



Pacini Editore & AU CNS

Regular article

Heroin Addict Relat Clin Probl 2010; 12(2): 9-18

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Adherence and social antecedents in relation to outcome in Methadone Maintenance Treatment (MMT)

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Summary

Numerous reports of the effectiveness of methadone in reducing opiate use as well as mortality, criminality, prostitution and the risk for HIV-infection have been published during the last forty years. However, poor adherence to treatment, continuing drug use and increasing rate of premature termination may lead to less than optimal outcome results or in too many cases death. The aim of this paper is to investigate which of the background variables, collected at the admission procedure, that can be used to tell which type of patient will adhere to the treatment regime and succeed or who will fail and who either need special considerations or ought not to be accepted for a methadone treatment (MMT). As much as 86 percent of the compliers in this study did benefit from the treatment and were rated as medium to very much improved according to CGI-I. The group not improved or worse had significantly more background problems such as school problems, a history of non-opioid abuse, many non-MMT treatment episodes, low age at drug debut and opioid debut than the group much or very much improved. Those moderately improved is usually situated somewhere in between the others.

Key Words: MMT; social antecedents; adherence to treatment

1. Introduction

Methadone maintenance is the primary treatment modality for opiate addiction and has been used since the 1960s [8, 9, 26, 31]. Numerous reports of its effectiveness in reducing opiate use as well as mortality, criminality, prostitution and the risk for HIV have been published [10, 11, 38, 17, 14, 20, 4, 15, 1]. During recent decades methadone maintenance treatment has received wide acceptance in many countries with the new object in reducing HIV risk behaviour [1]. Adherence to methadone treatment is associated to low HIV risk behaviour [36].

Although methadone treatment has demonstrated clear effectiveness in treating heroin addicts, poor adherence to treatment [35], continuing drug use and increasing rate of premature termination [24] may lead to less than optimal outcome results or death [17]. Haskew and co-workers [23]

found that 42 percent were partial or poor adherers to their prescribed methadone medication. Some studies report a yearly retention rate below 50 percent in methadone maintenance treatment for injecting heroin users [2]. Lehmann and co-workers [28] tried to predict retention and absence of opiates in the urine. Because they only found foster care before the age of 15 to be associated with success they concluded that until better predictors are available all applying for MMT should be admitted. Maremmani and colleagues [30] showed that there are statistically time effects in methadone treatment. Between three and twelve months of treatment they found that there were a decrease in opioids use and an improvement in clinical status.

The National Swedish Methadone programme in Uppsala had during 1967-1990 a yearly retention rate of 80-100 % (mean 90%) and resulted in 70-80% patients with paid jobs on the Swedish labour market [20, 21, 15]. When heroin

addicts are accepted for methadone treatment it is of great interest to know if there are differences in outcome that are related to background history. Some patients will remain in treatment for years while others will drop out early or will be expelled due to program rule violations or imprisonment [21]. For clinical purpose, at admission, it is important when drawing up the individual treatment plan to know if there is a way to tell which type of background that is associated with treatment adherence and success and which is associated with partial or no recovery. The present paper tries to define the success and failures within our treatment system and to clarify to what extent outcome was associated with various background factors. Outcome was measured by global ratings of clinical success, using the CGI-I (Clinical Global Impression of Improvement) scale by Guy [22]. This rating instrument has been validated by Dhalke et al [7] and Benke & Rasmus [3] and is worldwide used [5].

The aim with this paper is to investigate which of the background variables, collected at the admission procedure, that can be used to tell which type of patient will adhere to the treatment regime and succeed and who will fail and who either needs special consideration or ought not to be accepted for a methadone treatment program. In this study treatment outcome is evaluated by clinicians using a global assessment scale of treated patients. Adherence is operationalized as following the treatment regime in taking the prescribed methadone at correct doses, be mainly free from other drugs and not to be involved in criminality to such level that the patient cannot remain in treatment. Non-adherence is operationalized as not taking the prescribed methadone dose and/or using other illegal drugs and/or involvement in criminality to such an extent that the patient is expelled from treatment.

