



## **Chasing a Chained Dragon: Methadone Abuse and Misuse**

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According to a report from the National Drug Intelligence Center (NDIC) of the U.S. Department of Justice, the number of methadone-related deaths increased 390% from 1999 to 2004. 2004 was the last year that national data on opioid deaths was available for analysis. Selected data from state health department indicates that methadone poisoning deaths continued to increase through 2006.

### **Death and Diversion**

While the increase in methadone deaths (390%) exceeds the increase in other opioid deaths (90%) during the same time period, the overall death toll is higher for other opioids (i.e., 3,849 methadone-related deaths versus 5,242 other opioids-related deaths in 2004). These “other opioids” include oxycodone (Oxycontin, Percodan, Percocet), morphine, hydromorphone (Dilaudid), and hydrocodone (Vicodin). However, there has been a consistent yearly increase of the percentage of methadone-related deaths within all opioid-related deaths reported to the Centers for Disease Control and Prevention from 1999 to 2004. Methadone-related deaths were 22.2% of the total opioid-related deaths in 1999 (the first year methadone deaths were tracked independent of other opioids); in 2004 methadone-related deaths were 42.3% of the total opioid-related deaths. Most of these deaths can be attributed to the abuse of methadone diverted from hospitals, pharmacies, practitioners, and pain management physicians as methadone is now used more often to treat chronic pain.

Methadone gained popularity among physicians in recent years for treating medical problems such as chronic pain because it's cheaper and longer acting than other

commonly prescribed pain medications such as morphine, Vicodin and OxyContin.<sup>1</sup> The total amount of methadone legitimately distributed to businesses increased from 2001 through 2006. The greatest percentage of this change occurred at the practitioner level, suggesting that pain management and general practitioners are dispensing the drug more frequently for pain management. This increased availability and use of methadone to treat chronic pain seems to be a primary reason behind the above noted increase in overdose deaths from methadone.

Some methadone deaths and nonfatal overdoses occur because physicians may not have properly cautioned individuals about the dangers of taking the drug in ways other than those prescribed, including taking it in combination with other drugs and/or alcohol. Some doctors also wrongly prescribe methadone for temporary pain, such as a migraine headache, menstrual cramps, or a pulled tooth. Methadone's delayed narcotic effect and its lack of a potent high are important reasons the drug can be so dangerous, especially with opiate-naïve patients. “By the time they've actually overdosed, no one is with them to see what's happening,” said Kimberly Johnson, director of the Maine Office of Substance Abuse.

The NDIC report suggested that retail-level distribution of diverted (stolen) methadone may be occurring more frequently than law enforcement reporting indicates. Diversion from pain management facilities, hospitals, pharmacies, general practitioners, family and friends and, to a lesser extent, narcotic treatment programs (NTPs) increased availability, primarily at the retail level. But retail-level methadone is frequently obtained through traditional prescription drug diversion methods such as doctor-shopping, prescription fraud and, to a much lesser extent, rogue Internet pharmacies. Methadone can also be misused by patients being treated for chronic or cancer pain who obtain the drug using legitimate prescriptions. “The availability of methadone for treatment and pain has put people who would not normally be in a position to divert drugs in that position,” said Sgt. Scott J. Pelletier, who works for the

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<sup>1</sup> “In September 2007 the price of 90 tablets of 5-milligram methadone ranged from \$14.82 to \$20.22, the price of 90 tablets of 5-milligram oxycodone ranged from \$65.52 to \$65.77, and the price of 90 tablets of 5-milligram hydrocodone ranged from \$88.58 to \$121.04. Prices were retrieved from the prescription drug cost comparative web site [www.cu.destinationrx.com](http://www.cu.destinationrx.com), endorsed by Consumer Reports.” Quoted information taken from the NDIC report.

Maine Drug Enforcement Agency. For these reasons, methadone has become one of the fastest growing prescription drugs of abuse.

