

## Factors Related to Retention Duration of Patients in the Methadone Maintenance Treatment in Taiwan

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**Objective:** Opioid dependence is a chronic and relapsing disorder. In Taiwan, the methadone maintenance treatment (MMT) has been introduced since 2005. But high dropout rate from the MMT patients has been high. In this study, we intended to explore the related factors for patients' retention duration in the MMT program in Taiwan. **Methods:** This is a retrospective cohort study. We reviewed the charts of subjects enrolled in the MMT program at four sites in central Taiwan. Totally, 1,944 heroin users in the MMT program were enrolled consecutively from January 1, 2007 to May 31, 2009. Five groups of the MMT duration were divided into 1-30, 31-90, 91-180, 181-360, and more than 360 days. **Result:** The retention rate of the MMT was gradually decreased with the time. Only 290 (14.99%) subjects stayed in the MMT for more than 360 days. Higher dosage of methadone was found in subgroups of longer retention of MMT. Elderly patients who stayed in the MMT, were found to be staying longer than younger ones ( $p < 0.05$ ). Patients staying longer in the MMT had longer duration of heroin use ( $p < 0.05$ ). Unstable dosage of methadone was found to be more in those patients before their withdrawal from the MMT program. **Conclusion:** Our study gained important information that higher dosage and older age would be a favorable factor for longer retention duration in the MMT in Taiwan. Furthermore, dramatic changes in dosage could lead to patients' withdrawal from the MMT program.

**Key words:** methadone, dosage, dropout rate, factor  
(*Taiwanese Journal of Psychiatry* [Taipei] 2015; 29: 244-52)

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Received: January 14, 2016; revised: February 27, 2016; accepted: February 28, 2016

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## Introduction

Opioid dependence is a chronic or long-term and relapsing disorder. Dole et al. [1] believed that long-term heroin use can cause a permanent metabolic deficiency in the central nervous system and an associated physiological disease, requiring regular administration of opiates to correct the metabolic deficiency. The methadone maintenance treatment (MMT) is an effective therapy for heroin dependence [2, 3]. Crude mortality rates and the risks of death of opioid users are substantially higher than those in the general population [4]. Opiate addicts are at high risk for mortality during prolonged waiting periods for admission to the MMT program in a previous study [5]. Opiate substitution treatment has a greater than 85% chance of reducing overall mortality among opiate users if the average duration approaches or exceeds 12 months [6]. The MMT can lower morbidity and mortality rate in heroin addicts, and patients' longer retention of the MMT can lower mortality, and lower relapse rate, as well as improve their life quality [6-8].

Several factors may affect patients' duration of staying in the MMT. Patient's higher methadone dosage has been found to be associated with their longer retention in the MMT [9]. Booth et al. [10] reported that factors associated with retention include higher methadone dose, free treatment, greater contacts with the clinic, and higher counselor's rating on the cooperation from patients. Magura et al. [11] reported that constructive clinic responses to patient's problems, higher methadone dosage, more patients' treatment strengths, as well as less heroin and cocaine uses in the MMT are associated with their longer MMT retention.

In Taiwan, the MMT has been introduced since 2005. But high dropout rate from the MMT program has been noted. In Liu et al.'s study, only 26.6% of participants still remain in the MMT after 48 weeks [12]. To our knowledge, no paper has been published on variable factors and the MMT duration in Taiwan. To realize patients' MMT duration being an important factor contributing to better outcomes, we conducted a retrospect cohort study. The objective of the study was intended to explore the related factors for patients' retention duration at the MMT program in Taiwan.

## Methods

### *The study protocol*

The study protocol was approved by the institutional review board of Chung Shan Medical University Hospital without the need to obtain written consent from the study patients. No commercial funding existed in this retrospective cohort study. We reviewed medical records of heroin users enrolled in the MMT program at four sites in Central Taiwan: Changhua Christian Hospital, China Medical University Hospital, Chung San Medical University Hospital, and Changhua General Hospital.

