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## **Women, Pregnancy and Methadone**

**Loretta P. Finnegan**

### *Summary*

The abuse of psychoactive drugs by women of childbearing age has placed an untoward burden on the fetus, new-born and child. This included: marijuana-2.9%; cocaine-1.1%; with lesser percentages of other illicit drugs. Effective methadone maintenance prevents the onset of opioid abstinence syndrome for 24-36 hours, reduces or eliminates drug craving, and blocks the euphoric effects of illicit narcotics. Because of the extremely high risk environment of the pregnant drug-dependent woman, her infant is predisposed to a host of neonatal problems. Infants exposed to methadone in-utero, with mothers receiving prenatal care, generally have higher birth weights and a decreased incidence of premature birth and other medical complications. Infant medical complications are usually influenced by maternal prenatal care, incidence of maternal complications, and multiple drug use by the mother causing an unstable intrauterine milieu complicated by withdrawal and overdose. Infants exposed to methadone generally have a higher incidence and a longer duration of abstinence. The majority of this increased cost has stemmed from drug-affected infants born with significant/major medical needs and premature delivery related to maternal drug abuse. Over three-fourths (77%) of drug-affected infants have had significant/major medical needs compared with 27% of all new-borns. Seventeen per cent of drug-affected infants were born prematurely, compared with 6% of all new-borns. The total cost in 1997 for longer, specialised, and more intensive medical care for Florida's drug-affected infants is estimated at \$ 6.7 million.

When pregnant women abuse drugs, they affect their own health and that of their unborn child.

**Key words:** Women - Pregnancy - Methadone

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The abuse of psychoactive drugs by women of childbearing age has placed an untoward burden on the fetus, new-born and child. In many countries, estimates of the human and financial burden have not yet been calculated, nor have solutions been contemplated or implemented. The use of these psychoactive substances has led to a steadily increasing number of individuals suffering from the chronic, relapsing disease of addiction. This problem affects all socio-economic and ethnic classes within the world population and it is widely recognised that millions of individuals use illicit drugs regularly. Millions more are addicted to nicotine, alcohol or both. Mortality data are greatly influenced as a result of nicotine's role in heart and lung disease, and cancer. The effects of alcoholism have wreaked incalculable damage across generations throughout societies for centuries. Men, women and children continue to suffer as a result of the effects of addiction in destroying families. As the 21st century begins, pregnant, drug-dependent women continue to present to medical facilities after receiving little, if any, prenatal care, so putting their infants at risk through the double jeopardy of in-utero psychoactive drug exposure and the effects of maternal morbidity, including infection, hypertension and anemia.

In the United States, reasonably good estimates of tobacco, alcohol, marijuana, heroin, and cocaine use by Americans are available (12). According to the 1997 National Household Survey on Drug Abuse (15), among a population of 275 million individuals, there were 64 million tobacco users, 18 million alcoholics, 13.9 million users of illicit drugs (80% of these are marijuana users), 810,000 heroin addicts (comprising 180,000 treated with methadone) and 1.5 million cocaine addicts (data reflecting use during the 30 days preceding the survey). The U.S. Centres for Disease Control and Prevention recently reported a 1997 survey which found that 48 million Americans smoke cigarettes (24% of the population).

Numbers of pregnant users of psychoactive agents were systematically calculated in 1992. At this time, of the 4 million births in the United States, the National Pregnancy and Health Study (National Institute on Drug Abuse) found that 5.5 percent, or 221,000, used some illicit drug during pregnancy (15). This included: marijuana-2.9%; cocaine-1.1%; with lesser percentages of other illicit drugs. Most striking was the finding that 18.8% used alcohol and 20.4% smoked cigarettes. In the NHSDA, combining 1996 and 1997 data on pregnant women aged 15-44, 2.5% used illicit drugs, 1.3% were binge drinkers (5 or more drinks on the same occasion at least once in the past month), and 19.9% smoked cigarettes. By contrast, women of the same age who were not pregnant, had percentages of 10.4%, 16.7%, 33.3%, respectively, suggesting that many women resume their drug and alcohol use after giving birth. This drug use by mothers does not provide the most auspicious environment for the new-born infant. Depending on location within the national boundaries, socio-economic status and educational level, these percentages can be much higher or negligible. Whether the percentages are high or low, any form of psychoactive drug use should be discouraged in pregnant women, so that the fetus has the best possible chance of normal development. These data also reflect the fact that any attempt to ascertain direct etiologies of infant morbidity as a

result of some perinatal effect will encounter inherent difficulties due to the nearly universal occurrence of multiple drug use by individual pregnant women.

Medical complications in pregnancies involving drugs are generally quite common due to customary lifestyle and the high incidence of zero prenatal care (4; 7; 14; 16; 18). The most frequent complications encountered in injecting drug users include: infections such as cellulitis, hepatitis A, B, and C, pneumonia, bacterial endocarditis, sexually transmitted diseases and HIV infection; anemia, thrombocytopenia, thrombophlebitis, overdose and multiple injuries from trauma.

With cocaine use, medical complications may include myocardial infarction, cardiac arrhythmias, rupture of the ascending aorta, cerebrovascular accidents, seizures, and a range of psychiatric disorders such as dysphoric agitation. However, with both narcotic and stimulant addictions, there is a high incidence of mental health disorders estimated at 40-60 percent.

Obstetric complications add to the in-utero burden for the fetus, with potential adverse effects upon the new-born. The incidence of obstetric complications in women maintained on methadone is less than that found in heroin users. Fetal wastage occurs as a result of spontaneous abortion, intrauterine death, amnionitis, chorioamnionitis, gestational diabetes, premature rupture of the membranes and septicemia. Placental disorders that may occur include abruption, infarction and insufficiency. Because of the lack of prenatal care, many women are predisposed to pre-eclampsia or eclampsia. The most commonly seen obstetrical complications are preterm birth and intrauterine growth retardation. Addicted women should be closely observed for postpartum hemorrhage.

For three decades, methadone maintenance has been recommended for opioid dependence in pregnancy (5). It has been clearly demonstrated that treatment with methadone, when delivered with comprehensive services that include prenatal care, can reduce the incidence of obstetric and fetal complications, and that of neonatal morbidity and mortality (2). Effective methadone maintenance prevents the onset of opioid abstinence syndrome for 24-36 hours, reduces or eliminates drug craving, and blocks the euphoric effects of illicit narcotics. Methadone maintenance therapy for the pregnant woman also prevents erratic maternal opioid levels and protects the fetus from repeated episodes of withdrawal, decreases women's risk of HIV infection or hepatitis and reduces drug-seeking behaviours, such as prostitution, which increases the chance of sexually transmitted diseases. Methadone-maintained women frequently experience signs and symptoms of withdrawal as pregnancy progresses, and require increasing doses to maintain the same plasma level and remain withdrawal free. Higher doses of methadone in the third trimester have been associated with improved fetal growth and longer duration of gestation; as a result, more liberal methadone dosing in pregnancy may improve initial and long-term neonatal outcome (2; 3; 5; 11).

Drug dependence during pregnancy is not only a perinatal issue but a complex biopsychosocial problem that presents multiple challenges (9). When assessing the impact of addiction on the pregnant woman and ultimately her infant, one must put into

perspective the milieu within which she must survive. The cycle of addiction not only includes illicit and licit drug use, medical and obstetric complications and psychiatric disorders, but also family dysfunctions, physical and sexual abuse, social issues, legal problems and educational deficits leading to employment failure and economic loss. Additional problems that affect drug-addicted women include: poor interpersonal skills, chronic crises and chaos, violence, low self-esteem, past or present prostitution, previous incarceration, ineffective parenting, poor nutrition, lack of organising or problem-solving abilities and homelessness or the lack of a stable environment.

Because of the extremely high risk environment of the pregnant drug-dependent woman, her infant is predisposed to a host of neonatal problems. In heroin-dependent women, a significant portion of the medical complications seen in their neonates is due to low birth weight and prematurity. Therefore, conditions such as asphyxia neonatorum, intracranial hemorrhage, respiratory distress syndrome, intrauterine growth retardation, hypoglycemia, hypocalcemia, septicemia, and hyperbilirubinemia may occur. Infants exposed to methadone in-utero and whose mothers receive prenatal care, generally have higher birth weights and a decreased incidence of premature birth and other medical complications. However, symptoms of neonatal abstinence are common. Infant medical complications are generally influenced by maternal prenatal care, incidence of maternal complications, and multiple drug use by the mother causing an unstable intrauterine milieu complicated by withdrawal and overdose. The latter may predispose the infant to meconium aspiration.

Narcotic abstinence contributes considerably to neonatal morbidity. However, not all infants born to drug-dependent mothers show withdrawal symptomatology. Literature reports indicate a variable incidence between 60 and 90 % (6). It is not surprising to find varying descriptions and experiences in reports from different centres, because the biochemical and physiologic processes governing withdrawal are still poorly understood. Polydrug abuse, erratic drug ingestion, with vague and inaccurate maternal histories and methods of analysing body fluids to detect prenatal exposure, all confound the type, time of onset, duration and severity of symptoms.

Methadone-exposed infants generally have a higher incidence and a longer duration of abstinence. In comparative studies involving heroin exposure, however, doses of heroin were unknown and the figures may not be comparable. Other studies have shown that infants manifest moderate to severe abstinence when their mothers are maintained on adequate doses of methadone (17). Since the relationship between methadone dose and neonatal abstinence severity has been difficult to establish, and the studies have shown inconsistent results, this rationale should not be used to demand low doses during pregnancy. There is no compelling evidence to reduce maternal methadone dose to avoid neonatal abstinence. To do so may promote illicit drug use and increased risk to the fetus, since methadone eliminates the need for illicit opioid use, prevents erratic maternal opioid drug levels, and protects the fetus from repeated episodes of withdrawal.

Narcotic abstinence syndrome is described as a generalised disorder characterised by signs and symptoms of hyperirritability of the central nervous system, gastrointestinal

dysfunction, respiratory distress and vague autonomic nervous system symptoms that include yawning, sneezing, mottling and increased temperature. Initially the infants develop mild high frequency, low amplitude tremors that progress in severity. A high pitched cry, increased muscle tone, irritability, increased deep tendon reflexes and an exaggerated Moro reflex are all characteristic of the syndrome. The rooting reflex is usually strong, and sucking of fists or thumbs is common, yet infants show great difficulty with feeds and regurgitate frequently. The feeding difficulty occurs because of an uncoordinated and ineffectual sucking reflex. The infants may develop loose stools and so become susceptible to dehydration and electrolyte imbalance.