The NDIC report also suggested that methadone deaths received more media attention than oxycodone or hydrocodone-related deaths because of the drug's association with NTPs. They noted that "A 2004 Substance Abuse and Mental Health Services Administration (SAMHSA) study reported that most methadone deaths involve abuse or misuse of methadone diverted in ways other than from NTPs and taken in combination with other drugs and/or alcohol." This point should be emphasized. Although methadone is a safe and effective drug when used as prescribed, when it is misused or abused—particularly in combination with other prescription drugs, illicit drugs, or alcohol—death or nonfatal overdose is likely to occur. It is more likely that methadone dispensed outside of NTPs will be abused. The media attention given to the overdose deaths of Anna Nicole Smith and her son Daniel in 2006 indicated they both used methadone; and methadone was cited as one of the drugs responsible for the death of Daniel.

Public concern over the rise in methadone overdoses led two US senators, Charles Grassley (R-Iowa) and Jay Rockefeller (D-W Va.), to ask for stronger FDA warnings on the drug. "What's happening with methadone underscores how serious it is that the FDA make dramatic improvements to how it scrutinizes drugs after they're on the market," Grassley said. Added Rockefeller: "The serious problem of methadone overdose requires much greater scrutiny and the FDA needs to immediately improve its oversight efforts. For far too long the FDA has been lax on drug safety, which is unacceptable for an agency whose mission is to protect consumers. If the FDA fails to act quickly, Congress must step in and force the FDA to do its job."

In November of 2006, the FDA issued a public health advisory to provide patients, their caregivers and healthcare professionals with safety information to prevent serious complications from methadone use like those noted above. The advisory stated:

Prescribing methadone is complex. Methadone should only be prescribed for patients with moderate to severe pain when their pain is not improved with other non-narcotic pain relievers. Pain relief from a dose of methadone lasts about 4 to 8 hours. However, methadone stays in the body much longer, from 8 to 59 hours after it is taken. As a result, patients may feel the need for more pain relief before methadone is gone from the body. Methadone

may build up in the body to a toxic level if it is taken too often, if the amount taken is too high, or if it is taken with certain other medications or supplements.

The top ten states with the highest percent increase in methadone-related deaths from 1999 to 2004 were: West Virginia (2,400%), Ohio (1,650%), Louisiana (1,500%), Kentucky (1,400%), New Hampshire (1,359%), Florida (1,300%), Oregon (1,250%), Pennsylvania (1,150%), Tennessee (1,150%) and Wisconsin (950%).

### **Sudden Cardiac Death and Methadone**

Several research studies have noted the association of occasional sudden cardiac death while using therapeutic levels of methadone. In “Community-Based Evaluation of Sudden Death Associated with Therapeutic Levels of Methadone,” the authors reported on a 4-year study of all patients with sudden cardiac death who were investigated by the medical examiner in the metropolitan area of Portland, Ore. Only individuals with a therapeutic blood level of methadone were included; patients with recreational drug use or any drug overdose were excluded. Detailed autopsies were conducted, including the detection and quantification of all substances in the blood.

A total of 22 sudden cardiac death cases with therapeutic levels of methadone were identified and compared with 106 consecutive sudden cardiac death cases without evidence of methadone. The most common indication for methadone use was pain control (n = 12, 55%). Among cases receiving methadone therapy, sudden death-associated cardiac abnormalities were identified in only 23% (n = 5), with no clear cause of sudden cardiac death in the remaining 77% (n = 17). Among cases with no methadone, sudden death-associated cardiac abnormalities were identified in 60% (n = 64,  $P = .002$ ). The researchers concluded from these findings that methadone was a likely cause of sudden death. “The low prevalence of identifiable cardiac disease or structural abnormalities in the cases with therapeutic levels of methadone (<1 mg/L) strongly suggests a causative role for methadone in the pathogenesis of sudden cardiac death among this group.”

## **Methadone Maintenance: Treatment or Social Control?**

Methadone is a Schedule II controlled substance, meaning that it has a high potential for abuse, with the possibility of severe addiction following abuse. Under tight restrictions, it was approved for the “maintenance treatment” of opiate addiction in the 1960s. The goal of methadone maintenance treatment (MMT) is to reduce the illegal drug use, crime, death and disease associated with opiate addiction. Less and less do you hear mentioned another original goal of MMT, namely to provide a gradual, controlled decrease in dosage; ultimately allowing the MMT patient to be drug (methadone) free.