Good adherence to treatment may increase the possibilities to succeed at lower doses of medication which may decrease the risk for side effects that are dose-dependent and may also decrease the risk of leakage of methadone to the illegal market.

2. Method

2.1 Subjects and procedure

This study includes 345 opiate addicts (102 female and 243 male addicts) admitted to a National methadone maintenance program at the University Hospital in Uppsala, Sweden. Detailed data of the sample are given elsewhere [20]. The set of background data combines variables obtained from medical and official records, criminal justice system and social agencies' registers with self-reported data and filed according to a standardised model developed by Frykholm et al [13]. Subjects were admitted during 1966-1990 with all outcome data prospectively collected. There was a stand-still in intake of new patients during 1979-1984 due to political struggle around methadone treatment in Sweden [19]. Intake

criteria have remained the same since the introduction of this program in 1966 with a minor change when HIV-infection showed up in 1984 [8, 18, 16, 4].

The reliability and validity of data have been examined for congruence by using an admission committee evaluating each admission procedure. All subjects were aware at the admission that the staff already knows their official history as they had given their written permission to collect all obtainable data. At the end of each intake interview a urine specimen was collected.

2.2 Treatment process

Participation in this methadone program was voluntary and the methadone induction phase was with a few exceptions conducted as inpatients at a special unlocked treatment ward with medical trained personnel and social workers. Subjects received a standard medical and psychiatric examination including blood sampling and if needed treatment for withdrawal distress. Mean methadone dose in milligrams was 80 mg followed-up by controlling plasma levels of methadone [24, 20]. In recent years the mean doses have increased to some degree and the present doses are around 100 mg in the program. During their stay at the treatment ward subjects left urine specimens under direct observation on a randomly assigned day and always after longer visits outside the ward. Subjects have weekly individual counselling sessions with paramedical and university trained counsellors who also served as counsellor during the outpatient phase of treatment.

Our program philosophy is non-repressive and favours a rapid return to a working-life in a non-abusing society. Each patient is introduced to the program rules and together with the psychiatrist, and counsellors a complete rehabilitation plan with network system are set up. After the 6 week induction phase each patient are transferred to the outpatient team and now receives his/her daily methadone doses from the local pharmacy, sometimes adjusted according to treatment progress. Urine samples are delivered under observation at a frequency that corresponds to treatment progress. Thus, when the patients adhere to treatment rules and are improving, the frequency of mandatory urine samples will be lowered. Those who do not adhere to the main rules of treatment, such as remaining drug-free and free of criminal activity are running a risk to be expelled from the programme. However, we have earlier shown that those forced to stop taking methadone are at high risk for an early death [17].

2.3 Factors

The study design was based on two factors, Clinical Global Impression Scale (CGI-I) and gender. One special type of global rating scales refers to the change or improvement of patients during treatment after entry of a treatment modality [22].

Clinical Global Impression Scale (CGI-I) is a universally used rating scale for global clinical assessments for disease severity and change of a disease under influence of a treatment [22, 7, 3]. The CGI-I-scale is subdivided into seven grades from marked worsened through no change to marked improvement of a treatment variable. The rating scale has proved to have a high relevance to the individual patient in the evaluation of the efficacy of a treatment program. In a review of 24 different clinical trials the therapeutic impact was measured by global ratings in 14 out of 17 studies [27].

Five counsellors working in the methadone program in Uppsala were asked to rate all patients in the study sample of methadone patients with the CGI-I-scale. Their average clinical experience with methadone treatment was 7.4 years (range 2-17 years). In the preparation before the rating took place each counsellor rated ten other patients in order to become familiar with the scale. During the rating process of the 345 patients each counsellor had beyond their personal experience with the patient's access to all case histories through patient records and other written documents. The instruction to the raters was to take the whole treatment period into consideration with emphasis on the last five years. The interrater reliability was calculated with the average value of the Spearman rank correlation coefficient between the 5 counsellor's CGI ratings to be $r=0.82$ showing good correspondence between the raters, [12].

2.4 Variables

The variables can be grouped into six areas, (1) Heredity with two variables, (2) Childhood and adolescence with five variables, (3) Adult age with three variables, (4) Drug abuse with eight variables, (5) Treatment with six variables and (6) Criminality with four variables.

