

•Original research article•

Cross-sectional study of the severity of self-reported depressive symptoms in heroin users who participate in a methadone maintenance treatment program

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Background: Methadone maintenance treatment (MMT) is widely recognized as an effective method of combatting narcotic addiction. MMT reduces heroin withdrawal symptoms and, thus, makes it possible to provide the psychological and social support that is essential to the rehabilitation of drug users.

Aim: Compare the severity of depressive symptoms in heroin users who are currently receiving MMT to that of heroin users who are not receiving MMT.

Methods: We administered the 13-item version of the Beck Depression Inventory (BDI-13) and a demographic history form to 929 heroin users who had been receiving MMT at nine methadone treatment clinics in three Chinese cities for an average of 9 months and to 238 heroin users who had enrolled in a MMT program at the centers but had not yet begun MMT.

Results: Seventy-nine percent (188/238) of the untreated individuals reported depressive symptoms compared to 68% (628/929) of the individuals receiving MMT ($\chi^2=11.69$, $p<0.001$). The median (interquartile range) BDI score in the untreated group was 10.4 (7.9-11.4) compared to 8.0 (5.7-11.6) in the MMT group ($Z=2.75$, $p=0.006$). In the MMT group, there was a negative correlation between the severity of reported depressive symptoms and the duration of participation in the MMT program ($r_s=-0.24$, $Z=2.88$, $p=0.004$). Multivariate linear regression analysis showed that after adjusting for all demographic variables the treated group still had less severe depressive symptoms than the untreated group. After adjusting for the effect of MMT treatment, depressive symptoms were more severe in heroin users who self-reported poor family relationships (standardized regression coefficient [beta]=0.118, $t=6.56$, $p<0.001$) and in those who were divorced (beta=0.120, $t=3.73$, $p<0.001$).

Conclusions: Moderate to severe depressive symptoms are common in heroin users. MMT is associated with lower levels of depressive symptoms in heroin users, but prospective randomized controlled trials are needed to determine whether or not MMT actually improves depressive symptoms in heroin users. Poor relationships with family members are also associated with depressive symptoms in heroin users; this suggests that treatment of heroin addiction needs to incorporate methods for helping heroin users repair the severed social relationships that their addiction has caused.

Keywords: methadone maintenance treatment; heroin abuse; depression; China

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1. Introduction

Heroin use is a global public health problem that seriously affects the users themselves, their families, and the economic and social stability of their communities. Chronic use of heroin can directly cause physical

problems and is often associated with comorbid psychiatric disorders, particularly depression.^[1-4] Methadone maintenance treatment (MMT) is a widely recognized method for reducing narcotic addiction that involves the long-term use of methadone to

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reduce cravings for narcotics combined with various psychological and behavioral treatments aimed at restoring social functioning.^[5] The present study compares the severity of depressive symptoms between heroin users currently participating in voluntary outpatient MMT programs in nine locations around China to that of heroin users who have registered at the clinics but have not yet started MMT.

2. Methods

2.1 Participants

As shown in Figure 1, the selected participants were heroin users from nine voluntary outpatient methadone clinics in three cities – seven clinics in Xi’an (Shaanxi Province), one clinic in Beijing, and one clinic in Taiyuan (Shanxi Province). The participants were either already receiving MMT in October 2012 (the MMT group) or newly enrolled patients at the clinics (from October 2012 to April 2014) who had not yet started the MMT program (untreated group). Participants in both groups meet screening criteria for the outpatient use of MMT in heroin users in China:^[6] (a) 20 years of age or older; (b) registered as a permanent resident of the local community; (c) had full legal capacity for civil conduct; (d) had two court-imposed periods of compulsory drug rehabilitation or one period of ‘re-education through labor’ (i.e., legal incarceration for drug abusers); and (e) provided written informed consent to participate in the study.

2.2 Intervention

The MMT at the nine clinics was provided by clinicians who had been trained to provide MMT according

to national standards established by experts in the China Drug Dependence Center.^[7] This involves the administration of daily doses of 10 to 100 mg of methadone that is directly observed by the treating clinician. All the patients in MMT group had at least one month of MMT treatment before enrollment in the study; at the time of enrollment their mean (sd) duration of MMT treatment was 8.9 (3.7) months and their mean MMT dosage was 47.7 (22.2) mg/d.

The protocol for this project was approved by the Ethics Committee of Beijing University. Informed consent was obtained from all participants.