High doses of methadone (60 to 120 mg daily) can block the effects of heroin and other opiates, thereby discouraging continued opiate use (and thus decrease its related behavior and health problems) by addicts under treatment with methadone. Standard MMT recommendations suggest at least 12 months of daily use, effectively assuring that tolerance and dependence to methadone will occur. Sixty milligrams is 8 times the recommended daily dosage when methadone is initially used to treat chronic pain in “opiate-naïve” patients.

### ***Harm Reduction/Corrective Treatment***

There is a dramatic lifestyle change in the initial stages of MMT for many people. Testimonies and research suggesting that methadone is a wonder drug that saves lives abound. Stability and the resumption of an almost normal life are possible. Methadone maintenance patients can work in any capacity for which they are trained, live normal lives with their families and, if not infected with HIV or hepatitis C, or afflicted with other potentially fatal illnesses, show improvements in their health status. And if infected, methadone-maintained patients can more easily access medical help than untreated addicts.

There is also a social benefit to MMT, with decreased drug use, reduced addiction-related crime, reduced transmission of infectious diseases and reduced addiction-related mortality. The Institute of Medicine and the National Institute of Health have indicated “that methadone maintenance with relevant ancillary services is the most effective treatment for opiate addiction.” No more illegal activities to obtain your drug; no more chaos; a return to normal living. Sounds like a dream come true. But methadone maintenance is a *corrective*, not a *curative* treatment for opiate addiction,

meaning “It may be necessary for patients to remain in treatment for indefinite periods of time, possibly for the duration of their lives.”

Given the high social costs from illegal opiate addiction, and the high rate of relapse to active opiate use among MMT patients attempting to taper off of methadone, a “harm reduction” treatment model of long term and even lifelong opiate replacement has been suggested by some addiction professionals, including the authors of a 2001 review of the outcomes of post discharge patients from methadone maintenance programs (“Leaving Methadone Treatment: Lessons Learned, Lessons Forgotten, Lessons Ignored”). In addition to recommending long term opiate replacement therapy, this study also underscores the sharp differences between an abstinence-based and a harm reduction approach to opiate addicts.

The authors call to reduce the “social stigma” of methadone maintenance treatment and to expand access to it. This recommendation is controversial, especially within the abstinence-based community of addiction professionals who question “the ethics, wisdom, necessity, and expense” of maintaining addicts on opiate replacements such as methadone and buprenorphine (a newer maintenance treatment medication for opiate abuse) indefinitely. Nevertheless, they suggested that: “Until more is learned about how to improve post-discontinuation outcomes for methadone patients, treatment providers and regulatory/funding agencies should be very cautious about imposing disincentives and structural barriers that discourage or impede long-term (chronic) opiate replacement therapy,” and at the same time, not “pressure” patients to accept abstinence by touting its “supposed desirability or superiority.” In other words, find ways to keep opiate addicts in ongoing MMT without them feeling pressured by therapy staff to accept abstinence as a treatment goal. In fact, you should probably discourage patients from setting an abstinence-based treatment goal for an indefinite period of time.

### ***Social Stigma or Social Control?***

Conventional wisdom is that under medical supervision, an extended taper to withdraw from methadone will prevent discomfort. But virtually all the studies of “post-discharge outcomes” from MMT programs reviewed in the article showed high rates of relapse to opiate use. This held true even for those who were identified as therapeutically ready for discharge and approved for a gradual reduction of their

dosage, known as a tapering schedule. Most patients left treatment before completing their tapering schedule. The majority resume active opiate use and illegal activities to support their addiction.

The presence of a “withdrawal phobia,” a fear of experiencing opiate withdrawal symptoms, and a concomitant belief that withdrawal from methadone was more severe or protracted than from heroin, were noted as contributing to MMT patients being fearful or reluctant to taper off of methadone. One study even noted the development of what they said was an “organic mood syndrome” in patients undergoing slow detoxification from methadone maintenance that was associated with “a poor outcome.” So co-occurring mental health issues, as well as irrational or mistaken beliefs about methadone withdrawal and detoxification were contributing factors to the high rates of relapse into active opiate use for patients discharged from MMT.