Time of onset of symptoms is variable. At delivery, the serum and tissue levels of in-utero drugs begin to fall. The new-born continues to metabolise the drug(s) and abstinence signs occur when critically low tissue levels have been reached (13). Because of the variation in time of onset and degree of severity, a spectrum of abstinence patterns may be observed. Withdrawal may be mild and transient, delayed in onset or characterised by a stepwise increase in severity. It may be intermittently present, or have a biphasic course that includes acute neonatal withdrawal followed by improvement and then an exacerbation of acute withdrawal. Severe symptoms seem to occur in infants whose mothers have taken large amounts of drugs for a long time. Usually the closer to delivery a mother takes a narcotic, the greater the delay in onset of abstinence and the more severe the symptoms in her baby. The maturity of the infant's metabolic and excretory mechanisms plays an important role since preterm infants generally excrete the prenatal drug(s) more slowly, and seem to show a less vigorous onset. The duration of symptoms varies from a few days to several months.

One advantage regarding the pharmacological treatment of opiate dependence with methadone is that breast feeding can be considered if the mother is not abusing other drugs. Only small amounts of methadone have been detected in the breast milk of mothers on dosages up to 50 mg. Since such small amounts of this medication appear in the breast milk, this is not adequate treatment for the new-born undergoing abstinence. However, the immunologic and bonding benefits of breast feeding are absolutely essential in the opiate-dependent mother. If the mother is abusing drugs, or if there are infections such as HIV or hepatitis, breast feeding is contraindicated.

In the early period of the cocaine epidemic in the late 1980's, there was a rush to obtain information about the perinatal effects. Although many reports give detailed descriptions of the detrimental effects of cocaine on infant morbidity, many have not been substantiated by subsequent studies (1; 14; 16; 18; 19). Assessments of the impact of cocaine on human pregnancy have not always considered other concomitant drug use and associated variables such as poverty, inadequate prenatal and postnatal care, deficient nutrition, varying types of cocaine use, sexually transmitted diseases and the possible presence of toxic adulterants that are mixed with or, used to process, cocaine. Consistent findings of in-utero cocaine exposure include the impact of maternal morbidity, impaired growth, smaller head circumferences, and preterm birth. Inconsistent findings include the occurrence of congenital abnormalities, and abnormal

neurobehaviour. Transient findings include electro-encephalographic abnormalities and tortuous iris vasculature in the eye grounds. Studies are in progress to determine the potential of subtle effects in infants and children as a result of in-utero cocaine exposure.

New-borns affected by maternal addiction often require intensive, specialised and lengthy hospital care, which increases the cost of medical services to infants. A recent hospital costs survey from the Florida Agency for Health Care Administration reported that in 1997 the average cost of care for one drug-affected new-born was \$11,188 (17). This is more than twice the average cost of care for a new-born not affected by drug abuse. The majority of this increased cost stemmed from drug-affected infants born with significant/major medical needs and premature delivery related to maternal drug abuse. Over three-fourths (77%) of drug-affected infants had significant/major medical needs compared with 27% of all new-borns. Seventeen per cent of drug-affected infants were born prematurely, compared with 6% of all new-borns. The total cost of longer, specialised, and more intensive medical care for Florida's drug-affected infants was estimated at \$6.7 million for 1997.

The impact of prenatal drug exposure has many ramifications when pharmacological agents are complemented by varying amounts of maternal medical and obstetric complications coupled with environmental influences. Drug exposure in-utero may be further complicated by the risk of child abuse and neglect, lack of access to medical care, homelessness, loss of caregiver and subsequent foster care (8; 10). The infant is sent home too early for appropriate medical observation, and maternal caregiving ability may not be adequately assessed. Prolonged abstinence, preterm birth or asphyxia may result in tremulousness, agitation and hypertonicity, or hypotonicity with difficulty in eating and sleeping. This predisposes a tenuous maternal-child relationship to failure with the potential for the occurrence of developmental delays, behaviour and learning problems in the child.

Although drug abuse has existed for centuries, in entering the new millennium, an escalation of problems is emerging as a result of the vast numbers of individuals impacted. When pregnant women are abusing drugs, they are affecting their own health and that of their unborn child. The influence of drug abuse is not only of a physical and psychological nature; it also impacts the environment in which the new-born must attempt to survive. We have made great strides in the medical care of new-borns who experience drug exposure in-utero, but there have been inadequate resources for determining the many unknown variables in perinatal addiction that would improve the outcomes of the pregnant woman and her drug-exposed infant. Specialised treatment resources for childbearing women and their children are insufficient and, sadly, many medical professionals do not see this as an important area for their research and treatment efforts. Addiction is a chronic, relapsing disorder which encompasses every system in the human body. The numerous issues to be addressed acutely and the chronic relapsing nature of addiction make the clinician's task enormous when contemplating the rehabilitation of the maternal-infant dyad. The intergenerational transmission of addiction and its multiple problems, including HIV, become inevitable if methadone

maintenance with comprehensive services is *not* provided for the opioid-dependent women and her child. We must endeavour to end the physical, psychological and sociological disabilities resulting from this most pervasive disorder that not only destroys individuals but the fibre of our societies – the family.

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## **Sexual Dysfunction Associated with Methadone Maintenance: Treatment with Bromocryptine**

**Marc S. Shinderman and Sarz Maxwell**

### *Summary*

Sexual dysfunction, a side-effect of methadone maintenance treatment, may be caused by opioid-induced hyperprolactinemia; on this basis, a dopamine agonist could reverse the effect. We treated 34 (23 male; 11 female) patients with bromocryptine, 2.5-10mg/d. 65% of males and 36% of females reported a positive response. Responders and non-responders had a similar age (44 vs 40 yrs), time in MMT (45.5 mos), and use of serotonergic antidepressant therapy (21.1% vs 26.7%). Responders took higher doses of methadone (220.3 vs 165.6 mg/d), and were more likely to be taking bupropion or methylphenidate (42.1% vs 26.7%). Alternative therapies with other dopaminergic agonists are discussed.

Key Words: Methadone Maintenance; Sexual Dysfunction;  
Psychiatric Comorbidity

### **Introduction**

Sexual dysfunction is not an uncommon complaint among patients on methadone maintenance treatment (MMT) (12). Sexual side-effects of medication are seldom spontaneously reported (16, 17); the incidence is thus difficult to accurately determine. When sexual symptoms are attributed to MMT by the patient and are not satisfactorily addressed by the physician, adverse outcomes may result. Cocaine use, the reduction of methadone dosage, and the discontinuation of MMT are some strategies patients may use to attempt self-treatment of sexual dysfunction (SD).

Elevated prolactin levels have been reported in association with the chronic administration of opioid agonists (5, 8, 15, 18, 19, 20) by a mechanism involving the  $\mu$ -

opiate receptor (9,13). Medical conditions associated with hyperprolactinemia (e.g. pituitary prolactinoma) commonly cause sexual dysfunction (4). Bromocryptine (BRC), which decreases prolactin by increasing dopaminergic tone (19), has been utilised in the treatment of pituitary adenomas (4). Decreasing prolactin levels in these BRC-treated patients are correlated with the normalisation of testosterone and other hormone levels, the resumption of menses, the reversal of erectile dysfunction, and the restoration of libido in both sexes (6).

Tagliamonte (personal communication, 1998) reported that 17 male MMT patients complaining of loss of libido and exhibiting high serum prolactin levels responded to BRC therapy with restoration of libido. We thus began to utilise BRC in the treatment of MMT patients suffering from SD. We report herein our clinical experiences with this modality.

### **Methods**

Patients in methadone maintenance treatment were self-referred for a medical evaluation of sexual dysfunction associated with MMT. Patients were evaluated and treated by one of the authors. Patients were included in the study if they had been on MMT for at least six months, were stable on their methadone dose and ancillary medications, did not have a medical condition associated with organic SD (e.g. IDDM), and were willing to take a medication that was not FDA-approved for their complaint. The symptoms evaluated for the purpose of the study were, for males, erectile dysfunction (difficulty in achieving or maintaining an erection) and, for females, lack of libido. Response was measured by patients' reports of subjective alleviation of the target symptoms. Patients were followed with at least monthly physician visits. Data were collected by reviewing the clinical charts. Due to cost concerns, only 4 patients agreed to laboratory evaluation of serum prolactin levels.

### **Results**

Thirty-four patients took bromocryptine; 23 were male and 11 female. The mean age was 41.1 years (range 29-59; 37.8 for females; 44.5 for males). Average time under methadone maintenance treatment was 45.5 months, and mean dose of methadone 196.2 mg/d. The overall response rate was 55.9%. 65% of males and 36% of females had a positive response to BCR therapy. The non-responders did not differ from responders with respect to age (40 vs 44 yrs), time on MMT (45.5 vs 45.5 months), or use of selective-serotonin-reuptake-inhibitor antidepressants (SSRIs) (26.7 vs 21.1%). Responders tended to be taking higher doses of methadone (220.3 mg./d) than non-responders (165.6 mg/d), and were more likely to be taking ancillary medications with dopaminergic activity (bupropion and methylphenidate) (42.1% vs 26.7%). 100% of non-responders discontinued BCR before 90 days of tx; most (73.3%) because of non-efficacy. Responders also had a high attrition rate; only 4 (21%) continued BCR up to 90 days. Reasons for discontinuation were sedation (10.6%) and cost (68.4%).

Table 1. Characteristics of patients under MM treated for sexual dysfunctions		
	Non-responders n=15	Responders n=19
Age	40.4 years	43.9 years
Time on in MMT	45.5 months	45.5 months
Methadone Dose	165.6 mg/d	220.3 mg/d
Ancillary meds.: Dopaminergic	26.7%	42.1%
Ancillary meds.: SSRI	26.7%	42.1%
D/C for SE of BCR	12.6%	10.5%

## **Discussion**

The data from this clinical survey are preliminary, but we have formed some clinical conclusions based on examination of the trends. It is not surprising that more males than females had a positive response to BCR treatment; this is true in the treatment of SD of any aetiology (10). The tendency for responders to have a higher mean methadone dose than non-responders is somewhat puzzling until it is juxtaposed with the data regarding ancillary medications (Table 1). Responders had a higher methadone dose, and were no more likely to be taking SSRI antidepressants (which may cause SD), but were more likely to be taking ancillary medications with dopaminergic activity. These observations are in agreement with the findings that methadone causes sexual dysfunction via opioidergic stimulation of a dopamine-sensitive system, e.g. prolactin (9,18).

Only four patients had serum prolactin levels performed; the two with lower levels (16 and 21 ng/ml [reference range 0-18 ng/ml]) were non-responders, and the two with higher prolactin levels (22 and 44 ng/ml) responded to bromocryptine treatment. These data are insufficient to allow an attribution of even clinical significance, but the trend continues to agree with the science. It is this consistent agreement with the established scientific findings previously referenced that lends credence to the observations made in this uncontrolled series of cases.