### *Data collection*

We collected data on demographic characteristics, including educational level, criminal history, age at the first use of heroin, number of times in abstaining from heroin use, heroin use duration, expense for acquiring of heroin before joining the MMT, and methadone treatment duration. We also collected laboratory data, including antibodies to HIV, hepatitis B surface antigen, and antibodies to HCV. But there were missing data in this retrospective cohort. Totally 1,944 heroin users in the MMT were enrolled consecutively from January

1, 2007 to May 31, 2009. Five groups of methadone staying duration were divided into 1-30, 31-90, 91-180, 181-360, and more than 360 days.

### **Statistical analysis**

We analyzed study variables for the differences of retention factors in five groups of the MMT patients. We analyzed the differences of categorical variables with the Chi square test, and those of continuous variables with the independent t test or repeated measures of analysis of variance (ANOVA).

Statistical analyses were performed using Statistical Package for Social Science software version 10 for Windows (SPSS Inc, Chicago, Illinois, USA). The differences between groups were considered significant if *p*-values were smaller than 0.05.

## **Results**

Totally, 1,617 males (84.97%) and 286 females (15.03%) were recruited in this study. Table 1 lists demographic data of the MMT patients. Figure 1 presents data of patients' cumulative retention in the MMT program. Figure 2 describes methadone dosage distribution of five MMT duration groups. Figure 3 shows patients' average daily dosages of methadone in the MMT duration. And Figure 4 depicts methadone dosage change and methadone duration in each group.

## **Discussion**

Methadone is the most effective in relieving craving for opioids when properly dosed, often in the daily range of 80 to 120 mg [13]. Heroin users can be benefited rapidly and continuously from the MMT program. Longer retention in the MMT program may be associated with a better quality of

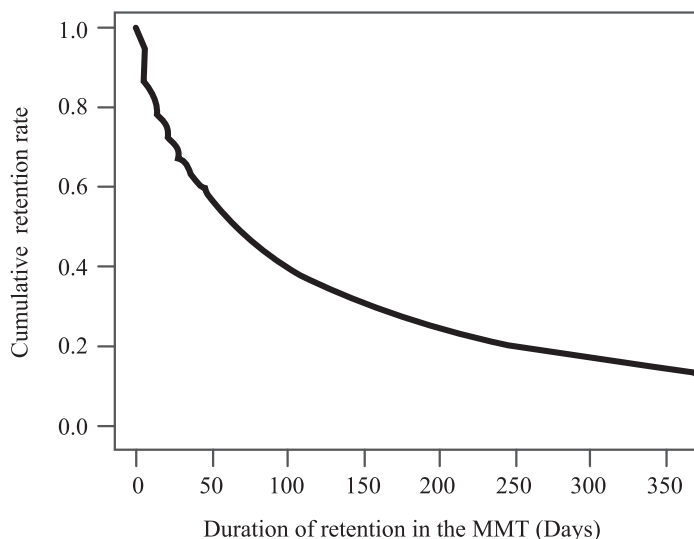
life [7]. In our study, we found a retention rate of 14.99% after one year (Figure 1). The retention rate in our study is lower than that in others. In a Sweden study, the one-year retention rate is 84%, and the two-year rate 65% [14]. In an Israel's study, the retention rate in the MMT at one-year is 74.4% [15]. The retention rates at the end of one year are 73.6% and 61.6% in studies in Tel-Aviv, Israel and Las Vegas, USA, respectively [16]. To pay attention to high drop rate of MMT program is important, but we need to consider several factors: First, Taiwan began the MMT in 2005 with only four pilot hospitals, and then expanded to whole country in 2006. Our data were collected between 2007 and 2009. In the early period of the MMT program, patients and clinicians did not understand the MMT well. Some patients and physicians worried about methadone would be addictive after patient's long-term treatment in the MMT. Some patients worried about side effects of methadone, especially about the damages in the liver and kidney. Besides, physicians prescribed low dosages of methadone in Taiwan. The averaged dosage of methadone used in Taiwan is lower than that in other countries. Those practices might lead to early discontinuation of MMT patients in Taiwan. What's more, other countries have MMT programs more than 10 years, or even 50 years. The experience in the MMT gained in Taiwan would help in increasing the retention rate. In another point, the definition of retention rate of one-year in the MMT is not clear. The major reasons of withdrawal from our MMT might be variable, such as heroin relapsed, legal problems other than substances, physical problems, and even recovery. Monetary subsidy is one of the factors to affect the sustainability of addicts to receive the MMT. A previous study in Taiwan showed that reimbursement is related to high compliance in the MMT [17]. To pay more atten-