Heredity comprised two variables; fathers or mother's psychiatric disorder and/or drug abuse. The measure was based on the individuals' self-report and confirmed by means of medical and social agency records, police files and through contact with relatives.

The childhood and adolescence period generated five variables and they were based on the individuals self-report and confirmed by means of medical and social agency records, police files and through contact with relatives. Abnormal childhood experience was a global index and based upon the other four measures in such a way that if the individual had one of the other problems he or she was considered having an abnormal childhood experience. Foster-home was measured as a child below the age of seventeenth living in a home with none of its parents or other close relative. Broken home was measured as coming from a home where the parents were divorced. The variable school problem was measured as being bullied, truancy or having writing and reading problems. Completed compulsory school was defined as the completion of secondary school to eighth or ninth grade depending on

how old the individual was and what the requirement was when he/she was in school.

Adult age generated three variables and they were based on the individuals self-report and confirmed by means of medical and social agency records, police files and through contact with relatives. Own residence was measured as renting or owning the living space. Work experience was measured as having had a paid work of part-time or more. Partner, active addict was measured as having or not having a partner who used illegal drugs.

Drug abuse was described in eight variables and was based on the individuals self-report and confirmed by urinalysis, medical and social agency records, police files and through contact with relatives. If opioid was the first drug was measured as, either the first illegal drug was any opioid or the first drug was another illegal drug (alcohol was not counted). Frequent heroin ODs (overdoses) was measured as having a history of more than yearly heroin OD:s. The presence or absence of a history of non-opioid abuse was measured as use on a more regular basis of illegal drugs other than opioids (alcohol was not counted) and divided into three categories: No additional drug, one additional drug and more than one additional drug.

Age at first drug use was measured as a discreet variable based on the individuals self-reported age and confirmed by means of medical and social agency records, police files and through contact with relatives. Age at first use was defined as the age at first use, whether oral or intravenous, of cannabis, amphetamine, opioids, barbiturates, cocaine or the illegal use of benzodiazepines. Alcohol use was excluded as first use of drugs. Age at first use of opioid was measured as a discreet variable based on the individuals self-reported age and confirmed by means of medical and social agency records, police files and through contact with relatives. Years between drug debut (Yrs. btw. Drug) and opioid debut was measured as the time in years with one decimal between age at first drug and age at opioid use. Years of abuse was measured as the time in years between age at first drug and age at start of methadone maintenance treatment. Years of opioid abuse was measured as the time in years between age at opioid use and age at start of their first methadone maintenance treatment.

There were six treatment variables and they were based on the individuals self-report and confirmed by means of medical and social agency records, police files and through contact with relatives. Short-term hospital treatment episodes was defined as a non-MMT in treatment period of one week or less and long-term hospital treatment episodes was defined as a non-MMT in treatment period of more than one week. Months in treatment community was measured as the time in voluntary or involuntary in drug-free treatment community of various kinds. Age at entering MMT was measured as the age with one decimal when first entering MMT. Age at first treatment was measured as the age with one decimal

Table 1. Presence of background variables of potential importance for the prognosis (heredity, childhood and adolescence, work, earlier treatment, court sentence and drug abuse pattern) in the case histories of 345 MT patients subdivided according to CGI-I rating of improvement

