the criminal justice system declines so the government saves money (Joseph et al., 2000; Lind, Chen, Weatherburn, & Mattick, 2005); heroin relapses decline (Johnson et al., 2000; Mattick et al.,2009); new infections with HIV decline (Gowing, Farrell, Bornemann, & Ali, 2004; Metzger, Navaline, & Woody, 1998); patients are more compliant with HIV medication schedules (Malta, Strathdee, Magnanini, Bastos, 2008; Spire, Lucas, & Carrieri, 2007); and many return to productive employment (Appel et al., 2001; Joseph et al., 2000). Intermittent heroin suppresses the immune system while stable methadone or buprenorphine doses do not have this effect (Sacerdote et al., 2008). (Immune system suppression is a particular problem for those who infected with HIV or Hepatitis C.) Similar findings of efficacy are found for buprenorphine as for methadone (Mattick, Kimber, Breen, & Davoil, 2008; McKeganey, Russell, Cockayne, 2013). These findings constitute the evidence base for the efficacy of Medication Assisted Treatment.

Heroin is a very dangerous drug. Heroin overdose was the leading cause of death in a cohort group of the addicted followed for 33 years by Smyth, Hoffman, Fan, & Hser (2007), with 8% of the cohort dying by overdose at a much younger age (late 20s and 30s) than from other causes of death. Long term studies of the opiate addicted followed out 20-33 years does confirm the high rate of death at an early age due to risky behavior and overdose (Hser, Anglin, &

Powers, 1993; Vaillant, 1973). Cohort studies and comparisons of overdose death before and after expansion of MAT suggest that overdoses decline with MAT (Brugal et al., 2005; Langendam, van Brussel, Coutinho, & van Ameijden, 2001; Schwartz et al., 2013), although buprenorphine is more effective than methadone on decreasing overdose deaths (Schwartz et al., 2013).

In the U.S., opiate agonist treatments are limited to methadone and buprenorphine. In Europe, some Medication Assisted Treatment programs provide long-acting morphine or heroin (Strang, Groshkova, & Metrebian, 2012). Europeans view provision of a patient's drug of choice as treatment. Reduced-harm outcomes, similar to those observed with methadone and buprenorphine maintenance, are observed when addicts are supplied with heroin in a structured manner from treatment centers (Strang et al., 2012).

Assumption that addicts cannot achieve a stable life without some type of opiate. Vincent Dole and Maire Nyswander, pioneers in the development of methadone maintenance clinics, argued that exposure to opiate drugs permanently altered the addict's body in such a way that abstention was no longer possible (Dole, 1988). The only way to normalize physiology and return an addict to productive citizenship was provision of a drug that could continuously stimulate mu-receptors. SAMSHA seems to have accepted a similar assumption with regard to continuous opioid agonist treatment. SAMSHA's (2012, p. 117) recommends discouraging those who wish to pursue withdrawal from MAT. Citing Magura and Rosenblum (2001; see Joseph 1994, for similar citations) that 80% of those who leave MAT treatment relapse within a year of treatment termination, SAMHA's goal is to retain clients (SAMSHA, 2012, p. 78). With regard to a client's request to lower a dosage, SAMSHA (2012, p. 78) recommends "These situations require physicians or other staff members to educate patients and their significant

others about the importance of adequate dosage and how individual differences in absorption, body weight, metabolism, and tolerance can affect the dosage necessary to achieve stability."

Can sobriety ever be achieved? There are data both "for" and "against" Dole and Nyswander's assumption that heroin addicts can never achieve sustained sobriety. Data from soldiers returning from Viet Nam, present a contrasting version to Dole and Nyswander's prediction. Forty-five percent of all soldiers returning from Viet Nam had used heroin, and 20% of those who had used it became addicted. After returning to the United States only fifty percent of those addicted in Viet Nam tried opiates in the States, with 12% having short period of state-side addiction and only 5% continuing to be addicted during the three year follow-up interval (Robins, 1993).

In addition to the data from the Viet Nam veterans, several studies of a California cohort speak to the possibility of long term abstinence in those who were at one point addicted to heroin. Hser et al. (1993) conducted a study with a sample size of 581 addicts from the California criminal justice system, only 10% of whom were engaged in methadone maintenance. They found that years later, if death at an early age was avoided, sizable percentages did not test positive for opioids. The numbers were as follows: 37.8% interviewed at 10 years out and 41% interviewed at 20 years out did not test positive for opiates; at 20 years out, 18.9% of Hser et al. sample had been opioid abstinent for at least three years. In a subsequent 33 year follow-up of the same sample, 79.3% were negative for heroin and 46.7% had been abstinent for more than 5 years. On the other hand, even after 15 years of abstention, ¼ of opiate addicts did relapse (Hser, Hoffman, Grella, & Anglin, 2001).