**Table1. Demographic data study patients in the methadone maintenance treatment program (N = 1,617) of each group**

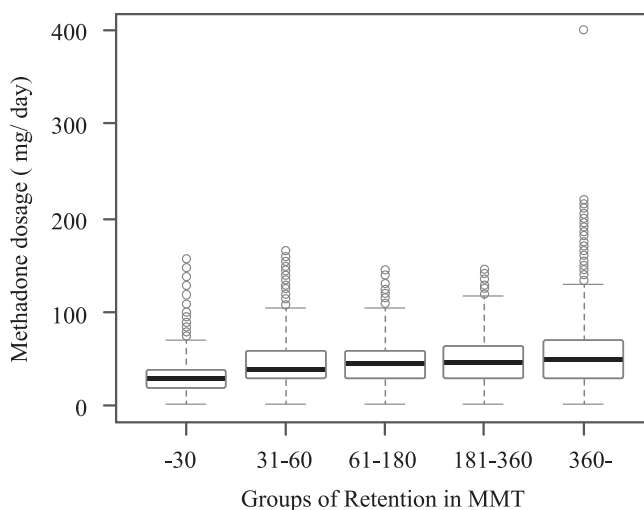
	Time (days)	-30	31-60	61-180	181-360	360-
Number of Subjects		629	471	290	255	290
Age (mean $\pm$ SD, years)*		35 $\pm$ 7.7	36.2 $\pm$ 8.1	35.9 $\pm$ 8.1	36.5 $\pm$ 7.9	36.4 $\pm$ 7.7
Age of first time heroin using (mean $\pm$ SD, years old)		23.1 $\pm$ 10	23.5 $\pm$ 9.7	23.2 $\pm$ 9.8	22 $\pm$ 10	23.6 $\pm$ 10.7
History of duration of heroin use (mean $\pm$ SD, years)*		12.2 $\pm$ 9.7	12.9 $\pm$ 9.2	12.6 $\pm$ 9.9	14.6 $\pm$ 10.3	13.1 $\pm$ 10.1
Methadone dosage (mean $\pm$ SD, mg/day)		34.9 $\pm$ 17.5	45.7 $\pm$ 22.2	47.1 $\pm$ 21.9	49.1 $\pm$ 24.5	53.2 $\pm$ 28.1
Gender	Female (%)	100 (16.08)	63 (13.73)	36 (12.72)	33 (12.99)	54 (18.95)
	Male (%)	522 (83.92)	396 (86.27)	247 (87.28)	221 (87.01)	231 (81.05)
Marital status	Single (%)	321 (52.97)	249 (55.7)	164 (59.64)	133 (53.2)	152 (54.29)
	Married (%)	149 (24.59)	101 (22.6)	59 (21.45)	59 (23.6)	73 (26.07)
	Divorced (%)	136 (22.44)	97 (21.7)	52 (18.91)	58 (23.2)	55 (19.64)
	Widowed	4	1	3	1	1
	Separated	6	3	2	3	3
	Education level	no	2	4	4	0
	Primary school	46	38	27	14	25
	Junior high school	339	248	143	131	142
	Senior high school	225	159	100	102	106
	College	4	8	6	5	7
	9 years less (%)	387 (62.82)	290 (63.46)	174 (62.14)	145 (57.54)	169 (59.93)
	9 years more (%)	229 (37.18)	167 (36.54)	106 (37.86)	107 (42.46)	113 (40.07)
Employment status	unemployed	268	206	133	111	124
	employed	351	248	149	143	161
Anti-HBsAb	Negative (%)	194 (53.59)	121 (45.49)	92 (51.98)	96 (53.04)	99 (50)
	Positive (%)	168 (46.41)	145 (54.51)	85 (48.02)	85 (46.96)	99 (50)
Anti-HCV	Negative (%)	59 (16.39)	45 (16.98)	20 (11.36)	22 (12.22)	26 (13.4)
	Positive (%)	301 (83.61)	220 (83.02)	156 (88.64)	158 (87.78)	168 (86.6)
HIV	Negative (%)	315 (91.04)	224 (88.89)	142 (83.53)	157 (91.81)	160 (87.91)
	Positive (%)	31 (8.96)	28 (11.11)	28 (16.47)	14 (8.19)	22 (12.09)
Criminal Record	No	38 (7.88)	21 (5.9)	12 (5.69)	12 (6.45)	14 (6.64)
	Yes	444 (92.12)	335 (94.1)	199 (94.31)	174 (93.55)	197 (93.36)
Heroin spent before MMT (mean $\pm$ SD, NTD/day)		2950.9 $\pm$ 3064.25	3180.97 $\pm$ 3274.41	3284.53 $\pm$ 2639.5	2947.95 $\pm$ 2871.75	3558.33 $\pm$ 4034.58