Variable	Total sample N=345	Much or very much improved N=130	Moderately improved N=132	Not improved or worse N=83	Chi (df)
Gender (males)	243 (70)	98 (75)	82 (62)	63 (76)	7.1 (2)*
Heredity					
Psychiatric disorder and/or drug abuse, father§	85 (27)	25 (21)	35 (29)	25 (34)	3.9 (2)
Psychiatric disorder and/or drug abuse, mother§§	58 (17)	18 (14)	23 (18)	17 (22)	2.1 (2)
Childhood and adolescence					
Abnormal childhood experiences	239 (69)	77 (59)	97 (73)	65 (78)	10.4 (2)**
Foster-home	94 (27)	32 (25)	33 (25)	29 (35)	3.3 (2)
Broken home	182 (53)	57 (44)	76 (58)	49 (59)	6.7 (2)*
School problems	222 (64)	67 (52)	89 (67)	66 (80)	18.2 (2)**
Completed compulsory school	254 (74)	110 (85)	93 (70)	51 (61)	15.1 (2)**
Adult age, treatment and criminality					
Own residence	183 (53)	85 (65)	67 (51)	31 (37)	16.4 (2)**
Work experience	232 (67)	97 (75)	88 (67)	47 (57)	7.5 (2)*
Partner, active addict	108 (31)	40 (31)	44 (33)	24 (29)	0.5 (2)
Compulsory treatment	135 (39)	38 (29)	52 (39)	45 (54)	13.3 (2)**
Court sentences	275 (80)	88 (68)	111 (84)	76 (92)	20.4 (2)**
Drug abuse					
Opioid as first drug	79 (23)	37 (28)	24 (18)	18 (22)	4.0 (2)
Frequent ODs	118 (34)	20 (15)	50 (38)	48 (58)	41.8 (2)**
History of non-opioid abuse					
No additional drug	175 (51)	89 (68)	52 (39)	34 (41)	
One additional drug	97 (28)	31 (24)	47 (36)	19 (23)	
More than one additional drug	73 (21)	10 (8)	33 (25)	30 (36)	38.1 (4)**

*p<0.05 **p<0.01

Figures in parenthesis are percent, § n=314, §§ n=337

when the person was first treated in hospital or community treatment. Compulsory treatment was measured as a history of being compulsory in treatment.

Criminality was described in four variables and were based on the individuals self-report and confirmed by means of medical and social agency records, criminal agencies, police files and through contact with relatives. Court sentence was defined as found guilty and sentenced due to criminal activity. Number of probation's was measured as the number of sentence where the punishment was probation. Months of imprisonment was measured as the total number of month received in court sentence. Periods of imprisonment was measured as the number of separated times the individual were sentenced to imprisonment.

2.5 Statistics

Statistical analyses were performed using the SAS program [34]. Two way analysis of variance were conducted for continuous variables and chi-square tests for categorical variables. The mean rating from the five counsellors' on each patient was used in the calculations. Interrater reliability was calculated with the Spearman rank correlation.

3. Results

3.1 Treatment outcome

Table 1,2a and 2b shows background variables of importance for the prognosis according to the CGI-I rating of improvement. The CGI-I rating gave rise to three groups of improvement from methadone treatment, much or very much improved (N=130, 38%), moderately improved (N=132, 38%) and not improved or worse (N=83, 24%).

In earlier studies [21, 20, 17] the patients were grouped according to their status of attendance in MMT. In the present study the sample was grouped according to the CGI-I ratings. We then compared the two ways of group allocation. In the group much or very much improved 15 % (19 individuals) had been discharged due to rule violations or imprisonment and were regarded as non-compliers. In the group of moderately improved 21 % (28 individuals) had been discharged due to rule violations or imprisonment and were regarded as non-compliers. In the group of not improved or worse 59 % (49 individuals) had been discharged due to rule violations or imprisonment and were regarded as non-compliers (see figure 1). To put it in another way, the counsellor's rated 14 % (34 individuals) of those not discharged due to rule

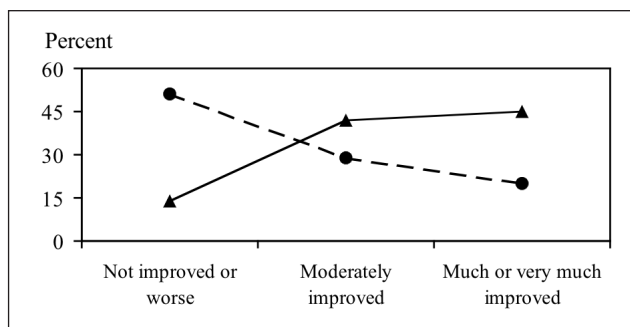


Figure 1. Comparison between Compliers (solid line and filled triangles) and Non-compliers (broken line and filled circles) with regard to improvement according to CGI-I ratings ($p < 0.001$).

violations or imprisonment to be not improved or worse. Thus, 86 percent (125 individuals) of the compliers have benefited from the treatment. More exactly 42 % (104 individuals) of the compliers were moderately improved while 45 % (111 individuals) were much or very much improved. The comparison between compliers and non-compliers with regard to the CGI-I improvement groups yielded a significant difference ($\chi^2 = 20.2, df = 2, p > 0.001$) with more non-compliers falling into the not improved or worse group and

more compliers in the moderately and much and very much improved groups (see figure 1).