Many of the recent longitudinal studies addressing long term outcomes of opiate addicts fail to distinguish whether clients are in methadone programs and thus the data are not relevant to

evaluating probability of sobriety without treatment. However, an early study conducted when methadone maintenance was less available found that 21.6% who were living in the community, were not using narcotics at the 20 year follow-up (Nurco, Bonito, Lerner, & Balter, 1975). Of those who elected to leave methadone treatment in an early Dole and Nyswander study, 34% were doing well without criminal or drug involvement at two-year follow-up (Joseph et al., 2000). Thus, there is considerable variability in the "natural course" of the disease.

An early rationale for methadone proffered by Dole and Nyswander was that opiates change the brain (Dole, 1988). Similar arguments regarding chemicals changing the brain are made for other chemicals of abuse. For the most part, the addiction literature suggests that the same brain changes are common to all drugs of abuse (Nestler, Hyman, & Malenka, 2009; Sankey, Dobrin, & Roberts, 2011; Sankey & Nestler, 2011; Volkow & Li, 2011). If this is the case, we can look to rates of sobriety for alcoholics and stimulant abusers. If they do not die, many alcoholics do achieve meaningful sobriety (Vaillant, 1995). The logic then supports the expectation of eventual sobriety for some opiate addicts. Some explanation of why the brain changes induced by opiate use is so much more extreme than brain changes induced by other drugs needs to be advanced before dismal outcomes are assumed to be "just part of the disease".

Consistent with the possibility of more severe brain changes induced by opiates as opposed to other drugs of abuse, short term recovery rates for those who abuse opioids are lower than for those who abuse stimulants and less than 5% of heroin addicts seek treatment voluntarily (Hser et al., 1993; Hser, Evans, Huang, Brecht, & Li, 2008). This might reflect more severe brain changes in those abusing opioids than those who abuse other drugs (viz., alcohol and cocaine). It is also possible that these rates may reflect the differences of various drugs in the physical effects on the body. Heavy drinking and cocaine are very punishing on the body

both in the long and short term. In contrast, opiates derived from the poppy family, when not associated with use of unsterile injection methods and when associated with a reliable access so withdrawal is avoided, produce limited damage on the body (DaSilva & Hazar, 2011; Friedman, 2011; Haber & Batey, 2011; Kwasnicka & Haber 2011). Moreover, as attested to by the favorable employment patterns of many persons in MAT, and the fact that motor vehicle problems are not elevated in MAT patients, opiates, when consumed on a routine basis, exert little impairment of function (Joseph et al., 2000). Unlike other drugs of abuse (viz., alcohol and stimulants), opioids have fewer inherent downsides on the body.

Can findings from drug-addicted cohorts of earlier times be extrapolated to the new population of addicts? In contrast to the rather limited recovery rates for heroin addicts from older studies, Magura (2009) raises the question of whether these findings can be generalized to prescription opioid abusers, a new population of persons addicted to opiates. It should be noted that the new addicts can also include seniors. Compton and Volkow (2006) also state, "Most of what we know about opioid abuse and addiction has been learned from heroin addiction in 20 to 40 year old individuals", p. 104. Thus, whether the current new population of addicts will be more similar to addicts who returned from Viet Nam, the addicts who initiated their addiction with street heroin, or different from both, is unclear. McKeganey et al. (2013) present findings suggesting that those in MAT remain dependent on opioids for a longer period than do those who are not involved with MAT. Magura, similar to the McKegancy et al. (2013), questions whether participation in methadone maintenance will further solidify the drug dependence of prescription opioid abusers.

A Closer Look at Why People in Twelve Step Recovery Object to Methadone and Buprenorphine

People in Twelve Step programs pursue freedom from all mood and mind altering chemicals. The assumption is that using one addictive chemical will undermine abstinence from one's drug of choice. SAMSHA (2012) suggests that "The terms 'substitution treatment' should be avoided because it incorrectly implies that long-acting opioid medication act like heroin and other short-acting opioids", p. 9. In this section, we'll consider whether buprenorphine and methadone are different from other opiates. We will consider whether medication assisted treatment results in addiction defined as compulsive pursuit of chemicals.