Clinically, however, bromocryptine seems to be a poor treatment, mainly for practical (financial) reasons. There was an acceptably low rate of discontinuation ascribed to side-effects (10.5% of responders; 12.6% of non-responders), and the side effects reported (sedation and nausea) are not difficult to manage clinically. However, an unacceptably high proportion of responders (68.4%) discontinued the medication because of cost. This finding relates to the effectiveness of a medication – a parameter that takes into account not only efficacy but general acceptability of the treatment. Bromocryptine seems to be efficacious, but not effective, in the treatment of methadone-

induced sexual dysfunction.

These clinical findings are encouraging, however, as bromocryptine is certainly not the only dopaminergic agonist available in our pharmacopoeia. We are having good early responses to two of the dopaminergic medications we commonly use in psychiatric treatment of opiate-dependent patients: bupropion and methylphenidate. Patients in the "responder" bromocryptine treatment group were more likely to be taking these medications; response may have been partly due to the action of these ancillary medications. Bupropion is an effective antidepressant, and its dopaminergic profile has been associated with decreased cravings for cocaine (1). In the United States it also has an FDA-approved indication for treatment of nicotine dependence. The hypothesised mechanism of action is, again, dopaminergic alleviation of cravings (14). The use of such an agent could thus have a triple effect: reversing sexual dysfunction, treating depression, and alleviating cravings for other drugs of abuse. Surely the use of bupropion deserves further investigation.

The use of methylphenidate in patients with addiction disease is controversial, but the controversy is based on a misunderstanding of the nature of addictive disorders. The common lay perception of addiction is: The problem with addicts is that they use drugs, therefore the solution to addiction is to remove the drug(s). However, addiction is not a behavioural choice but an Axis I disorder caused by a chemical imbalance in the brain, and judicious pharmacotherapy is usually the most effective treatment for Axis I disorders. Pharmacotherapy is particularly crucial in the treatment of addicts with additional Axis I disorders. There has been interest recently in the high incidence of Attention Deficit Hyperactivity Disorder, Adult Type (ADHD-A) in patients with addictive disorders (3). In the United States, treatment of choice for ADHD, in adults or children, in addicts or non-addicts, is stimulants (11). In patients who have ADHD-A and sexual dysfunction associated with methadone treatment, stimulants may be doubly effective: Treatment of the ADHD-A and alleviation of the sexual dysfunction.

Thus, careful evaluation for psychiatric comorbidity is crucial in choosing the proper pharmacological agent for a patient complaining of sexual dysfunction in association with MMT. A diagnosis of depression would indicate bupropion; that of ADHD-A would indicate methylphenidate as a first line of treatment. Concomitant cocaine abuse would tend to contraindicate the use of stimulants, unless the patient also has ADHD-A, in which case stimulant therapy is indicated (11). A patient with bipolar disorder should be treated prophylactically with mood stabilisers, and monitored carefully.

Another avenue for further investigation is treatment of the weight gain associated with opiate substitution therapy. This effect is also probably related to hyperprolactinemia (7). This side-effect can be severe – 30 to 50 pounds in three to six months is not unusual. It is very distressing to patients, and very difficult to manage. This side-effect does not seem to respond to non-pharmacological treatment (e.g. diet and exercise), and it commonly occurs in patients who have never been overweight before methadone maintenance treatment. We hypothesise that this side-effect may lead patients to abuse

of illicit stimulants (e.g. cocaine), undertreatment (trying to minimise the side-effect by decreasing the dose), and discontinuation of opiate substitution therapy. Because of the association of this weight gain with opioid-induced hyperprolactinemia, this effect may respond to dopaminergic treatment (7). This theory has been advanced for the treatment of weight gain induced by antipsychotic medications (2).

It is arguably true that we are observing greater frequency and severity of methadone side-effects because we tend to treat patients with higher doses than some practitioners. This is possible, as the mean dose for patients in this study (196.2 mg/d) is significantly higher than the average methadone dose for the clinic as a whole (119 mg/d) and very much higher than the average dose in some other clinics. However, this argument is tautological. Most side-effects of most medications are dose-related; this is not an argument for insufficient doses. Naturally patients will have fewer side-effects when treated with homeopathic doses. This is not an indication to withhold efficacious doses. With methadone, as with any other medication, the management of side-effects is preferable to the discontinuation of therapy.

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## **Attitudes and Beliefs Towards Methadone of Staff Working in Substance Abuse Treatment**

**Peter Vossenber**

### *Summary*

This study investigates the possible use of the Abstinence Orientation Scale (AO-scale), which has been developed to study the impact of attitudes towards methadone maintenance treatment (MMT) on treatment retention.

Method: participants at two conferences were asked to complete a questionnaire. Physicians who were known to work on substance abuse treatment received the questionnaire by mail.

Results: 167 persons returned the questionnaire. An AO-scale could be confirmed. Scores recorded for staff groups differed, with physicians working on MMT being least abstinence-oriented. Programme size is correlated with scores on the AO-scale. Scores on knowledge were low among social workers.

Key words: Attitudes and beliefs - Methadone Maintenance

One of the more important parameters for measuring the success of Methadone Maintenance Therapy (MMT) is treatment retention. On leaving treatment, most patients return to the use of heroin (1). In the last few years it is becoming increasingly clear that many factors influence retention. Some of these, such as the need for an adequate dose (10) are almost obvious. The capacity to deliver comprehensive services, such as vocational rehabilitation and medical services, also seems to be important (9).

As early as 1970 (9), both treatment staff and clients saw abstinence as a more desirable goal of treatment than sustained methadone treatment. A few years later (2), the same researcher found that staff viewed methadone clients as even more inferior than before to abstinent clients.

In several recent studies (3; 4) it has been shown that staff attitudes towards MMT

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are a factor that has great impact on retention. In these studies, a distinction is made between an abstinence-oriented and a maintenance-oriented attitude. With the help of an attitude-scale, which has been developed in these studies, programmes or individual professionals can be described as more or less abstinence-oriented. A one-point shift on a five-point Abstinence Orientation Scale almost doubled early dropout from treatment (5). The scale has already been used in several countries: Australia (7), USA (6), Germany (Gerlach R., Caplehorn, JRM, 1997 unpublished manuscript).

This study investigates the possible use of the Abstinence Orientation Scale in the Netherlands. It also compares the scores that would be obtained in the Dutch sample if the US or Australian scales were used.

### **Subjects and method**

The questionnaire contained 33 questions, taken from the Australian questionnaire. Seven questions were added by the investigator. Ten questions that provided an estimate of knowledge regarding methadone treatment were included in this questionnaire. It was distributed at two seminars, and included some items focusing on personal experience with substance abuse (other than tobacco). Because this yielded no extra information, these items were not used in the mailed version. No attempt was made to identify persons or programmes and respondents came from all regions of the country. At present, more than 60 different sites provide methadone. One question on the size of the programme was added, as were questions covering areas like experience and training.

Fifteen medical students (residents) who were completing the last six months of practical training before they obtained their medical degree, were used as a control group. With one exception, none of them had any practical experience of substance abuse treatment. All the students worked in the same hospital. All the physicians who were known to work on substance abuse treatment received the questionnaire by mail. Not all the physicians work on outpatient methadone treatment. The other respondents were attending two seminars, which were held on the same day. One seminar was organised for substance abuse treatment staff in the eastern part of the country; the second seminar was the first of its kind, and was specifically organised for nurses working on substance abuse treatment, mainly MMT. All the data were entered by the author. Analysis was then performed using Statgraphics. The preliminary results are as follows.

### **Results**

At the time of this analysis, 167 persons had returned the questionnaire. At both seminars the response rate was approximately 50%. At the time of this presentation, 50% of the physicians working on substance abuse treatment had responded. This was before a reminder was sent to them.

On average, physicians had been working for 6.9 (SD 6.7) years on MMT, nurses 5.7 years (SD 4.2), social workers 3.3 years (SD 3.4) and other staff 3.7 years (SD 3.4). Physicians and nurses scored above average on knowledge, while social workers and

other professionals scored lower than residents (Table 1). More than half the non-medical staff think that long-term MMT damages kidneys or liver. They also think that methadone worsens depressive symptoms.

Analysis failed to confirm a Dutch Disapproval of the Drug Use scale. Factor

	Average	SD
Physicians	0.742	0.239
Nurses	0.622	0.240
Social Workers	0.410	0.235
Other Professionals	0.427	0.253
Residents	0.461	0.237
ANOVA $p < .0001$		

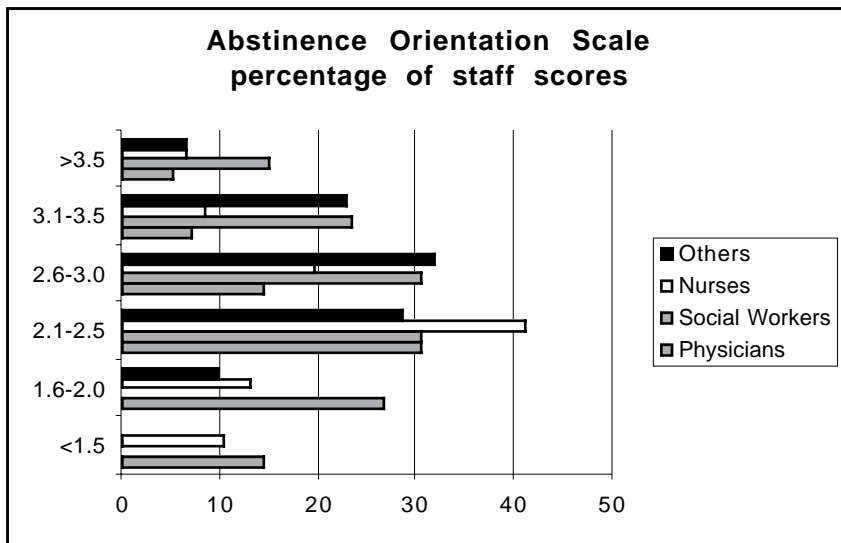


Figure 1. Scores on the Abstinence Orientation Scale: scores grouped in six classes. Lower scores indicate less abstinence-oriented

Table 2. Abstinence Orientation: six most typical statements. Score ranging: 1=disagree completely 5=agree completely				
	Physic.	Nurses	Social Workers	Other Profess.
The main goal of a clinician should be to prepare a MMT patient for a drug-free living (including no methadone): factor loading: 0.82	2.00	2.00	2.54	2.44
A maintenance patient who ignores repeated warnings to stop using cocaine should be gradually withdrawn from methadone: factor loading: 0.78	1.86	2.04	2.46	2.31
A maintenance patient who ignores repeated warnings to stop using heroin should be gradually withdrawn from methadone: factor loading: 0.77	1.81	2.25	3.00	2.28
Abstinence from all opioids (including methadone) should be the principal goal of MMT: factor loading: 0.73	2.37	2.32	3.31	2.50
A MMT patient who no longer uses heroin should be gradually withdrawn from methadone factor loading: 0.70	2.61	2.77	3.23	2.63
Someone on MMT who continues to use heroin should get less methadone: factor loading: 0.65	1.81	2.40	2.85	2.67

	Score	SD
Physicians	2.27	0.73
Nurses	2.49	0.76
Social Workers	2.97	0.56
Other Professionals	2.67	0.51
Residents	3.86	0.49
ANOVA $p < .0001$		

analysis confirms an Abstinence Orientation scale (AO-scale) consisting of 10 items (Table 2). A higher score on this five-point scale indicates a more abstinence-oriented attitude. Residents score significantly higher on this AO-scale, whereas physicians have the lowest score (Table 3 and Figure 1). Correlation of the results, using either the Dutch, German, Australian and USA scales in the Dutch sample, are between 0.91 and 0.94 (Pearson  $r$ ).