Of the 96 patients discharged due to rule violations or imprisonment 20% (19 individuals) were regarded as much or very much improved prior to the discharge and 29% (28 individuals) were regarded as moderately improved prior to the discharge. The remaining, 51% (49 individuals), were regarded prior to discharge as not improved or worse (see figure 1). According to a chi-square test this difference in proportion was significant ($\chi^2 = 54.4, df = 2, p < 0.001$).

Heredity as a set of background data showed no significant difference between the three CGI-I improvement groups.

Among background variables during childhood and adolescence only time spent in foster-home before methadone treatment showed no significant group difference between CGI-I rated groups. Abnormal childhood experiences were lowest in the much and very much improved groups and highest in the not improved or worst group. Broken homes were most common in the not improved or worst group and most rare in the much or very much improved group. The experiences of school problems were more usual in the least improved group and most rare in the most improved group. A higher proportion of those most improved had completed compulsory school and fewer in the least improved group

Table 2a. Presence of background variables of potential importance for the prognosis (heredity, childhood and adolescence, work, earlier treatment, court sentence and drug abuse pattern) in the case histories of 243 males and CGI-I rating of improvement

Variable	Much or very much improved N=98	Moderately improved N=82	Not improved or worse N=63	Chi (df)
Heredity				
Psychiatric disorder and/or drug abuse, father§	16 (18)	19 (25)	5 (27)	1.9 (2)
Psychiatric disorder and/or drug abuse, mother§§	11 (11)	16 (20)	14 (24)	4.6 (2)
Childhood and adolescence				
Abnormal childhood experiences	52 (53)	58 (71)	47 (75)	9.8 (2)**
Foster-home	24 (24)	20 (24)	23 (37)	3.4 (2)
Broken home	41 (42)	44 (54)	34 (54)	3.3 (2)
School problems	53 (54)	53 (65)	50 (79)	10.7 (2)**
Completed compulsory school	80 (82)	63 (77)	38 (60)	9.5 (2)**
Adult age, treatment and criminality				
Own residence	58 (59)	34 (41)	17 (27)	16.7 (2)**
Work experience	72 (73)	60 (73)	35 (56)	6.9 (2)*
Partner, active addict	19 (19)	23 (28)	14 (22)	1.9 (2)
Compulsory treatment	31 (32)	28 (34)	35 (56)	10.3 (2)**
Court sentences	70 (71)	69 (84)	59 (94)	13.1 (2)**
Drug abuse				
Opioid as first drug	28 (29)	15 (18)	14 (22)	2.7 (2)
Frequent ODs	12 (12)	26 (32)	34 (54)	32.3 (2)**
History of non-opioid abuse				
No additional drug	67 (68)	32 (39)	28 (44)	
One additional drug	22 (22)	33 (40)	14 (22)	
More than one additional drug	9 (9)	17 (21)	21 (33)	26.2 (4)**

* $p < 0.05$ ** $p < 0.01$

Figures in parenthesis are percent, § $n = 221$, §§ $n = 236$

Table 2b. Presence of background variables of potential importance for the prognosis (heredity, childhood and adolescence, work, earlier treatment, court sentence and drug abuse pattern) in the case histories of 102 females and CGI-I rating of improvement