Or could it be that even when a gradual withdrawal from an addictive substance taken on a daily basis over months and years occurs, there is a concomitant depressed mood, as is evident with the protracted withdrawal of other addictive substances? The “mistaken belief” of a more protracted withdrawal from methadone than heroin has a basis in fact. And in this sense, it could be more severe than heroin withdrawal. Methadone has a slow metabolism and very high fat solubility, making it longer lasting than morphine-based drugs like heroin. Its metabolism rates vary greatly between individuals, up to a factor of 100, ranging from as few as four hours to as many as 130 hours or more. This is apparently due to genetic variability in the production of the associated enzymes. A longer half life with methadone (22 to 25 hours versus 2 to 4 for other agonists) allows for administration only once per day in MMT programs. The analgesic activity of methadone is shorter than the pharmacological half-life; so dosing for pain control usually requires multiple doses per day. Both the increase in overdose deaths from methadone and its reputation as a harder drug to “kick” have a basis in the simple biochemical facts of how methadone is metabolized, some of which make it attractive for use as an opiate replacement drug. And by the way, a “withdrawal phobia” from heroin was one of the original reasons that methadone maintenance was proposed to begin with. Sooner or later you have to unchain yourself from the dragon if you want to be truly free of it.

The study also pointed out that the number of “long term” stable patients (5 years or more of MMT) has never been very large. In fact, nationally, one half of all

admissions to MMT leave within one year; in Texas, three quarters leave within a year. But the authors seemed to feel that certain barriers to opiate addicts remaining in MMT contributed to the high dropout rate. The identified disincentives included program policies and state regulations that discourage long term MMT, poor physical clinical facilities and marginally trained and demoralized staff. Again, the challenge seemed to be for “medical and political leadership” to promote MMT as the “gold standard” for opiate dependency treatment. Staff members need to be highly trained in the benefits of opiate replacement treatment and encouraged to believe that they offer a viable treatment alternative that empowers the opiate addict to find a better life with opiate replacement therapy. The call was to challenge the “stigma” of addiction in general, and methadone maintenance in particular.

It seems that influential members of the medical and political community agree. In order to treat hundreds of thousands of untreated heroin users nationwide, the Institute of Medicine (IOM) and National Institute of Health (NIH) recommended the expansion of existing MMT programs, the training of more health personnel on the benefits of methadone maintenance, and the relaxation of regulations on federal, state and local levels to permit the opening of new programs and the development of new models of treatment for opiate addiction. “Effective medical and political leadership is necessary to reduce the social stigma surrounding addiction and methadone treatment in order to effectively implement these changes.”

### ***Chained to the Dragon***

But could the high dropout rate and failure to retain larger numbers of “long term” stable patients in MMT be the result of methadone maintenance ultimately being a fundamentally flawed approach to opiate treatment? Methadone maintenance, even at the relatively shorter time periods of twelve to eighteen months, attempts to isolate and “treat” opiate addiction by dispensing a Schedule II controlled substance to treat dependency problems with a Schedule I controlled substance: heroin and other Schedule II controlled substances like morphine and oxycodone. Schedule II controlled substances mean that a) there is a high potential for abuse, b) they have a currently accepted medical use in the US, with or without severe restrictions and c) abuse of the drug may lead to severe psychological or physical dependence. Schedule I controlled substances also a) have a high potential for abuse, but b) have no currently accepted

medical use in the US. MMT “treats” dependency to heroin, a substance with a high potential for abuse, with methadone—*another* substance with a high potential for abuse and psychological or physical dependence!

But is this “treatment” or an attempt at social control? Long term, daily methadone use essentially ensures physical dependency on the drug; and creates a pool of “patients” who face potential lifelong maintenance treatment. Instead of being at the mercy of drug dealers, MMT patients are at the mercy of the medical and treatment personnel who dispense methadone. As the saying goes: “It was sweet as honey in my mouth . . .” Methadone is the “honey” made available to the opiate addict: freedom from the pain of withdrawal; a chance to live an almost normal life; a chance to stop the madness of chasing the dragon. And it is honey . . . for awhile; then it turns to vinegar: “. . . but when I had eaten it my stomach was made bitter.” (Revelation 10:10)

By the time the opiate addict realizes that he’s simply traded chasing a free dragon for a chained one, it’s often too late. Unfortunately for him, the dependency to methadone forms much more slowly than to heroin or morphine and he often doesn’t recognize the dependency until after it develops. He then adds methadone to his list of abused and dependent drugs, perhaps without even realizing he’s dependent. But methadone can be a tougher drug to “kick” than heroin and other opiates. Remember the longer acting half life of methadone? Also, how many opiate addicts are well-supplied enough with their opiate of choice to avoid withdrawal pangs for even 12 months straight, let alone 24 or 48 months. The methadone addict who seeks to eventually withdrawal from methadone and remains abstinent has to walk through a gauntlet of their own making: a daily methadone intake for the entire time they were active with MMT. No wonder so many fail to complete their tapering schedule.