\* $p < 0.05$ 

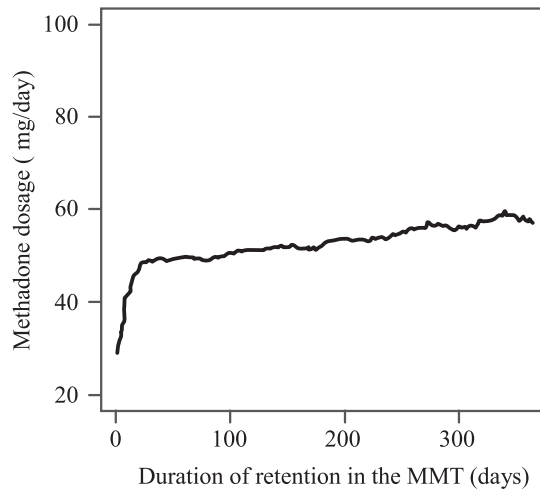
HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; SD, standard deviation



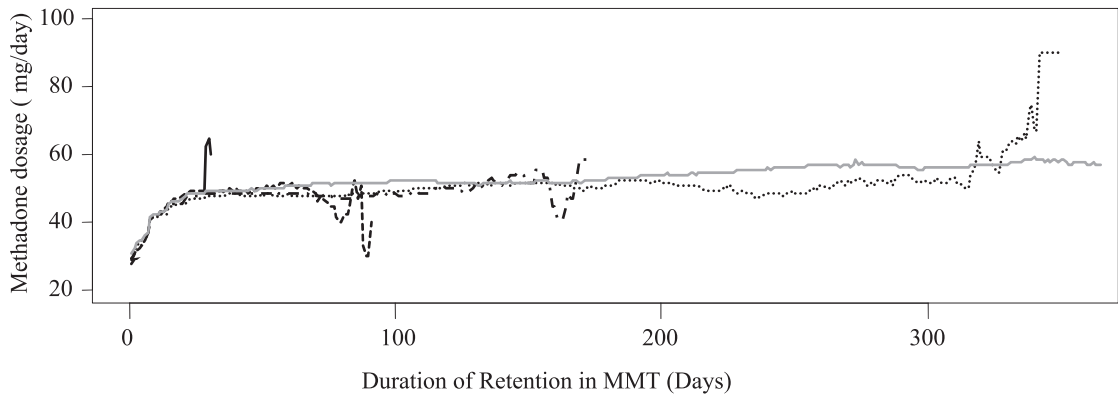
**Figure 1.** The cumulative retention in the methadone maintenance treatment. Most patients withdrew from MMT in early periods. There were 629 (32.51%), 471 (24.34%), 290 (14.99%), and 255 (13.18%) dropped out from the MMT within 30, 31-90, 91-180, and 181-360 days, respectively. Only 290 (14.99%) patients stayed in the MMT for more than 360 days.