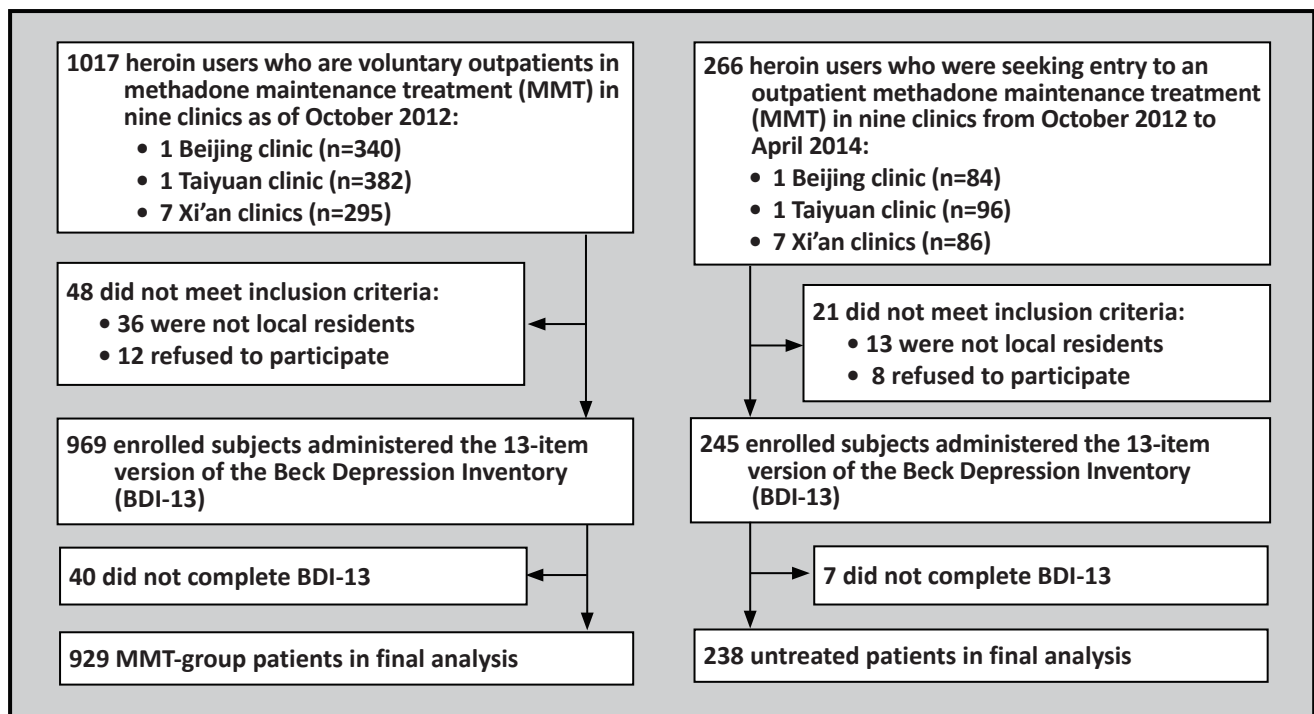
2.3 Assessment

We developed an expanded demographic and current treatment form to collect information on the demographic characteristics and pattern of heroin use of participants. We also administered the short 13-item version of the Beck Depression Inventory (BDI-13),^[8] which has been shown to have good reliability and validity when evaluating the severity of depression in substance abusers.^[9] The BDI items are scored on 4-point Likert scales (0-4) resulting in a range in total scores of 0 to 52, with higher scores representing more severe depression. Total scores of 0 to 4 indicate no depression, scores of 5 to 7 indicate mild depression, scores of 8 to 15 indicate moderate depression, and scores of 16 or more indicate serious depression.

2.4 Statistical analysis

Epidata (version 3.1) was used to double enter the data, and SPSS 11.3 was used to conduct the statistical analysis. Chi-square tests, t-tests, and rank tests were

Figure 1. Flowchart of patient enrollment in the study



used to compare characteristics between the two groups. We used Spearman correlation coefficients to assess the relationship between the duration of MMT treatment and the severity of depression in the treated group. We used multivariate linear regression analysis to identify the factors independently associated with the severity of depressive symptoms. All statistical tests were two-tailed and the level of statistical significance was set at $p \leq 0.05$.