There are significant differences in the scores of some medical staff on the AO-scale, which is correlated with the size of the MMT-programme (Table 4). Physicians who do not work on MMT are more abstinence-oriented than physicians who are involved in MMT. Nurses from smaller programmes are significantly more abstinence-oriented than those from larger programmes. After weighting for the number of years spent working in the field and checking for profession, knowledge has no significant correlation with the score on the AO-scale.

## **Discussion**

The score on the knowledge questions is low among social workers and other, non-medical staff. Compared with the scores on similar questions in an Australian sample (5), where an average of 64% of participants staff gave correct answers, in this sample only physicians, with 73%, gave correct answers, scoring significantly higher than average. Social workers recorded the lowest scores on these questions. So far there has been no formal training programme for professionals who start working on substance-abuse treatment. This is true, not only of social workers, but also of nurses and physicians.

The results show that this AO-scale is able to measure differences. The questionnaire, as used here, was not designed to measure differences between programmes. Instead,

Table 4. Score on Abstinence Orientation Scale (medical staff only)		
Size of programme	Physicians n=55	Nurses n=45
less than 50 patients	1.80	3.10
50-75 patients	1.97	2.60
76-100 patients	2.00	2.43
more than 100 patients	2.99	2.21
not working on MMT	2.99	n.a.
ANOVA	p<0.001	p<0.05

differences between groups of professionals have been measured, as well as a possible correlation of AO-scores with programme size.

Social workers are significantly more abstinence-oriented than medical staff, especially physicians. In the Netherlands, much of the most intensive counselling is provided by social workers. It is quite possible that the differences in attitude found between social workers and physicians is sending a conflicting message to patients on the question of methadone.

Compared with results from a survey among New York MMT-programme (7), scores on the AO-scale among professionals in this study are quite similar. However, scores from both doctors and social workers in New York sample are 0.25-0.50 points lower than in the sample chosen in this study. This may indicate that staff in the Netherlands is more abstinence-oriented than staff in New York. A possible explanation for the slightly more Abstinence-Oriented attitude in the Netherlands may be that, until the mid-80's, most programmes were officially aiming for abstinence. This is still reflected by an average methadone dosage of less than 40 milligrams in 1997 (source: IVV), compared with an average dose of 35 milligrams in 1990 (8). In fact, there are several programmes where the maximum dosage is 70 milligrams or less (personal communications).

Physicians who are not involved in MMT seem more abstinence-oriented. This may partly be due to a lack of knowledge. Their score on knowledge is 0.58, compared with an average score of 0.74 for physicians working on MMT. Some of these physicians, however, will sometimes be dealing with patients on MMT, e.g. in inpatient treatment or as a substitute in case of the absence of the physician, who is normally in charge of the programme.

Nurses have more frequent contacts with MMT patients than doctors do. The influence of a nurse on a patient can therefore be quite important. If nurses and physicians working on the same treatment programme have a different attitude towards MMT, this may send a conflicting message to patients.

### **Conclusions**

Despite the superior long-term results of MMT over abstinence-oriented methadone treatment, many still seem to see abstinence as a goal that should be pursued with many patients. A factor that may be influenced relatively easily is knowledge. Staff should be made more aware of the objective benefits of MMT. It also is important that treatment staff, both medical and non-medical, share a similar attitude towards MMT. Because of the important role of local authorities in the funding of MMT, they too should be provided with objective information.

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## **Is Prescribing Higher Doses of Methadone Likely to Promote Elevated Drop-out Rates?**

**Carlo Vetere**

TO THE EDITOR: During my daily reading in various libraries, I have found in the summer issue of JDI, Journal of Drug Issues, published by Florida State University, an article by Wim van den Brink, Director of the Amsterdam Institute of Addiction and Research and Professor of Psychiatry, on the "Medical co-prescription of heroin to chronic treatment resistant methadone patients in the Netherlands" (1). Among the reasons quoted there for the resistance to methadone, is an "unwillingness to give up heroin use by taking higher doses of methadone because higher methadone doses would prevent [patients] from experiencing the euphoric effects of heroin. Consequently prescribing higher doses of methadone is likely to promote elevated drop-out rates". The quotation is from Korf DJ, Lettink D and Bouma, in a paper written in Dutch and published in the Amsterdam Bureau voor Onderzoek en Statisticj, 1998. As the author is a major authority in the field of addiction, this hypothesis about a minority of drug addicts should be taken into consideration.

Might it be advisable to open a discussion?

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## **The Pacific Drug Policy Institute and Research Findings that Led to Its Founding**

**Donald C. Smart**

### *Summary*

The failure of currently employed drug control measures is caused by what I call the “drug/crime subsidy”. Because the drug/crime subsidy is caused by our government’s \$17 billion investment (per annum) in drug control measures. Apologists for the war on drugs argue that the illegal drug could be controlled, if we would just enforce the drug laws. As well as being the primary victims of the drug/crime epidemic, drug users are also major carriers in the contagions of drug use and addiction. Experts estimate that addicts consume 80% of illegal drugs. An estimated 20% of illegal drugs is consumed by recreational or casual drug users. We could eliminate 20% of the drug/crime subsidy by serving the drug-related needs of these users.

Key words: drug/crime subsidy - illegal drug - drug control -  
public health strategy - black market

### **Origin and Mission of the Institute**

PDPI’s mission is to improve the quality of public information relating to the drug/crime epidemic and its control. This is to be done by engaging researchers, educators, and practitioners in the further development of a new interdisciplinary field of drug/crime studies. To expedite the work, PDPI plans to: 1) conduct and fund research on topics necessary to rational policy formation, 2) conduct conferences and seminars, 3) publish monographs on research findings, 4) publish a Journal of Drug/Crime Studies, and 5) manage public dissemination of the information product. Improvement of drug policy is one expected effect of the Institute’s work. The research findings that led to the founding of PDPI are set forth in comparatively weighty writings, referred to below as “the literature”. They are available in hard copy and at the PDPI web-site. This paper provides a quick overview of only the most important findings.

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### **Principal Findings Re Drug/Crime Epidemic**

Surprisingly, the literature includes the first attempt at a comprehensive analysis of the social dynamics of the “drug/crime epidemic” (defined below). The analysis relies heavily on the work of other observers for many details, but it also contains many new insights, and important myths are exploded. The integration of details is unique in the drug policy literature. The findings support two conclusions of major importance: first, that the war on drugs has failed and cannot be fixed, and, second, that the entire epidemic is vulnerable to control by tested, proved and inexpensive public health measures, without legalizing private enterprise in drug manufacturing and distribution. The failure of currently employed drug control measures is caused by what I call the “drug/crime subsidy”. This is defined as the super-profit reward to black-market entrepreneurs for producing and bringing drugs to the consumer market and for promoting drug consumption. Why call profit a subsidy? Because the drug/crime subsidy is caused by our government’s \$17 billion investment (per annum) in drug control measures. These measures induce the scarcity that causes drug prices to range from 70 to 170 times real economic value. The latter numbers mean that the estimated \$70 billion annual drug sales figure consists almost entirely of a subsidy to the crime syndicates. With \$70 billion at their command, the criminals can readily purchase the failure of law enforcement. In fact, in their eager efforts to harvest the drug/crime subsidy, black-market drug suppliers have made drugs readily available everywhere in our society – including our jails and prisons. Apologists for the war on drugs argue that the illegal drug could be controlled, if we would just enforce the drug laws. On the contrary, the failure of drug control in jails and prisons demonstrates that the drug/crime subsidy has made the drug laws unenforceable – even under totalitarian conditions.

The drug/crime subsidy is also the energy source that drives all of the currently rampant pathologies of the “drug/crime syndrome”. The latter is the increase in pathologies that is caused by ongoing drug use under the conditions of war on drugs. The syndrome includes the extraordinary prevalence of all of the following pathologies: drug use and addiction; blood-borne diseases; over-dosing; emergency admissions; school dropouts; educational failure; youth rebellion; prostitution; teen pregnancy; domestic violence; absenteeism; accidents; prenatal injury; gangsterism; gang violence; criminalization of youth; incarceration; husbandlessness; fatherlessness; homelessness; dependency; money laundering; corruption of the criminal justice system, politics and business; and still more. These pathologies complete a vast positive feedback loop\*. They stimulate public demand for drug war measures to “keep drugs out”. As we have seen above, the real effect of these measures is to magnify the economic reward for bringing drugs in and promoting their use.

The drug/crime epidemic, then, is defined as the evolving social catastrophe that embraces 1) the social pathologies of the drug/crime syndrome, plus 2) the causal connections linking these pathologies, plus 3) the entire positive feedback loop that is

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\* A positive feedback loop in an array of events in which each event in the series causes or stimulates its successor, and the last event in the series causes or stimulates the first.

completed by public demand for intensified war on drugs, plus 4) the energy source that drives the loop – the drug/crime subsidy.