Variable	Much or very much improved N=32	Moderately improved N=50	Not improved or worse N=20	Chi (df)
Heredity				
Psychiatric disorder and/or drug abuse, father§	9 (31)	16 (35)	10 (56)	3.2 (2)
Psychiatric disorder and/or drug abuse, mother§§	7 (23)	7 (14)	3 (15)	1.1 (2)
Childhood and adolescence				
Abnormal childhood experiences	25 (78)	39 (78)	18 (90)	1.5 (2)
Foster-home	8 (25)	13 (26)	6 (30)	0.2 (2)
Broken home	16 (50)	32 (64)	15 (75)	3.5 (2)
School problems	14 (44)	36 (72)	16 (80)	9.4 (2)**
Completed compulsory school	30 (94)	30 (60)	13 (65)	11.5 (2)**
Adult age, treatment and criminality				
Own residence	27 (84)	33 (66)	14 (70)	3.4 (2)
Work experience	25 (78)	28 (56)	12 (60)	4.3 (2)
Partner, active addict	21 (66)	21 (42)	10 (50)	4.4 (2)
Compulsory treatment	7 (22)	24 (48)	10 (50)	6.5 (2)*
Court sentences	18 (56)	42 (84)	17 (85)	9.3 (2)**
Drug abuse				
Opioid as first drug	9 (28)	9 (18)	4 (20)	1.2 (2)
Frequent ODs	8 (25)	24 (48)	14 (70)	10.4 (2)**
History of non-opioid abuse				
No additional drug	22 (69)	20 (40)	6 (30)	
One additional drug	9 (28)	14 (28)	5 (25)	
More than one additional drug	1 (3)	16 (32)	9 (45)	15.1 (4)**

*p<0.05 **p<0.01

Figures in parenthesis are percent, § n=93, §§ n=101

had done so (See table 1, 2a and 2b).

During adult age fewer in the not improved or worse group had own residence and earlier work experience compared to the other two groups. The group much or very much improved had the highest proportions. The reverse was true for compulsory treatment and court sentences where the least improved group were in top and the most improved group at bottom. No significant difference was found with regard to if the partner was an active addict or not.

No differences in proportion between the three groups were found with regard to opioids as first drug. Frequent over-doses on the other hand were far more common among those not improved or worse than among those that were much or very much improved with those moderately improved in between. A history of non-opioid use was least common among those most improved and most common among those least improved with moderately somewhere in between.

In table 3 the continuous background data in this study is presented according to the CGI-I rating of outcome. The three groups did not differ according to years between drug and opioid debut, years of abuse before MMT, years of opioid abuse before MMT, months in treatment community before MMT nor age at entering MMT.

Six of the continuous background variables show signifi-

cant difference between the outcome groups. Thus, those most improved have a higher age at drug debut, opioid debut and age at first treatment than the not improved or worse group, with the moderately improved group situated in between on the first two variables but have the lowest age at first treatment. Both short- and long-term treatment episodes are fewer for the most improved group and they have fewer number of probation's than the least improved group, while the moderately improved group are situated in between.

When it comes to criminality only numbers of probations differ between the groups while neither periods of imprisonment nor months of imprisonment differ significantly between the groups.

The age at drug debut and opioid debut are not significantly different between men and women (see table 4), nor are the years of drug abuse or opioid abuse before methadone treatment. Despite the nearly same age at debut of drugs and opioids there is a slight, but significant, difference (8 months) in time between drug debut and opioid debut. Men move quicker from general drug use to the heavier opioid use than women do. Women have significant more short-term treatment episodes, long-term treatments episodes and months in treatment community than men. Men have a significantly higher number of probations, months in imprisonment and

Table 3. Mean±sd main effect of continuous background data for patients in methadone treatment, subdivided according to CGI-I ratings of improvement. Type III sum of squares are used

Variable	Total sample N=345	Much or very much improved N=130	Moderately improved N=132	Not improved or worse N=83	F
Dug Abuse					
Age at drug debut	15.7	16.8±4.5	15.2±3.1	14.8±3.1	8.76**
Age at opioid debut	19.1	20.1±4.5	19.0±3.3	17.8±3.3	8.90**
Yrs btw drug and opioid debut	3.4	3.3±3.4	3.8±3.3	3.0±2.9	0.47
Years of abuse	14.1	13.9±5.7	14.4±5.7	14.0±5.5	0.15
Years of opioid abuse	10.7	10.6±4.8	10.7±4.5	11.0±4.7	0.19
Treatment					
Short-term treatment episodes	7.7	6.0±6.5	8.0±8.2	10.1±10.3	7.14**
Long-term treatment episodes	4.4	3.8±2.8	4.3±3.9	5.3±4.7	3.96*
Months in treatment community	5.5	4.0±9.3	7.1±13.4	5.6±7.7	2.76
Age at MMT entering	29.8	30.6±5.9	29.7±5.1	28.9±5.5	2.87
Age at first treatment§	22.9	23.9±5.2	22.6±4.2	21.7±4.0	6.50**
Criminality					
Number of probation's	2.5	2.1±2.6	2.7±2.6	3.0±2.5	3.13*
Months of imprisonment	16.9	15.2±27.3	14.5±27.3	23.5±29.8	0.98
Periods of imprisonment	1.9	1.6±3.2	1.6±2.9	3.0±4.1	1.68