3. Results

There were 929 patients in the MMT treatment group and 238 in the untreated group who completed the assessment; completion rates in the two groups were 95.9% (929/969) and 97.1% (238/245), respectively. As shown in Table 1, there were several statistically significant differences in the characteristics of the two groups. Compared to individuals in the untreated group, individuals in the MMT group were less likely to

Table 1. Comparison of the demographic characteristics of heroin users who are or are not enrolled in an outpatient methadone maintenance treatment (MMT) program

Characteristic	MMT group n=929	untreated group n=238	statistic	p-value
Male gender ^a n (%)	770 (83.2%)	218 (92.8%)	$\chi^2=13.45$	<0.001
Mean (sd) of age in years	39.7 (6.4)	37.0 (8.4)	$t=-4.46$	<0.001
Educational level ^b n (%)				
primary school	80 (8.7%)	31 (13.1%)		
junior middle school	405 (44.2%)	140 (59.3%)		
technical school	87 (9.5%)	11 (4.7%)	$\chi^2=30.31$	<0.001
senior high school	285 (31.1%)	47 (19.9%)		
associate degree or above	60 (6.5%)	7 (2.9%)		
Marital status ^c n (%)				
single	189 (20.5%)	33 (13.9%)		
cohabitation	26 (2.8%)	3 (1.3%)		
married	548 (59.3%)	171 (71.8%)	$\chi^2=128.35$	<0.001
divorced	144 (15.6%)	30 (12.6%)		
separated	17 (1.8%)	1 (0.4%)		
Occupation ^d				
employed	110 (12.0%)	23 (9.8%)		
self-employed entrepreneurs	220 (24.0%)	149 (63.1%)	$\chi^2=136.43$	<0.001
unemployed	409 (44.7%)	40 (16.9%)		
other	177 (19.3%)	24 (10.2%)		
Quality of family relationships ^e				
excellent	252 (28.3%)	91 (41.0%)		
good	332 (37.3%)	81 (36.5%)	$\chi^2=18.16$	<0.001
average	265 (29.7%)	46 (20.7%)		
poor	42 (4.7%)	4 (1.8%)		
Monthly income in Chinese Renminbi (RMB)(1\$US=6.27 RMB) ^f				
none	184 (19.8%)	26 (11.0%)		
1-3000	300 (32.3%)	24 (10.1%)	$\chi^2=110.04$	<0.001
3001-10,000	403 (43.5%)	141 (59.5%)		
over 10,000	41 (4.4%)	46 (19.4%)		

^a 4 MMT-group and 3 untreated-group participants missing data on gender

^b 12 MMT-group and 2 untreated-group participants missing data on educational level

^c 5 MMT-group participants missing data on marital status

^d 13 MMT-group and 2 untreated-group participants missing data on occupation

^e 38 MMT-group and 16 untreated-group participants missing data in quality of family relationships

^f 1 MMT-group and 1 untreated-group participant missing data on monthly income

be male, were older, had a higher level of education, were less likely to be married, were more likely to be unemployed, had lower monthly incomes, and reported poorer family relationships.

As shown in Table 2, the total daily dose of heroin at the time of enrollment in the MMT program was similar in the two groups, but the average single dose of heroin and the maximum single dose of heroin in the week prior to enrollment was greater in the MMT group than in the untreated group. However, the duration of heroin use and the frequency of daily use were greater in untreated individuals than in treated individuals.

The BDI-13 score was not normally distributed, so we used rank tests and Chi-squares to compare results between groups. Both analyses show that the reported severity of depressive symptoms was significantly greater in the untreated group than in the treated group. Among the 929 patients in the MMT group, longer participation in MMT was associated with lower scores on the BDI-13 ($r_s=-0.24$, $Z=2.88$, $p=0.004$).

We considered the treatment status and all assessed sociodemographic variables in a multivariate linear regression analysis ($n=1138$) to determine which variables were independently associated with the reported severity of depression. As shown in Table 3, depressive symptoms were significantly more severe in persons who reported poor family relationships, in persons in the untreated group, and in persons who were divorced. Other variables, including gender, age, educational level, income level, and employment status were not independently associated with the self-reported severity of depressive symptoms.

4. Discussion

4.1 Main findings

We found that the prevalence of depressive symptoms among heroin users (79% in the untreated group and 68% in the MMT group) is much higher than in the general population,^[10] a finding that is similar to several other studies of substance users.^[11] The depressive symptoms frequently reported by heroin users include pessimism, dissatisfaction, guilt, self-denial, work-related difficulty, fatigue, and anorexia.^[12] These symptoms can be exacerbated immediately after drug withdrawal and by social-environmental stressors including the stigma and discrimination that many drug abusers must often endure.^[13] Several studies have shown that depressive and anxiety symptoms in heroin users are important causes of relapse after detoxification,^[14] so addressing these symptoms needs to be a key component of drug rehabilitation programs.