### **The General Nature of the Public Health Remedy**

I use the phrase “public health measures” with the same very narrow meaning that the phrase had when first coined: public health measures control diseases by interrupting their contagious processes. In contrast, medical practice treats diseased individuals. Public health measures are also “systemic” – again, in relation to the contagious process, rather than in relation to a disease process in an individual. The pioneers of public health discovered that, to interrupt a contagious process, one must first properly understand the relationships between its three key elements: the agent of the disease, the carrier, and the host (or victim). In yellow fever, a classic example, the disease agent is a virus that inhabits the carrier, a mosquito. The latter transmits the disease to the victim’s blood while feeding on it. Understanding these relationships empowered public health officials to control the contagion by draining mosquito swamps. Similarly, a public health strategy to control addiction must be founded on a proper understanding of the relationships between the disease agent (drugs and the drug culture), the carrier (the black-market drug supply system), and that system’s victims (drug users). As well as being the primary victims of the drug/crime epidemic, drug users are also major carriers in the contagions of drug use and addiction. For this reason, treatment and harm-reduction measures for addicts and drug users act as systemic controls against the contagious processes of all the disorders in the drug/crime syndrome. (We will see how below.) Consequently, the countries that use treatment and harm-reduction measures reap benefits across the board; this shows up in all of their health and social statistics. Our drug warriors make little or no use of these measures, and it shows in our deplorable statistics. On the surface, typical drug war measures may look systemic in relation to the contagion of drug use and addiction. That is, drug interdiction, drug crop destruction, crop substitution, and drug busts do target drugs and their sources. These measures are not systemic. They are based upon a misconception of the epidemic’s real processes, and, as a result, they fail. The misconceptions most responsible for the failure relate to two key relationships: 1) that between the addict and the drug, and 2) that between the addict and the drug supplier. As to the first relationship, drug warriors see addiction as a moral fault, so they prescribe punishment. Punishment fosters addiction: it forces drug use under ground, ruling out early interventions that could nip addiction in the bud; it dooms the addict to repeated jail terms that do not fix the disease. Rather than address the real relationship between the addict and the drug, drug-war policies exclude most addicts from treatment: 1) with long waiting lists, 2) with arbitrarily high admission thresholds, 3) by punishing relapse with expulsion from therapy, and 4) with treatment regimens many addicts find worse than the disease. In contrast, experience elsewhere proves that we get far better results by understanding addiction as a physiologically based, recurrent disease and making treatment readily available. Contrary to the drug-war myth, addicts want and seek treatment. They do use it when it is available. Why not?

It helps them to recover and lead normal, productive lives. Treatment is also much less costly than jail, and it reduces all related pathologies.

As to the relationship between addicts and their drug suppliers, our present massive failure to treat addicts leaves them as the captive money-cows of black-market drug suppliers. The obscene profits gained from exploiting their money-cows motivate drug suppliers to seduce still more victims. Untreated, many addicts are unemployable and must earn the cost of maintaining their addiction (\$10,000 plus per year) through the characteristic crimes of addicts: robbery, theft, prostitution, drug-pushing, and seducing new drug users. These crimes further enrich the criminal syndicates. Experts estimate that addicts consume 80% of illegal drugs. If so, by defining addiction as a disease and providing acceptable treatment on demand, we could: 1) relieve addicts of their worst suffering, 2) eliminate 80% of the \$70 billion drug/crime subsidy, 3) eliminate well over 80% of the related pathologies of the drug/crime syndrome, and 4) cut social costs. Instead, war on drugs fertilizes the mosquito swamp. An estimated 20% of illegal drugs is consumed by recreational or casual drug users. We could eliminate 20% of the drug/crime subsidy by serving the drug-related needs of these users. Overdosing from drugs of uncertain potency would be ended, as well as sickness caused by adulterated black-market drugs.

In face-to-face and day-to-day contact with drug users, an agency empowered to serve their needs would be well positioned to steer them toward less dangerous drugs, to teach self-protective measures, to refer troubled drug users to counselling and therapy, and to encourage early quitting. Instead, we wage war against these primary victims of the drug/crime epidemic, so fertilizing the mosquito swamp. Up to this point, we have looked only at treatment and harm-reduction measures. Still another class of devices for substance control is the governmental (or governmentally-authorized) public health monopoly.

For the first example, let's consider the "state alcohol monopolies". These are used to supply existing demand and prevent private profiteering in drink. All of the Scandinavian countries have extensive experience with this general type of monopoly. So does 1/3 of the United States. Sweden is a good example. Prior to joining the European common market, Sweden prohibited private enterprise in alcohol distribution. That prohibition generated no black-market gangsterism, such as the U.S.A. experienced in the 1920's. The state alcohol monopoly (the Systembolaget) prevented black-market sales by supplying existing demand. In doing so, it also eliminated the economic incentive for the creation of new demand. As a result, Sweden's indices for alcohol-related pathologies ranked with the lowest in the industrial world. Another example: the pharmacy system that is common in the U.S. is a state-authorized public health monopoly. For the protection of public health, the right to engage in sales of pharmaceuticals is restricted by statute to pharmacies under state control. Purchase requires a prescription. The interesting point to us here is that, even though some medicinal drugs have a potential for recreational use, their sale by pharmacies – at normal prices – satisfies existing demand for these controlled substances and eliminates

profit opportunities in black-market sales. The result is that there are virtually none. Pharmacy sales at normal prices also explode the prominent drug-war myth that high prices for the illegal drugs keep them out of the hands of children. If high prices had that effect, kids would be using less. Looking at the long-term trend, they are using more. The obvious explanation is that high prices excite sales efforts enough to overcome the deterrent to demand.

The information presented above is evidence that a new public health strategy is feasible. The agent of this strategy is a monopoly empowered to serve all the drug-related needs of all drug users. The monopoly uses treatment and harm-reduction measures of the sort generally described above to eliminate the drug/crime subsidy and control all the contagious processes of the drug/crime epidemic. The name I have given to this strategy is “market interposition” (MI). I chose this name to call attention to the key characteristic that makes for its success: The agency for drug market interposition (ADMI) is designed and empowered to interpose itself between the supply and demand sides of the market and prevent their mutual stimulation. The interposition is effective when the agency satisfies demand. Under this condition: 1) drug gangsters cannot make enough sales to stay in their dirty business, so they abandon it; 2) there is no economic incentive to seducing new drug users, so that too stops; and 3) in face-to-face contact with drug users, the agency provides or facilitates treatment and harm-reduction measures.

If they are to be prevented from resorting to black-market sources, drug users must prefer the services and products of the agency, so the agency must defeat the black-marketeers in competition for customer loyalty. The literature identifies many ways this can be done, while advancing all relevant public health interests. There is no mystery here: both the alcohol monopolies and the pharmacy system defeat black-market commerce competitively, and they do it with less powerful tools than those proposed here. To illustrate the enhanced competitive power of the ADMI, let us consider the following. The drug supply industry includes a long series of industrial processes. The series starts with the planting of drug crops; it includes harvesting, purification, transport, storage, cutting, packaging, distribution and promotion, and ends with sale to the user. The changes of ownership that take place along the way make up the “drug commerce ladder”. At every stage or rung of this ladder, the respective trafficker must defray extraordinarily high operating costs that are consequent on the condition of illegality. The literature defines these extraordinary costs as “super-costs”, and seven separate categories of such super-costs are described. Not the least of these is “super-profit”. In this context, super-profit is defined as profit in excess of the normal rate, that each black-market entrepreneur on the commercial ladder requires to compensate him for assuming the extraordinary risks of conducting business under the condition of illegality. To sustain the necessary motivation in the entire system, the retail price to the final user must cover the sum of these super-profits and all other super-costs. To strangle the black market, all the ADMI must do is undercut the black market price enough to eliminate the marginal increment of profit that attracts black-market participation. The

ADMI can both do that and generate a positive cash flow because it operates legally, with only ordinary and necessary costs, and without distributing profit. Clearly, surplus revenue would be generated by supplying the needs of casual drug users. The surplus could be used to serve the needs of indigent addicts without cost to them. The analysis has not yet been done to test this point, but the entire program might be self-sustaining! By no stretch of the imagination could net cost remotely approach the \$17 billion now being spent on the drug war. The power to eliminate profit opportunities in illegal commerce makes MI an inherently effective strategy for substance control. Furthermore, since the ADMI has the capability to strangle black market commerce, its managers can be held accountable for any failure to do so. In contrast, drug warriors are never held accountable for the ongoing defeat of drug-war measures: wily and unscrupulous criminals take the blame for that, not the drug-war measures that now indirectly subsidize illegal commerce in drugs. It might be inferred that MI is a more appropriate strategy for use in control of the less dangerous substances. The opposite is true. The more dangerous the substance, the more urgent the need to prevent its unauthorized distribution, and the more compelling is the need to serve such demand as might otherwise make illegal commerce profitable. Not the least of its virtues is that MI works without compulsion and without punishment; it works simply by changing the incentives that influence the behaviour of drug users and suppliers. When we implement MI, illegal drugs will virtually disappear. They will remain available only through the authorized agency, only for licensed use by the initiated, and only under restricted circumstances designed to prevent contagion and to minimize harm. The public health monopolies prove it. Finally, the literature gives some attention to considerations in the design of the ADMI – in particular, to factors affecting choice as to its place in the institutional structure of our society, its powers, its mode of governance, and the MI planning process. At this early stage, there is no fixed recommendation on these matters. Indeed, there is no narrow prescription for any aspect of implementation. One task of PDPI will be to conduct research to support choice in these matters.

### **The Interpositionist Critique of Legalization**

The awful cost and continuing failure of the war on drugs mean that drug policy may be approaching political crisis. MI is not yet recognized as a policy option, so the danger implicit in this crisis is that the public may dump drug war for the visible alternative – legalization. Some free market economists and libertarians mistakenly read the failure of war on drugs to mean that all governmental measures for drug control must fail and breed social disorder. They would cut government out of drug control altogether and allow the drug supply industry to market its wares on exactly the same basis as merchants of ordinary economic goods. On the other hand, not even Milton Friedman, free market economist par excellence, wants to do that. He wants “legalization with controls”. That concedes a role for government. The question becomes “What role?”. Alcohol and tobacco have given us both recent and contemporary experience with “legalization with controls”. In the case of alcohol, two-thirds of our states use alcohol

control boards (ACB's) to regulate alcohol. The history of the ACB's suggests what we might expect, if we were to employ a similar institution to regulate a legalized commerce in drugs. Over time: 1) liquor licenses become very valuable; 2) the licensing process is corrupted; 3) the "regulated" alcohol industry co-opts the ACB; 4) the latter is gradually degraded into an agency merely for alcohol tax collection; 5) impoverished inner city neighborhoods (lacking political clout to defend themselves) are swamped with licensed liquor stores and liquor ads; 6) high rates of alcoholism, alcohol-related social pathologies and cirrhosis intensify the problems of urban poverty and blight, and 7) these sorry results give the government-haters fresh evidence of the inevitability of government ineffectiveness. In the meantime, the Systembolaget does better! No, "legalization with controls" is a formula for government failure. Where profit wars with public health, profit wins.

Legalization would decriminalize drug use and addiction, but do nothing to arrest them. It would end black-market drug commerce (and related evils), but it would let loose a profit-motivated drug supply industry. Legalized drug pushers could not be prevented from promoting and advertising their wares to the young and the gullible, just as today's merchants of alcohol and tobacco do. As in the cases of alcohol and tobacco, high rates of addiction would follow. Drug-induced psychosis, related violence, related spousal and child abuse, accidents from drug-induced incompetence, absenteeism, damage to health, and shortened life – all would at least continue, and maybe increase under the influence of legalized drug-pushing for profit. More, we would have continuing political struggle over minor drug control issues and measures. In all such struggles, the political clout of the drug industrialist would be added to that of the tobacco and alcohol industries.