*p<0.05 **p<0.01

§ the group "not improved or worse" has n=82 for this variable

Table 4. Mean±sd main effect of continuous background data for patients in methadone treatment, subdivided according to gender and the interaction between CGI-I ratings of improvement. Type III sum of squares are used

Variable	Men N=243	Women N=102	Gender F	Interaction CGI-Gender F
Dug Abuse				
Age at drug debut§§	15.8±4.0	15.2±3.6	2.39	1.15
Age at opioid debut§§	19.1±3.8	19.1±4.1	0.02	2.35
Yrs btw drug and opioid debut	3.2±3.1	3.9±3.4	3.88*	0.55
Years of abuse	14.0±5.8	14.4±5.3	0.34	0.09
Years of opioid abuse	10.8±4.8	10.5±4.3	0.42	0.02
Treatment				
Short-term treatment episodes§§	6.5±7.1	10.8±10.1	19.18**	1.43
Long-term treatment episodes§§	4.0±3.4	5.3±4.4	8.64**	0.94
Months in treatment community§§	4.5±8.7	8.1±14.4	5.62*	0.90
Age at MMT entering§§	30.0±5.6	29.5±5.4	0.19	0.87
Age at first treatment§	23.2±4.6	22.2±4.6	2.18	1.17
Criminality				
Number of probation's	2.7±2.8	2.2±2.1	5.47*	2.16
Months of imprisonment§§	21.1±31.2	6.9±14.4	17.75**	1.81
Periods of imprisonment	2.5±3.8	0.7±1.3	21.17**	1.40

*p<0.05 **p<0.01

§ for this variable there are 242 men and 101 women

§§ data and statistics for men and women on these variables are adapted from Gunne et al, 2005

periods of imprisonment than women.

Age at first treatment and age at entering MMT are not significant different between men and women. There are no significant interactions between CGI-I and Gender (see table 4).

4. Discussion

Our result that non-compliance to treatment is associated with poor outcome is congruent with earlier research [35]. In the present study 28% (96 patients) were discharged due to non-compliance to the program instructions for reason such as criminal activity/imprisonment or other rule violations (cheating with urine tests or drug use, usually poly drug use). Before discharge 51 % of them were regarded as not improved or worse. In the group with adherence to the treatment regime only 14 % were rated according to CGI-I-criteria by the counsellor's to be not improved or worse. Thus, 86 percent of the compliers have benefited from the treatment and were rated as medium to very much improved. The difference in improvement between compliers and non-compliers were highly significant. If the results are looked at from another angle significantly higher proportions of the CGI-I group not improved or worse were discharged at follow-up compared with the improved groups. Earlier studies [for instance 17, 37] have shown that the death rates are very high among those involuntarily discharged and drop-outs of methadone treatment. Our result that compliers had better improvement than non-compliers is consistent with the work by Maremmani and colleagues [30] who showed that there are statistically time effects in methadone treatment. Between three and twelve months of treatment they found that there were a decrease in opioids use and an improvement in clinical status.