Issue of Addiction. The concept of addiction has changed considerably in recent times. At an earlier point, addiction was defined as physical dependence on a chemical. Particular drugs that are taken continuously but then discontinued abruptly can result in the emergence of very troublesome symptoms (withdrawal symptoms). However, with the realization that many drugs (lithium, antipsychotics, antidepressants) are associated with withdrawal symptoms but do not lead to compulsive use has led to the abandonment of physical dependence as the core feature of addiction (Nestler, 2004; Nestler, Hyman, & Malenka, 2011; Sankey & Nestler, 2011). As discussed previously, methadone and buprenorphine are associated with withdrawal phenomena. However, withdrawal phenomena are no longer considered the defining feature of addiction.

Neuroscientists such as Eric Nestler, Peter Kalivas, Marina Wolf emphasize compulsive drug seeking as a more accurate defining characteristic of addiction (Everitt & Wolf, 2002; Kalivas & Volkow, 2005; Nestler, 2004; Sankey & Nestler, 2011; Wolf, 2002). A current view of addiction is that the drug has captured the brain's motivational system. An addicted person works for the drug, because the individual's motivational system is a hostage to the drug (Dong

& Nestler, 2014; Nestler, 2004). This characterization comports well with Twelve Step representation of addiction: there is a loss of control and volition (choice) is no longer relevant.

Animal research on addictive drugs suggests the way a chemical is administered can determine whether the same chemical (for example cocaine or amphetamine) results in compulsive drug seeking. When drugs are administered on a regular routine basis, rather than intermittently, in the animal's home cage, compulsive-drug seeking does not occur (Caprioli et al., 2007; Robinson & Berridge, 1993). Coming daily to the methadone clinic and receiving methadone at the same time in a highly familiar setting may capture the extant prevailing conditions for the animals who fail to develop a compulsive use pattern. Thus, methadone and buprenorphine administered under routine conditions may indeed fail to produce the compulsive behaviors which constitute the essential features of addiction.

Opiates Are Not Safe Drugs

The evidence suggests that MAT will decrease the risk of opiate over-dose death for those who can't achieve sobriety. However, methadone and buprenorphine carry their own risks. As mentioned previously opiates can induce respiratory depression. The rates are 0.05% for morphine, 4.0% for methadone, and none for buprenorphine (Shipton, 2005). Not only are opiates associated with respiratory depression, but methadone (but not heroin) is associated with cardiac arrhythmias (Barceloux, 2012). The rate for methadone is 0.78% for torsades de pointes, a severe form of cardiac arrhythmia, and 0.29% for another indicator, QT wave prolongation (Leal & January, 2013; Preston, 2005; Seewald, 2013). Some antipsychotics and antidepressants are also associated with QTc prolongation, compete for the same enzyme for metabolism as buprenorphine or methadone, and thus potentiate the risk of sudden death (Beach et al., 2014; Haddad & Anderson, 2002; McCance-Katz et al., 2010). In terms of opiate medication

overdoses, 22% are associated with simultaneous use of alcohol (SAMSHA, 2015, p. 37) and alcohol makes buprenorphine an unsafe drug (Kintz, 2002). Studies of sudden death in those receiving prescription opiates suggests that concurrent use of opiates with antidepressants, antipsychotics, alcohol, and benzodiazepines potentiates risk (Kintz, 2001; Leece et al., 2015; Zedler et al., 2014; 2015).

Risk potentiation attributable to concurrent use of other chemicals with buprenorphine or methadone is particularly relevant for addicts entering MAT. According to the CDC, the new population of heroin addicts are often poly drug abusers (CDC, 2015). According to Joseph et al. (2000) approximately 20% of those entering methadone programs have extant alcohol problems. In Dole and Nyswander's original sample, 80% of those who were drinking heavily prior to methadone treatment continued to do so during methadone treatment (Joseph et al., 2000). A recent study by Cone (2012) found the about half of methadone clients were supplementing with other drugs. SAMSHA (2012) generally discourages dis-enrolling anyone from methadone maintenance for any reason (p. 179; p. 186) and SAMHSA suggests that urines containing evidence of illicit drug use be called "positive urines" rather than "dirty urines" (SAMSHA, 2012, p. 9).

In terms of limiting the danger for those MAT clients who abuse other drugs, onsite administration of methadone and buprenorphine can be required. The guidelines for buprenorphine specify that clients who abuse or are dependent on alcohol or sedative-hypnotics are not appropriate for office-based treatment (SAMSHA, 2004, p. 42). If overdose deaths of those in MAT are to be avoided, additional effective strategies for ensuring that MAT clients curtail use of other chemicals will need to be in place.

Will the Expansion of MAT Increase the Number of Addicts and Opiate Overdoses in America?