### **How Interposition Is (and Is Not) Likely To Be Adopted, and Why**

My studies have also addressed how MI might come to be adopted as public policy. My purpose in this study area has been to develop a general plan for the least costly route to policy change, considering major pertinent factors. The evidence to support the resulting plan came from three sources: 1) the standard model that political scientists use to describe the way our society typically processes public policy issues; 2) the history of political struggle and policy change relating to alcohol, tobacco and the currently illegal drugs; and 3) my own experience promoting MI. If correct, the resulting plan will focus effort for MI where it is most likely to be productive, bringing change sooner. As with any guide to action, the test of this plan is pragmatic, and it is subject to change on the basis of new evidence and experience. Abbreviated and shorn of most of the supporting evidence, the key observations or tenets of this plan are as follows.

1) Government forms policy pursuant to the demands of politically dominant constituencies. Therefore, policy change is dependent on changing the dominant constituencies, changing what they want, or both.

2) MI is the reform policy option most capable of uniting a politically dominant coalition for reform: the coalition would ally those who deplore drug war and its effects

with those who want effective means to bar hucksters of stupefying, addicting, and health-endangering products. Policy change can come only when the key constituencies for war on drugs (parent, teacher and employer groups) enter this coalition.

3) For information to rely and act upon, the key constituencies now have the leading ideologues of war on drugs and professionals with career interests in war on drugs. Policy change depends on creating a new source of expert information and policy leadership. To be credible to the key constituencies, the new source must be composed of prominent researchers, academics and professionals from criminal justice, health, economics, pharmacology, treatment, prevention, etc.

4) This new leadership can most quickly come into being through the research, educational, and organizing programme that PDPI has been created to conduct.

5) Very wealthy individuals can greatly expedite the change process by funding the agents of change – PDPI and political action groups motivated by PDPI's information product. With suitable resources supporting the change agents, policy change can come quickly. (For example, in 1930, John D. Rockefeller II switched sides, denounced alcohol prohibition, and launched the movement for the state alcohol monopolies. In two years the job was done.)

6) Appeals to “insiders” or “persons of power and influence” are not realistic alternatives to persuading the key constituencies in the manner described above. On the contrary, until the new information begins to reach the dominant constituencies, only few individuals will be positioned to make any use of either MI or the new critique of drug policy. A few examples point up some real obstacles to this illusory alternative: neither politicians nor drug war bureaucrats are likely to use MI. Politicians must wage war on drugs because the dominant constituencies want it. Bureaucrats are hired to implement adopted policy, not to change or oppose it. Foundations may be unlikely contributors: experience to date suggests that none is presently authorized to support PDPI in its intended role. If this is true, for a foundation to support PDPI, its authorization would have to be revised. Researchers in the drug policy and crime policy areas may not use it; they must serve the established funders, seeking answers to the problems the latter are authorized to pursue. Most academics and workers in drug-related professions will not use it; MI has little application to existing professions. Many may oppose it as contrary to their career ambitions. Others will be reluctant to support an idea that might offend persons in a position to obstruct their future career opportunities. The media are not likely to use it: MI and its potential will remain only a wish among many (and not news) until PDPI is funded to perform its role.

Impediments of the sort just described are not unique to MI. On the contrary, impediments of the same sort obstruct change in all public policy areas. Obversely, in all public policy areas, when change comes quickly, it is in the generic manner described in the first five tenets above.

7) Now, the top priority task in the shortest and least costly route to policy change is building PDPI and its related political action committee, gaining adherents where

possible, and recruiting funders. Whatever their skills, interested volunteers can play roles essential to both of these tasks.

### **An End Note**

Before a thing happens, it looks impossible. Afterwards, it seems to have been inevitable. It is simply harder to foresee the relevant causal processes and how they will shape the future, than it is to reconstruct how we arrived where we are. The reality is that society constantly invents new, and shucks worn-out institutions. Every social institution comes into existence in consequence of some foresight, act of invention and overt action. Just as we are the inheritors of the world built by earlier generations, so will we leave, as our legacy to future generations, the world as our acts will have reshaped it.

Contrary to what the government haters claim, drug war and the failure of drug control are not the fault of government; the buck stops with the electorate. We the people are responsible for the doings of our government. A bygone electorate made a mistake and institutionalized machinery they thought would work for drug control. We can see now how the machinery they created defies their good intentions and breeds social catastrophe. It falls to us in our time to fix it. Happily, we still have the tools that the founding fathers placed at our disposal – the institutions of a self-governing society. The rules of the self-government game require that we choose a plan that provides maximum benefits and minimum detriments for us and our values. Then, if we want to advance our interests and values, we have to act to persuade the majority that our plan serves their real interests too. When we fail to play the game, we betray our responsibility as citizens, and our failure endangers our democratic institutions and the future right of our progeny to govern themselves.

If we fail to fix the drug/crime epidemic, who will fix it, and when? The history of the last seventy years shows that the drug/crime epidemic becomes ever more menacing of social welfare over time – bringing an ever-greater threat of criminal rule. If we fail, will the next generation have a chance to succeed? We must not fail.

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## Discontinuation Symptoms are not Addiction/Dependence

Robert G. Newman

TO THE EDITOR: Another relevant analogy, this time involving the problems associated with termination of antidepressants and the concern that they may be viewed as evidence that the medication is “addictive”. In the *Journal of Psychopharmacology*, vol 13 #3, 1999, is an article by Healy and Tranter entitled “Pharmacological stress diathesis syndromes.” The authors refer to “issues surrounding the use of and problems following the discontinuation of antidepressants” and conclude they are “so different to those that follow opiate or cocaine use or discontinuation that to use the same terms – dependence, withdrawal reactions and addiction – to encompass both seems fundamentally mistaken.” Another article in the same issue is by Haddad entitled “Do antidepressants have any potential to cause addiction?” He concludes : “Despite extensive clinical experience over more than 40 years, including use in high risk groups (drug misusers and those with personality disorders) addiction with antidepressants is virtually unrecognized;” obviously, he does not consider symptoms associated with cessation of antidepressant medication as evidence of “addiction.” And finally, there is an editorial by Haddad and Anderson that concludes : “In summary, the key issue is for the public and health professionals to differentiate between discontinuation symptoms . . . and addiction/dependence. . .”

Seems to me that this type of thinking applies directly to methadone and to the nearly universal criticism that “It’s just another addictive substance” – as evidenced by the fact that if it’s discontinued abruptly withdrawal syndrome occurs. Methadone, I suggest, is no more “addictive” than antidepressants; both types of medications have in common the fact that when they are discontinued the discontinuation per se can cause symptoms; they also have in common the limitation that while they often reduce markedly the symptoms of disease, they do not reverse the disease processes, and relapse after medication stops is common.

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## Take-home and Compliance with Methadone Maintenance Treatment

Pier Paolo Pani and Roberto Pirastu

### *Summary*

One of the most important restrictions placed on patients during methadone treatment is the need for daily attendance at the outpatient unit providing the medication. While this may be obvious for patients beginning the treatment, many patients stabilized on appropriate doses of methadone complain of its interference with their activities (home, work, leisure). To see if take-home methadone promoted the retention of patients in treatment, we compared, on the basis of various demographic and clinical characteristics, the patients enrolled in the take-home programme with those attending the clinic daily. The opportunity to broaden the investigation by including the relationship between take-home policy and retention in treatment partly derived from the law which, between 1991 and 1993, prohibited the take-home option. The comparison of patients with and without the take-home advantage seems to show a longer retention in treatment for the first group, without specifying anything about the role of take-home in promoting retention. Our clinical practice suggests that when sufficient guarantees as to the reliability of the patient exist, take-home methadone practice may be a useful tool for promoting compliance and improving the retention rate of patients in treatment.

**Key Words:** Take home - Methadone Maintenance

By now there is a general consensus on the efficacy of Methadone Maintenance Treatment for opioid addiction. The success of this therapy largely depends on its ability to control the addictive search for, and use of heroin and deal with related problems (such

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as criminality, and psychological and medical complications), by favorably affecting various indicators of psychosocial rehabilitation (1; 2; 5)

The demonstration of the efficacy of the drug on the nuclear symptoms of addictive behaviour does not fully explain the good results achieved. As a matter of fact, the degree of usefulness of any treatment depends not only on a demonstration of its efficacy on symptoms, but also on a demonstration of its acceptance by patients and their willingness to follow it. This last factor represents a critical aspect of any treatment, and is able to affect its results.

The patient's compliance with the treatment is affected by various factors; it partly depends directly on the medication (its desirability, tolerability, etc.) and partly on the demands and restrictions that derive from the drug itself (frequency of administration, the need to carry out medical examinations, etc.), and also from the social setting where the treatment is given (accessibility of treatment services, availability of auxiliary services, cultural attitude toward drug addiction, etc.).

There is a large body of documentation on the desirability and tolerability of methadone. This does much to explain its ability to attract and retain patients in treatment programmes – an advantage not shared by other substances such as naltrexone. As to the demands and restrictions placed on the patient, the case of methadone calls for more detailed investigation for two reasons: a) it is a long-term treatment; b) it implies the use of a narcotic. These two components act in different directions: the first suggests the greatest possible reduction of all programme demands which may interfere with the daily life of the patient; the second suggests the adoption of precautions that aim to avoid the improper use of the drug, particularly its diversion on to the black market.

One of the most important restrictions placed on the patient during methadone treatment is the need for daily attendance at the outpatient unit providing the medication. While this may be obvious for patients beginning the treatment, many patients stabilized on appropriate doses of methadone complain of its interference with their activities (home, work, leisure).

One way to face the problem has been that of allowing reliable patients (those with negative urine, and good social adjustment) the chance to take the medication at home. It is a much-debated choice, above all for the intrinsic risk of facilitating the diversion of methadone on to the black market. In fact, the practice of giving take-home doses of methadone has been adopted in many programmes all over the world. In these situations, the risk of diversion of the medication on to the black market has been controlled through laws and regulations that aim to define the limits of acceptability of this practice.

In Italy the take-home of methadone has gone through several law-related phases: it was allowed until January 1991; then prohibited until April 1993; and has been allowed again up to now. The two years of prohibition came from the enforcement of a national law (Decree 445) which stated that the ingestion of methadone had to take place in the presence of a health professional.