The social context of receiving methadone at a NTP is different, and perhaps better, than buying heroin on a street corner, but the reality is the same for the addict: if they don’t get their drug, they’re going to go through withdrawal. So the methadone addict (for that’s what a MMT patient becomes) learns to do what they have to do to get their drug and avoid withdrawal; sometimes by remaining compliant with clinic expectations and sometimes by stepping outside those expectations. The so-called rhetoric of a “stigma” associated with methadone treatment reflects a basic philosophical disagreement on addiction treatment between abstinence and harm

reduction treatment models. Opiate replacement promises life, liberty and the pursuit of happiness at the cost of a chain around your neck . . . attached to methadone.

Watch the HBO documentary “Methadonia” for an unflattering look at the lives of several MMT patients in New York City. Steve, one of the persons followed in the film who’s trying to get off of methadone, said “Once they get you hooked, you’re nothing but a junkie. Come get your fix in the morning.” While the methadone addicts in the film are not representative of all MMT patients, you do see a side of MMT that is often ignored by its advocates.

### **The Merry-Go-Round of Cross Addiction**

Another complication with long term methadone maintenance is the frequent abuse of other drugs by MMT patients, particularly tranquilizers (like Xanax and Valium) or crack cocaine. This is not a fringe issue or isolated problem among a few MMT patients and poses one of the more insidious problems with long term methadone maintenance: cross addiction.

Lintzeris, Mitchell, Bond, Nestor and Strang (2007) noted that about 33% of methadone maintenance patients reported using benzodiazepines in any given month. The researchers found that high dose (40mg) diazepam was associated with time-dependent (1 to 3 hours from use) increases in the intensity of subjective drug effects with methadone and buprenorphine. These effects were usually independent of the opioid dose administered. The Lintzeris et al. study further reported that benzodiazepines were present in 40–80% of the opioid-related deaths reviewed for the study.

An Australian research study, “Benzodiazepine Use in Opioid Substitution Treatment,” was done to investigate the safety of benzodiazepines with methadone and buprenorphine. It noted that benzodiazepines were abused by 30 to 70% of methadone patients, with there being little research on their interaction.

An examination of the data available in October of 2000 (reported in “Methadone Maintenance Treatment (MMT): A Review of Historical and Clinical Issues”) indicated that 40% of methadone patients were using cocaine or crack upon admission to the MMT program. A 1970s study of MMT indicated that 20% of the methadone patients had serious alcohol problem upon admission to the program. Another study showed

that “alcohol-related diseases were major causes of death of patients in methadone treatment, and that approximately 23% of the terminations from treatment were related to alcohol.” The review noted that patients with “serious” anxiety and depression problems may abuse illegal substances if they are not properly diagnosed and treated, which should include psychiatric care and medication “as well as detoxification from non-prescription substances.” The medications of choice for treating anxiety are benzodiazepines. The lack of an effective “long-term medical” (think medication) intervention for cocaine addiction was lamented, but a “sharp and significant” reduction in cocaine use was reported in a study of 133 methadone patients who remained in treatment for 18 months and received “adequate doses of methadone.” Can you read between the lines of the report and see that what happened was a slow growing addiction to methadone, resulting in a lessening dependence upon cocaine?