The federal government is committed to expanding the availability of opiate treatment in the U.S. Basically, the current heroin epidemic was initiated by increased availability of opiates initiated by a change in the way medicine was practiced. The journalist, Sam Quinones (2014), tells the story of how the pharmaceutical houses promoted the idea that if a patient was in pain, that patient could not be addicted to an opiate. Key opinion leaders were paid to present the "evidence-base" at continuing education events. The FDA bought the argument that OxyContin, because of its timed released preparation, had little addictive liability. Sales representatives offered coupons to doctors which could be redeemed at pharmacies for free OxyContin. More physicians began assessing for pain and writing prescriptions (Compton & Volkow, 2006; Dhalla et al., 2009; Olsen, Daumit, & Ford, 2006) even for young people (Fortuna, Robbins, Caiola, Joynt, & Halterman, 2010). With more opiates in the family medicine chest, the family medicine chest became the gateway to opiate abuse for young people (Fortuna et al., 2010). Eventually, the downsides to this change in policy appeared. Report of an increase in opiate related overdoses in those filing claims with Workmen's Compensation was noted (Franklin et al., 2005), as well as an increased number of deaths and emergency room visits in the general population (Compton & Volkow, 2006; Dhalla et al., 2009). In 2007, the makers of OxyContin pled guilty to charges of deceptive marketing (Dhalla et al., 2009; Meier, 2007).

With the expansion of Medicated Assisted Treatment, there will be more methadone and buprenorphine in the general population. There are street markets for both methadone and buprenorphine (Clark, & Baxter, 2013; Duffy & Baldwin, 2012). Deborah Sontag (2013), in the *New York Times*, discusses the unscrupulous doctors who have established buprenorphine clinics

where they indiscriminately prescribe similar to the way in which OxyContin clinics increased the sales of OxyContin (as told by Sam Quinones, 2014). Surveys of knowledgeable individuals suggest that the supply of street buprenorphine comes from persons with legitimate prescriptions (Clark & Baxter, 2013; Johanson et al., 2009). From 2005 to 2010, emergency room visits for buprenorphine increased by a factor of 10, half of which involved non-medical use of buprenorphine (Clark & Baxter, 2013). With increased availability, more young people will be tempted toward casual use of chemicals which the federal government calls "medication".

Consistent with the concern that MAT will expand the number of people using prescription opiates, McKeganey et al. (2013) report that the overdoses from methadone exceed overdoses from heroin in some areas in Scotland. According to McKeganey et al. (2013), the health care system in the UK is now more focused on helping people move toward abstinence and continues to label methadone as opioid substitution. Methadone overdoses have also increased substantially since 2000 in the United States and throughout the world (Madden & Shapiro, 2011).

Bottom-lines: the evidence for MAT. A strong case can be made that engagement in MAT does allow people to return to better functioning and will decrease the risk of accidental death for the individual. As MAT expands, it will be important to monitor whether the number of addicts increases and, because the size of the pool of opiate using persons has increased, whether there will be an increase in the number of opiate deaths. Thus, while MAT may be the best "evidence-based" treatment for the individual, the impact of expansion of MAT on society may be another story.

Ambiguities

SAMSHA's recent policies reflect a major shift in strategies for dealing with addiction. As discussed previously, SAMSHA recommends including the severely addicted as well as the less severely addicted for MAT, and abstinence should be discouraged. Attitudes toward a broad range of drugs are changing in American society generally. Medical marijuana is legal in 23 states plus the District of Columbia and four states allow recreational use. Methamphetamine and cocaine are schedule II drugs, but 11% of children are diagnosed with ADHD and 6.1% of American children receive medications, primarily stimulants for ADHD (CDC, 2014). In fact, at a Brains and Behavior lecture presented by philosopher Nicole Vincent (2014) at Georgia State, she promoted the idea that Ritalin use should be required for physicians in practice because it improves performance. As attitudes and laws are changing, the need for some rational basis for deciding those behaviors we wish to encourage or discourage is sorely needed. Many persons in Twelve Step supported recovery are totally opposed to methadone and would not include maintaining physical dependence on an opiate under any definition of recovery. In Europe, some Medication Assisted Treatment Programs provide long-acting morphine or heroin (Strang et. al., 2012). Apparently, Europeans view provision of a patient's drug of choice as treatment. Buprenorphine is in clinical trials for treatment resistant depression (Clinical Trials, 2014; Fava et al., 2016), so the society may soon have to decide whether buprenorphine for the 9.5% of those meeting criteria for depression is acceptable (Kessler, et al., 2005). Opinions vary dramatically. Hopefully this essay will spur discussion so that a consensus on rational policy toward experience-altering substances can be reached.

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