Even though it cannot be said that these sudden changes of legislative orientation arose from scientific uncertainty, we must recognize that take-home practice is one of

the least studied aspects of treatment with opioid-agonists. What little research has been carried out has been focused on the use of take-home as a reinforcer, to facilitate interruption of the use of street opioids and compliance with some of the requirements of the treatment plan: counselling, psychotherapies, etc. (7; 12; 13).. On the other hand, no observations on the validity of this practice for the facilitation of retention in treatment are available. For this purpose we must remember that, since the efficacy of methadone maintenance has only been demonstrated during the course of treatment, a patient's retention in treatment is a pre-eminent indicator of its success (4; 6).

At our out-patient unit, the take-home practice has been a basic component of the therapeutic programme since its inception in 1980. Ethical reasons preclude the implementation of prospective randomized trials that aim to demonstrate its definite benefits. However, the data we have collected have given us the opportunity to clarify some aspects regarding the characteristics of patients who benefit from take-home. Moreover, a more detailed investigation of patients who have been subjected to the restrictive law mentioned above has given us an opportunity to verify the effect of prohibition of take-home on the retention of patients in treatment.

Before analyzing the results of these studies, we will take a quick look at the characteristics of our take-home programme.

### **The take-home programme at the SerT USL 21, Cagliari, Italy**

Since 1980 our service has given assistance to about 5,000 heroin addicts. The prevalent orientation has been that of methadone maintenance treatment. Until the enforcement of Decree 445 (8), the therapeutic plan included the opportunity to take methadone doses home. After six months of complete compliance with the programme, negative morphinuria results included, patients could come to the service once a week to carry out urinalyses, have clinical check ups, take a prescribed methadone dose and take methadone doses home for the rest of the week. The maintenance of the take-home privilege was subject to the maintenance of negative urine results for morphine.

### **Some characteristics of the population in the take-home programme**

To see if take-home methadone promoted the retention of patients in treatment, we compared, on the basis of various demographic and clinical characteristics, the patients enrolled in the take-home programme with those attending the clinic daily. In January 1991, before the enforcement of Decree 445, out of a population of about 1,000 patients, 850 were on methadone maintenance. Of these, 389 were granted the take-home privilege. We compared data collected from the clinical records of 223 patients, chosen at random among those in the take-home programme, with those of 200 patients not involved in the programme (10).

We did not observe significant differences in age, gender, marital status, length of heroin use, or length of methadone treatment. Conversely, we observed a significant difference in employment (75% employed among those in take-home versus 63% among daily attenders) and length of current methadone treatment (4.4 years among

patients in take-home versus 2.8 among daily attenders).

Unfortunately, these results did not allow us to conclude that take-home methadone increases retention in treatment, because another explanation is available – that only those patients who had a better psychosocial adjustment and compliance with the treatment, besides morphine-free urine, entered the take-home programme.

The opportunity to broaden the investigation by including the relationship between take-home policy and retention in treatment partly derived from the law mentioned above; between 1991 and 1993 it had prohibited the take-home privilege.

### **Consequences of take-home prohibition**

In January 1991, before the enforcement of Decree 445, 389 patients were involved in a take-home programme. In a service like ours, which had included take-home as an essential tool of the therapeutic programme, the enforcement of a law which imposed daily attendance at the clinic was a particularly strong stress factor.

The operational choice we made was to warn patients, six months in advance, that the take-home programme had to be interrupted. Whenever possible, we tried to reduce the practical inconveniences related to the enforcement of the new law and to minimize the emotional impact of the changes required, looking for alternative solutions, but confirming the need to comply with the new law.

In order to study the consequences of the change of perspective on the patients who had been allowed to take part of their supply of methadone home, at the end of the 6-month period following notification of the new law we compared retention in treatment of a group of 211 patients, chosen at random among those subjected to the new law, with that of a group of 200 patients, matched for demographic and clinical characteristics and chosen from 430 patients who were in the take-home programme one year before the announcement of the law (11)

The two groups of patients were evaluated at the end of a 6-month period, on the basis of the changes observed, which allowed division into four categories: those interrupting the programme, those continuing on take-home dosages, those assuming methadone daily on the service premises, and those completing detoxification successfully.

The results showed that, in the group of patients subjected to the new law, a significantly higher percentage dropped out of the treatment abruptly (19.9% versus 3.2%) or after detoxification (23.2% versus 3.6%).

It does not seem that these negative consequences were counterbalanced by the percentage of patients who completed detoxification (23.2%). In fact, three years later, we noticed that of these patients 10 were again under treatment and 5 had died.

### **Discussion**

Available studies seem to indicate that the take-home privilege may improve compliance with the treatment (7; 12; 13). Moreover, comparison between patients with and without the take-home advantage, seems to show a longer retention in treatment for the first group, without specifying anything about the role of take-home in promoting

retention (10).

From the point of view of the researcher, the issue of Decree 445 has worked as an "experiment of nature", by giving us an opportunity to study, even if indirectly, the effect of take-home on retention in treatment. The results obtained, though subject to the limitations of retrospective studies, are indicative of negative consequences deriving from the interruption of this practice (11). In support of this hypothesis some arguments can be recalled.

Among long-term psychiatric therapies, methadone maintenance is an exception. In no other therapies are patients systematically obliged to attend the service daily for years, Sundays and public holidays included. For the patient, taking medication at home means being allowed to organize the everyday routine of life on the basis of his or her needs (work, family, leisure, etc.), so it is obvious that the lack of this opportunity can have repercussions on compliance with the treatment. It is not hard to imagine what compliance with treatment in bipolar patients would be like, if they had to go to a psychiatric service every day to assume lithium.

In the case of addicted patients, the condition is worsened by the persistence of a particular sensitivity to events, affective states, and so on, which facilitates relapse (3; 4; 9). We can hypothesize that for patients stabilized at a clinical and behavioural level, the prospect of giving up the social achievements obtained to continue treatment with methadone constitutes a reason for severe stress, which is able to undercut the value of a life without heroin.

In conclusion, our work suggests that when sufficient guarantees as to the reliability of the patient exist, take-home methadone practice may be a useful tool for promoting compliance and improving the retention rate of patients in treatment.

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## **Methadone Dose and Retention in Treatment of Heroin Addicts with Bipolar I Disorder Comorbidity. Preliminary Results**

**Icro Maremmani, Stefania Canoniero, Matteo Pacini**

### *Summary*

We studied 71 opioid-dependent subjects, 19 with additional DSM-IV diagnosis of Bipolar I disorder and 52 with no psychiatric comorbidity. There were significant differences between these two groups regarding the methadone dose required for clinical stabilization, but not in the rate of retention in treatment. Patients with bipolar I psychiatric comorbidity required an average stabilization dose of  $146 \pm 80$  mg of methadone, compared with  $99 \pm 49$  mg/die for patients whose only Axis I diagnosis was Opioid Dependence. In the 990-day period considered there were no significant differences between the two groups of patients in terms of retention on treatment; even so, bipolar I heroin addict patients tend to be less compliant to treatment.

**Key words:** Heroin Addiction - Methadone Maintenance Treatment - Psychiatric Comorbidity - Bipolar I Disorder - Stabilization dosage - Treatment Retention Rate

### **Introduction**

It is clear that substance-related disorders occur frequently in bipolar I patients (1; 22), but only a few studies have investigated the outcome of manic-depressive illness with comorbid substance addiction. Alcoholism was common in bipolar I patients and, if alcoholism predated the onset of the affective illness, patients were less likely to have episodes in the follow-up period than if affective illness predated the onset of alcoholism (23). Alcohol and drug addiction, when present, tend to modify the course and expression of manic-depressive illness, making its diagnosis and treatment more complicated, and producing a poorer prognosis, especially in individuals with rapid cycling or mixed states. It is also has been observed that substance use is more

commonly encountered when these patients are manic than when they are depressed (8). Research also suggested that patients with bipolar I disorder and drug use have an impaired response to traditional pharmacotherapy (1; 6).

The opioid system may play an important role in the etiology and treatment of various mental disorders (21). Most clinicians report antidepressant activity of opioids in depressed opiate addicts, though some contradictory reports exist (2- 4; 7; 15). There are reports of opiates having efficacy in psychotic disorders, panic disorder, and mood disorders; these properties, by themselves, may attract subjects afflicted with the corresponding disorders to self-administer opioid drugs (13; 16; 17; 24). It has recently been reported that methadone can stabilize mood in heroin-dependent patients (14).

The present study looks more closely at the relationship between bipolar I psychiatric comorbidity, methadone stabilization dose and retention rate in treatment. It seeks to determine whether or not patients with and without bipolar I psychiatric comorbidity differ in regard to:

- 1) methadone dose required for clinical stabilization and
- 2) retention in treatment

## **Methods**

### ***Sample***

Patients meeting DSM-III-R and DSM-IV criteria for heroin dependence at the Addiction-Psychiatry Unit of the University of Pisa, were considered. Patients whose medical status or noncompliance precluded substance abuse treatment were excluded. Nineteen subjects (17 males; average age  $27\pm 6$ ) had a bipolar I psychiatric diagnosis in addition to Opioid Dependence. Fifty-two subjects (37 males; average age  $30\pm 6$ ) did not have any additional Axis I or Axis II mental disorder diagnosed, and are defined uncomplicated heroin addicts.

Most of the patients were male (76.1%), and single (73.2%). Only 37.7% were employed (15.9% white-collars and 21.7% blue-collars) and 69.1% had less than 13 years of formal education. Age ranged between 19 and 46 years (mean =  $29\pm 6$ ). There were no physical complications in 9.9%, no working concerns in 29.6%, no family concerns in 28.2%, no legal concerns in 29.6%, no sexual concerns in 70.4%, no leisure time concerns in 39.4%. 81.7% were polyabusers. The mean duration of drug addiction was  $104\pm 73$  months. Patients were followed during treatment for an average of  $337\pm 230$  days (min. 24 max. 990).

### ***Therapeutic protocol***

The Addiction-Psychiatry Unit of the Research Doctorate in Drug Addiction of Siena, Pisa and Cagliari Universities utilizes the following staff and intervention modality: the staff of six consists entirely of psychiatrists, psychiatric residents or Doctors (MD) or Candidates (MD) for a Research Doctorate in Chemical Dependence. Each of these six clinicians spends a mean period of four hours a day in contact with patients. Physicians administer methadone during a brief, time-limited visit. There are

no limits regarding dosage or duration of treatment; take-home privileges are given on the basis of clinical evaluation independently of methadone dose. Physicians provide counselling for patients in conjunction with visits for medication administration. There are no exclusion criteria for addicts who qualify for methadone maintenance treatment.