The group not improved or worse has significantly more background problems in childhood and adolescence than the group much or very much improved. Those moderately improved are usually situated somewhere between the others. For both men and women school problems and an uncompleted compulsory school history were associated with a low grade of improvement. For men abnormal childhood experience was also more common among those with lower grades of improvement. Although, broken-home was not significantly related to improvement neither among men nor women, there was a significant association in the combined group. In this sample there were no significant association between improvement and foster-home. When Lehmann and co-workers [28] defined positive outcome in MMT as one year retention in the program and urine samples negative for opiates they found that foster care before the age of 15 were the only variable of a large number that were associated with success. The differences between there sample and ours may have its origin in the difference between our Swedish social service and their Canadian counterpart. Although, Lehmann

and co-workers did not define less benzodiazepine use as a measure of success they found that working/studying, low criminal activity and being man were associated with low use of benzodiazepine.

In the present study work experience and to have had own residence was important for men's improvement, but not for women. For neither men nor women there was no association between improvements and if the partner was an active drug addict.

For both men and women to have a history of compulsory treatment was associated with low levels of improvement. To be young at first non-MMT treatment was associated with low level of improvement, while age at entering MMT was not significantly related to grade of improvement. There was no significant difference between men and women in age neither at first non-MMT treatment nor age at entering MMT.

To have a criminal record before MMT was associated with low level of improvement. To have a court sentence was negative for both men and women. Those less improved also had a higher number of probations, but not significantly higher numbers of months in prison or periods in prison. To have many short- or long-term treatments and need of treatment at an early age was associated with poor improvement, but number of months in a drug-free treatment community did not appear to be associated with improvement.

The drug-related variables had an impact on both men and women. Frequent overdoses (OD:s) and a history of non-opioid abuse were related to poor improvement. Low age at drug debut and debut of opiates appears to indicate a severe form of addiction that is hard to treat. For women an early initiation of drugs are also associated with selling sex at an earlier age [32]. Compared to the moderately improved the not improved or worse are one year ahead initiating drug and opiate use and need of treatment compared with the much and very much improved group. However, there was no association between initiating drug abuse with opioids or other drugs. Years of general abuse or opioid abuse did not appear to be associated with rate of improvement and neither did the time between drug and opioid debut. However, women's time between the initiation of drug use and the switch to opioid use were roughly 20 percent longer than the men's time.

There were no significant interactions on the continuous variables between improvement measured according to CGI-I and gender which can be interpreted to indicate that the association, if any, is in the same direction for men and women. However, there were an interesting difference between men and women regarding treatment and criminality. Women had a higher number of short- and long-term treatment episodes and months in treatment community while men had a significant higher number of probations, months of imprisonment and periods of imprisonment. Thus women are to a higher extent treated and men are punished.

Poirier, et al [33] found the response to be better to buprenorphine in opiate addicts with no family history of

addiction or mood disorder while we found no difference in improvement with regard to the combined index of psychiatric disorder and/or drug abuse neither on the father's side or the mothers. The difference in results between the studies can be due to the sample, the way family history was measured and the substitute (buprenorphine versus methadone). According to a review by Maremmani, Pacini and Pani [29] buprenorphine may have good effects in addicts with low severity and low psychiatric problems. Davstad and co-workers [6] found that those with a psychiatric diagnosis had an higher retention rate in MMT than those without such a diagnosis.

5. Clinical implications

The finding in the present study that non-improvement or worsening of addictive behaviour is associated with non-compliance and higher discharge rates provide a strong urge to find background variables that can be used to identify these individuals in advance so that they can receive special considerations. Consistent findings of risk factors in the whole group and in men and women are (1) the pattern of drug use with frequent heroin overdose (ODs), additional drug abuse beside opioid use, an early drug and opioid debut, (2) a treatment pattern with low age at first treatment, many non-MMT treatments and being convicted and (3) school problems. Thus, drug use pattern and treatment history together with school history can be used to identify risk groups that need extra consideration and treatment efforts. The results of the present study suggest that extra effort should be put in to enhance adherence to the treatment regime and thereby increase improvement, avoid involuntary discharge and prevent death.

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Acknowledgements

We thank Professor emeritus Lars Gunne for valuable comments on an earlier draft of this paper and for valuable discussions.

Role of funding source

No funds for this particular paper.

Contributors

The authors contributed equally to this work.

Conflict of Interest

None of the authors have any relevant conflict of interest to report in relation to the present study.

Received December 30, 2009 - Accepted April 18, 2010