We also found that reported depressive symptoms among heroin users engaged in a MMT program were less severe than the depressive symptoms reported by heroin users who are not engaged in a MMT program, and that this difference persists after controlling for key demographic variables. Moreover, individuals who had participated in the MMT program longer had less severe depressive symptoms than individuals who only recently started participating in the MMT program, suggesting – but not proving – that MMT was having a positive effect on participants' depressive symptoms. A similar study by Brienza and colleagues among 528 heroin users found that the rates of depression among individuals receiving MMT were lower than those of attendees

Table 2. Characteristics of heroin use and depressive symptoms among heroin users who are or are not enrolled in an outpatient methadone maintenance treatment (MMT) program

characteristic	MMT group	untreated group	statistic	p-value
	mean (sd) (n=929)	mean (sd) (n=238)		
total daily dose of heroin (gm)	0.80 (0.07)	0.65 (0.11)	$t=1.33$	0.184
dose of heroin each time used (gm)	0.33 (0.04)	0.21 (0.02)	$t=5.89$	<0.001
daily frequency of heroin use (times)	2.25 (0.72)	3.41 (0.81)	$t=12.56$	<0.001
maximum one-time dose of heroin (gm)	0.57 (0.05)	0.44 (0.03)	$t=3.64$	<0.001
duration of heroin use (years)	9.86 (3.10)	11.48 (3.21)	$t=3.89$	<0.001
median (IQR) BDI-13 total score ^a	8.0 (5.7-11.6)	10.4 (7.9-14.4)	$Z=2.75$	0.006
Classification of BDI-13 total score				
no depressive symptoms	301 (32.4%)	50 (21.1%)	$\chi^2=12.33$	0.006
mild depressive symptoms	148 (15.9%)	41 (17.2%)		
moderate depressive symptoms	301 (32.4%)	96 (40.3%)		
serious depressive symptoms	179 (19.3%)	51 (21.4%)		

BDI-13, 13-item Beck Depression Inventory^[9]

IQR, interquartile range

^a the distribution of BDI-13 total score in both groups was skewed, so the Mann-Whitney test was used

Table 3. Multivariate linear regression of factors associated with total score of the 13-item Beck Depression Inventory (BDI-13)^[7] among 1138 heroin users in China^a

factor	regression coefficient (β)	se	standardized regression coefficient (beta)	t	p-value
quality of family relationships ^b	3.427	0.527	0.118	6.56	<0.001
not receiving MMT treatment	2.925	0.507	0.012	5.30	<0.001
divorced ^c	2.559	0.605	0.120	3.73	<0.001
higher personal monthly income ^d	-0.616	0.403	-0.041	-1.41	0.119
higher educational status ^e	0.071	0.042	0.115	0.47	0.601
age (years)	-0.022	0.029	-0.009	-0.42	0.617
currently working	-0.045	0.032	0.092	-0.42	0.764
female	-0.259	0.572	-0.014	-0.35	0.613

MMT, methadone maintenance treatment

^a R²=0.431^b 1=excellent, 2=good, 3=average, 4=poor^c 1=not divorced (including all marital statuses other than divorced), 2=divorced^d 0=none, 1=1-3000 renminbi (RMB); 2=3001-10,000 RMB; 3=>10,000 RMB (1\$US=6.27 RMB)^e 1=less than middle school; 2= middle school and above

at a Needle Exchange Program (NEP).^[15] A one-year follow-up treatment study^[16] of adjunctive treatment with MMT and rehabilitation therapy (without a control group) in 485 heroin users reported that the prevalence of core depressive symptoms dropped from 26% to 11% over the course of treatment.

Our findings that divorce and poor family relationships are associated with more severe depressive symptoms in individuals who use heroin, a finding that remains robust even after adjusting for the effect of participating in a MMT program, highlight the importance of addressing environmental stressors while using methadone to reduce the physical addiction. Some studies^[17] report that providing psychological support to spouses and family members of heroin users both reduces the stress experienced by the family members and promotes the social rehabilitation and quality of life of the patient.