An article in *The American Journal of Forensic Medicine and Pathology*, “A Review of Methadone Deaths in Jefferson County, Alabama,” reported how its authors performed a retrospective study of 101 cases where methadone was detected in the blood when they noticed an increase in deaths resulting from the co-intoxication of methadone and benzodiazepines. Benzodiazepines were the most frequently detected co-intoxicant, found in 60 of 101 cases; just benzodiazepines were found in 30 of these cases. Pure methadone intoxication occurred in 15 cases. A mixture of methadone and non-benzodiazepines were found in the remaining 30 cases. The authors commented that higher levels of methadone could have occurred because benzodiazepines compete with methadone for methadone receptors. Higher levels of methadone could also have occurred as a result of the chronic abuse of methadone and benzodiazepines because over time, benzodiazepines inhibit the hepatic enzymes that metabolize methadone.

## **Conclusion**

Methadone maintenance is a corrective treatment for the high social toll of opiate use; but it doesn’t really treat opiate addiction. It “treats” the legal, medical and interpersonal negative consequences that result from a dependency to heroin and other opiates. But the price paid by the “patient” is that they must gamble on chaining themselves to a slowly developing dragon that may be harder to get away from than

the original chaos and potential death they sought to escape from in active heroin addiction.

*For more information on methadone, see the following sources used in this article:*

“Benzodiazepine Use in Opioid Substitution Treatment”: [http://www.turningpoint.org.au/research/wip/wip\\_2006/Benzo\\_use\\_in\\_opioid\\_substitution\\_treatment.pdf](http://www.turningpoint.org.au/research/wip/wip_2006/Benzo_use_in_opioid_substitution_treatment.pdf)

“Citing Overdoses, Lawmakers Ask FDA for Stronger Methadone Warnings”: <http://www.jointogether.org/news/headlines/inthenews/2006/citing-overdoses-lawmakers.html>

“Community-Based Evaluation of Sudden Death Associated with Therapeutic Levels of Methadone”: [http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6TDC-4RJ8KX9-G&\\_user=10&\\_coverDate=01%2F31%2F2008&\\_rdoc=14&\\_fmt=full&\\_orig=browse&\\_srch=doc-info\(%23toc%235195%232008%23998789998%23678117%23FLA%23display%23Volume\)&\\_cdi=5195&\\_sort=d&\\_docanchor=&\\_artOutline=Y&\\_ct=24&\\_acct=C00050221&\\_version=1&\\_urlVersion=0&\\_userid=10&md5=7098b4040657bc1e97c2900485528f22#sec4](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TDC-4RJ8KX9-G&_user=10&_coverDate=01%2F31%2F2008&_rdoc=14&_fmt=full&_orig=browse&_srch=doc-info(%23toc%235195%232008%23998789998%23678117%23FLA%23display%23Volume)&_cdi=5195&_sort=d&_docanchor=&_artOutline=Y&_ct=24&_acct=C00050221&_version=1&_urlVersion=0&_userid=10&md5=7098b4040657bc1e97c2900485528f22#sec4)

“Increases in Methadone-Related Deaths: 1999-2004”: <http://www.cdc.gov/nchs/products/pubs/pubd/hestats/methadone1999-04/methadone1999-04.htm>

“Leaving Methadone Treatment: Lessons Learned, Lessons Forgotten, Lessons Ignored”: <http://www.mssm.edu/msjournal/68/68162.shtml>

Lintzeris, N., Mitchell, T., Bond, A., Nestor, L. and Strang, J. (2007).

“Pharmacodynamics of diazepam co-administered with methadone or buprenorphine

under high dose condition in opioid dependent patients.” *Drug and Alcohol Dependence*, 91, 187-194.

“Methadone Diversion, Abuse and Misuse”: <http://www.usdoj.gov/ndic/pubs25/25930/25930p.pdf>

“Methadone Maintenance Treatment”: <http://www.cdc.gov/idu/facts/MethadoneFin.pdf>

“Methadone Maintenance Treatment (MMT): A Review of Historical and Clinical Issues”: <http://www.mssm.edu/msjournal/67/6756347.shtml>

“Methadone Medical Maintenance (MMM): Treating Chronic Opioid Dependence in Private Medical Practice — A Summary Report (1983–1998)”: <http://www.mssm.edu/msjournal/67/6756388.shtml>

“Report of the International Narcotics Control Board for 2006”: <http://www.incb.org/incb/index.html>

“A Review of Methadone Deaths in Jefferson County, Alabama”: <http://cat.inist.fr/?aModele=afficheN&cpsidt=13892050>