### **Assessment**

#### **Evaluation of Substance Abuse History Diagnostic**

Diagnostic Evaluation utilized the RSDA (Rating Scale for Drug Addiction) by Maremmani and Castrogiovanni (9). The RSDA is a multi-scale questionnaire comprising the following categories: physical health, mental health, substances abused, substance abuse and treatment history, social adjustment and environmental factors. The Scale rates 10 items: physical problems, mental problems, polysubstance abuse, previous treatment, combined treatments, occupational level, family situation, sexual problems, socialization and leisure time, drug-related legal problems. (The specific variables addressed are: hepatic, vascular and lymphatic pathology, gastrointestinal disorders, sexual disorders, dental pathology, HIV seropositivity; awareness of illness, memory disorders, anxiety disorders, mood disorders, aggression, thought disorders, sensory perception disorders; employment family, sex, socialization and leisure time, legal problems; use of alcohol, opiates, CNS depressants, CNS stimulants, hallucinogens, phencyclidine, cannabis, inhalants, polysubstance abuse; frequency of drug use, pattern of use, phase, nosology; previous therapies; modality, current therapy; and methadone dosage).

#### **Psychiatric Diagnostic Evaluation**

Diagnosis was made by two psychiatrists reviewed by a senior psychiatrist (I.M.) who had access to all clinical information, and reached consensus after independent face-to-face interviews, on the basis of the DSM-IV diagnostic criteria for bipolar I disorders.

#### **Outcome Criteria**

In analyzing the retention rate, a positive and a negative outcome are distinguished. "Positive" outcome refers to complete compliance with programme rules, improvement in social adjustment, having a DSM GAF score of 70-100 and having no more than one episode of positive urine toxicology in the previous thirty days. "Negative" outcome is assessed when these criteria are not met. Substance use was assessed by radioimmunologic assay (RIA) tests for heroin, cocaine, stimulants, and cannabinoids performed on patient urine specimens.

#### **Statistical Analyses**

Comparisons between bipolar I heroin addicts and uncomplicated patients were evaluated by chi-square analysis (categorical variables) and by two-tailed Student's T-Test (numerical items). Retention rates were evaluated by means of "life table" analysis

(according to the Kaplan Mayer Method).

**Results and Comment**

Table 1 shows differences in demographic data and in history of drug addiction of two groups. The majority of Bipolar I heroin addicts were educated for more than 13 years and have a poor economic status. The duration of their addiction and their age at 1st treatment are lower than in only addicted patients. Physical complications are fewer in Bipolar I Heroin Addicts, and none of them are HIV positive. About household concerns they tend to show problems with their partner. They use more alcohol, hypnotics and amphetamines than uncomplicated patients.

Although no differences were found between the two groups regarding the majority

Table 1. Characteristics of bipolar I heroin addicts compared with uncomplicated patients (only p<.05 significant differences are reported)				
	Bipolar I Heroin Addicts n=19	Heroin Addicts n=52	t/chi	p
Duration of Educational process (>13 years)	10/19 (52.6%)	11/49 (22.4)	5.84	.015
Economic status <sup>a</sup>	2.00±.9	2.72±1.1	-2.59	.014
Age at 1st treatment	24±5	28±7	-2.84	.007
Time in addiction (months)	78.47±67.2	124.90±74.5	-2.50	.017
Physical complications	2.15±1.4	3.07±1.9	-2.14	.030
HIV positivity	0/19 (0.0%)	11/52 (21.2%)	4.51	.033
N° of "stable" patients	1/19 (5.3%)	15/52 (28.8%)	7.69	.050
Problems with partner	8/10 (80%)	13/39 (33.3%)	7.07	.007
Alcohol Abuse	15/19 (78.9%)	23/52 (44.2%)	6.74	.009
Hypnotic Abuse	10/19 (52.6%)	12/52 (23.1%)	5.68	.017
Amphetamin Abuse	14/19 (73.7%)	25/52 (48.1%)	3.68	.050
<sup>a</sup> High scores signify good economic status "Stable" patients live in a way that is apparently in conformity with social conventions. They often manage to keep a job, in some cases quite an important one, and they do not get into trouble with the law. They do not wish to belong to groups containing other drug addicts.				

of clinical and toxicological characteristics, subjects with Bipolar I Disorder have fewer organic complications. It is probably the severity of psychopathology requiring a longer hospitalization period that cannot allow patients to have a repetitive addiction behaviour leading to somatic consequences. On the whole, social functioning fails to distinguish between the two groups. The main exception is that the relationships with the partner is more severely impaired in Bipolar I heroin addicts. Within the area of social functioning, occupational activity and leisure time are problematic, but do not differ between the two groups. Although age at the moment of first contact with heroin does not differ between these two groups, age during the 1st treatment and the duration of addiction are lower in Bipolar I Heroin Addicts. Shorter duration of addiction might account for the less severe physical complications in the bipolar I group. No differences are evident between the two groups for history of drug abuse. Most subjects had a daily pattern of use, and had periodic drug-free states and relapses. Both groups were "metabolic drug addicts", according to Maremmani's classification (12). According to the literature, Bipolar I heroin addicts are more frequently polyabusers (1; 22). As widely reported in the literature (18- 20), our subjects' psychiatric comorbidity coincides with an earlier request for help than is found in our uncomplicated patients.

In all patients the most common stabilization dose was 90 mg/day (9.9% of patients), but the curve is skewed in the direction of higher doses. Doses higher than 100 mg/day were common (45.1% of patients); doses higher than 250 mg/day were infrequent (2.8% of patients). Comparison of doses between the bipolar I heroin addicts and uncomplicated patients showed statistical significance ( $99 \pm 49$  vs.  $146 \pm 80$   $T = -2.39$   $P < .026$ ).

The retention rate of bipolar I heroin addicts expressed as a percentage of the total number of patients is high compared with lower-dose programmes (5) and does not differ significantly from that of uncomplicated patients (Log Rank Statistic = .70  $p = .40$ ). We register 5 events and 47 censored subjects (90.38%) in uncomplicated patients, and 3 events and 16 censored subjects (84.21%) in bipolar I heroin addicts during a maximum observation period of 990 and 635 days, respectively. Bipolar I heroin addicts tend to leave their treatment during the first few months; after 140 days none of these patients had left the treatment. For uncomplicated patients the maximum risk of leaving the treatment falls within a range of 170 to 260 days. As reported in Fig 1, the retention rate of bipolar I heroin Addicts is lower than that of uncomplicated patients over the whole observation period. No significant differences were found by stratifying the sample for sex (log rank .57  $p = .44$ ), civil status (married vs unmarried; log rank .54  $p = .46$ ), educational level (> of 13 years vs < 13 years; log rank .58  $p = .44$ ), and job (white-collars vs blu-collars vs unemployed; log rank 1.74  $p = .18$ ).

In a previous study we demonstrated that the methadone stabilization dose is positively correlated with the severity of psychopathology and the aggression scores resulting from patient self-evaluation at the start of treatment (11). We also demonstrated that patients with psychiatric comorbidity tend to stay longer in treatment (10). Patients with psychiatric comorbidity may well associate their never previously experienced improvement in mental health and emotional well-being with methadone, as a medication,

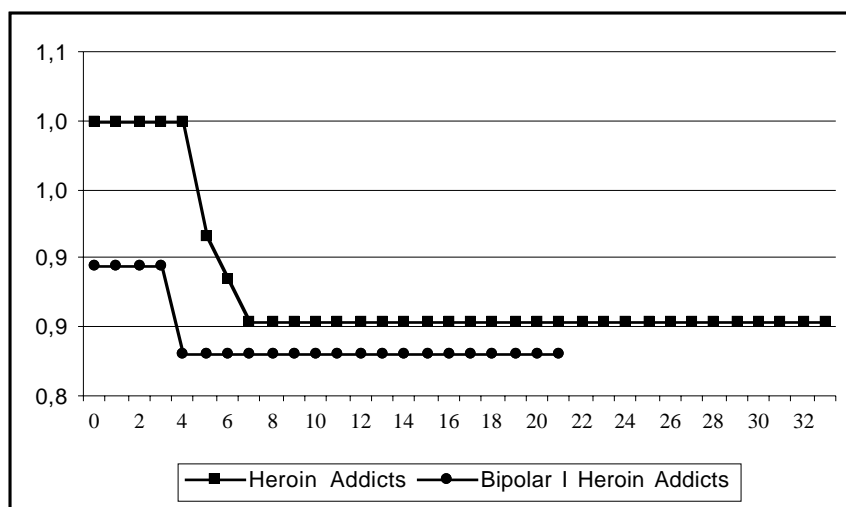


Figure 1. Survival Time on Treatment of Heroin Addicts. Effect of Bipolar I Disorder Double Diagnosis

and so (correctly) fear discontinuing it.

This study suggests that early retention is problematic with patients having psychiatric comorbidity especially with those suffering from Bipolar I disorder. Opioid-dependent patients with Bipolar I psychiatric comorbidity need significantly higher methadone doses during stabilization than those required by addicts with no diagnosis of additional Axis I mental disorder. If they survive early attrition, they tend to stay on treatment longer than those without psychiatric comorbidity, but, among heroin addicts with psychiatric comorbidity, they continue to be at risk both because they tend to leave the treatment and because they are less compliant with treatment.

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## Discontinuation Symptoms are not Addiction/Dependence

Robert G. Newman

TO THE EDITOR: Another relevant analogy, this time involving the problems associated with termination of antidepressants and the concern that they may be viewed as evidence that the medication is “addictive”. In the *Journal of Psychopharmacology*, vol 13 #3, 1999, is an article by Healy and Tranter entitled “Pharmacological stress diathesis syndromes.” The authors refer to “issues surrounding the use of and problems following the discontinuation of antidepressants” and conclude they are “so different to those that follow opiate or cocaine use or discontinuation that to use the same terms – dependence, withdrawal reactions and addiction – to encompass both seems fundamentally mistaken.” Another article in the same issue is by Haddad entitled “Do antidepressants have any potential to cause addiction?” He concludes : “Despite extensive clinical experience over more than 40 years, including use in high risk groups (drug misusers and those with personality disorders) addiction with antidepressants is virtually unrecognized;” obviously, he does not consider symptoms associated with cessation of antidepressant medication as evidence of “addiction.” And finally, there is an editorial by Haddad and Anderson that concludes : “In summary, the key issue is for the public and health professionals to differentiate between discontinuation symptoms . . . and addiction/dependence. . .”

Seems to me that this type of thinking applies directly to methadone and to the nearly universal criticism that “It’s just another addictive substance” – as evidenced by the fact that if it’s discontinued abruptly withdrawal syndrome occurs. Methadone, I suggest, is no more “addictive” than antidepressants; both types of medications have in common the fact that when they are discontinued the discontinuation per se can cause symptoms; they also have in common the limitation that while they often reduce markedly the symptoms of disease, they do not reverse the disease processes, and relapse after medication stops is common.

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Book Chapter:

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