4.2 Limitations

There are several limitations with the study that need to be considered. (a) Individuals included in the study voluntarily entered a MMT program after having participated in court-mandated compulsory treatment (which is typically a minimum of two years in China), so they have long histories of heroin use (10 years on average) and, thus, are not representative of individuals who have only recently started using heroin. (b) The level of use of heroin was assessed at the time of enrollment in the MMT program in both groups; for the untreated group the BDI-13 evaluated the level of depression at the same time period (i.e., depression at the time of enrollment), but for the MMT group the

BDI-13 assessed the individual's level of depression on average 9 months after the time of enrollment. This made it impossible to correlate the heroin use variables (other than the total duration of use) to the level of depression or to include these variables in the multiple linear regression model. (c) There were major unexplained differences in the demographic and heroin use variables between the two groups. Even though we controlled for these variables in the linear regression, these differences may reflect underlying differences in the groups that could have confounded the results about depression between the groups. (d) The prior treatment history of participants was not considered. (e) No formal diagnosis was conducted to distinguish patients who did and did not meet formal diagnostic criteria for depression. Finally, (f) this was a cross-sectional study, so the identified relationships are associations, not causal; we cannot conclude the MMT treatment improves depression in heroin users, we can only conclude that MMT is associated with lower levels of depression in heroin users. Randomized controlled studies are needed to determine whether or not MMT actually improves the depressive symptoms of persons who use heroin.

4.3 Importance

We found that concurrent depression is common in individuals who seek outpatient treatment for heroin addiction in China. Individuals who are participating in the comprehensive methadone maintenance therapy programs in China report substantially less severe depressive symptoms than heroin users who have enrolled in MMT programs but have not yet started

the treatment. Poor family relationships (including divorce) magnify the depressive symptoms experienced by heroin users, so programs aimed at rehabilitating heroin users need to develop and test creative ways for improving the emotional re-integration of heroin users back into their families after their physical addiction is under control.

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Conflict of interest statement

The authors declare no conflict of interest in the preparation of this manuscript.

Informed consent

Every outpatient who participated in this study signed a consent form at the beginning of the study.

Ethics approval

The biomedicine ethics committee of Peking University approved the study (approval number: 000010-13020).

Authors' contributions

WY was in charge of drafting the manuscript and gathering data; YS and QZ were in charge of quality control while gathering the data; LZ and BY were in charge of processing the data; and LZ was the principal investigator for the study; and all authors read and approved the final manuscript.

参与美沙酮维持治疗的海洛因成瘾者自我报告的抑郁症状严重程度：一项横断面调查

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背景: 美沙酮维持治疗 (methadone maintenance treatment, MMT) 是一种公认的有效降低毒瘾的措施。美沙酮维持治疗可以减少海洛因成瘾戒断症状, 并因此可以提供心理和社会支持, 对吸毒者的康复至关重要。

目标: 比较目前正在接受 MMT 的海洛因成瘾者和没有接受 MMT 的海洛因成瘾者之间的抑郁症状严重程度。

方法: 本研究运用了 Beck-13 (13-item version of the Beck Depression Inventory, BDI-13) 抑郁自评量表和人口学历史资料调查表, 对中国三个城市 9 个美沙酮治疗中心的 929 例正在接受 MMT 的海洛因成瘾患者 (平均已接受 9 个月 MMT 治疗) 和已经在中心注册参加 MMT 治疗但尚未开始的 238 例海洛因成瘾患者进行评估。

结果: 与正在接受 MMT 的成瘾者中有 68% (628 / 929) 报告抑郁症状相比, 79% (188/238) 的未治疗成瘾者报告有抑郁症状 ($\chi^2=11.69, p<0.001$)。未经治疗组的 BDI 评分中位数 (四分位区间) 是 10.4 (7.9-11.4), 而 MMT

组 BDI 评分中位数是 8.0 (5.7-11.6), 两者有显著差异 ($Z=2.75, p=0.006$)。在 MMT 组内, 自我报告的抑郁症状严重程度与参加 MMT 时间呈负相关 ($r_s=-0.24, Z=2.88, p=0.004$)。多元线性回归分析发现, 在控制所有人口学变量后, 治疗组的抑郁症状严重程度仍然轻于非治疗组。在控制 MMT 疗效后, 自我报告家庭关系较差 ($\beta=0.118, t=6.56, p<0.001$) 以及离异 ($\beta=0.120, t=3.73, p<0.001$) 的海洛因成瘾患者抑郁症状较严重。

结论: 中度至重度抑郁症状常见于海洛因成瘾患者。MMT 治疗与海洛因成瘾患者抑郁症状较轻相关, 但需要采用前瞻性随机对照试验来确定 MMT 是否确实改善了海洛因成瘾患者的抑郁症状。与家庭成员的关系较差也与海洛因成瘾患者的抑郁症状有关, 这表明对海洛因成瘾患者的治疗需要纳入一些方法来帮助海洛因成瘾患者修复由于他们成瘾造成的社会关系割裂。

关键词: 美沙酮维持治疗; 海洛因滥用; 抑郁; 中国

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