**Figure 2.** Methadone dosage distribution in each duration group. The retention rate of MMT was gradually decreased with the time and was shown in Figure 1. The mean daily dosages for 629 patients stayed in MMT for less than 31 days were  $34.9 \pm 17.5$  mg, for 471 patients stayed in MMT between 31 and 90 days were  $45.7 \pm 22.2$  mg, for 290 patients stayed in MMT between 91 and 180 days were  $47.1 \pm 21.9$  mg, for 255 patients stayed in MMT between 181 and 360 days were  $49.1 \pm 24.5$  mg, for 290 patients stayed in MMT more than 360 days were  $53.2 \pm 28.1$  mg, respectively.



**Figure 3.** The average daily dosage of methadone in the duration of the methadone maintenance treatment. The average daily dosage of methadone was  $49.97 \pm 25.8$  mg in the whole cohort. The average daily dosage was gradually increased with methadone duration.



**Figure 4.** Methadone dosage change and methadone duration in each group. The curve of methadone dosage of each group showed unstable dosage before the termination of the MMT. The unstable dosage of methadone of each group before withdrawal was clearly seen. — the < 30-day group; ----, the 31-90-day group; - · - ·, the 91-180-day group; · · · ·, the 181-360-day group; and — — —, > 361-day group.

tion to this issue is important. We suggest that further survey is needed to follow up the retention rate in the following year, and that to educate our clinicians and patients for a better understanding of the MMT is also urgent.

In the data obtained (Figure 2), we found that patients' methadone doses were gradually increased with the time. Previous studies [16, 18] suggested that higher dosage of methadone is a predictor of retention. The finding reinforces the

need for higher doses of methadone to increase the efficacy of the MMT. Besides, we found the unstable dosage changes in each group before the withdrawal from the MMT, except the group of more than 360 days. The reason of unstable dosage change could be attempting to taper off methadone. Patients who have attempted to taper off methadone dosage can expose themselves to risk the withdrawal of the MMT. Nosyk et al. [19] found that many patients attempting to taper off from MMT do not succeed. Success could be enhanced by gradual dose reductions interspersed with having periods of stabilization. When the patients attempt to taper off the dosage of methadone, we suggest that clinicians need to closely monitor to make sure that they have been enjoying periods of stabilization.

As shown in Table 1, we found that older patients remained in the MMT significantly longer than those younger patients ( $p < 0.05$ ). This finding is similar to that in the previous studies. Age more than 35 years also is a favorable factor for retention in MMT in another study in Taiwan [20]. Torrens et al. [21] reported that patient's age being older than 30 years is a predictive variable for the MMT retention. Peles et al.'s cumulative retention study showed that MMT patients who have been older than 40 years of age on admission have better MMT retention compared to those who were younger [15]. In Indonesia, older patients have better outcomes in the recent survey [22]. But, age has not been found to predict retention of MMT in Kelly et al.'s study in the US [23]. History of longer opiate use might be related with older age. The relationship between duration of opiate use history and age in predicting better patients' MMT retention is still unanswered. Therefore, we suggest that further studies are needed to answer this question.

### **Study limitations**

The readers are warned against over-interpreting the results of this study because of its having three major limitations:

- This study is retrospective in design which limits its data collection to variables only recorded in patients' clinical records.
- Inaccuracies and omissions of information in medical charts are possible.
- Four hospitals in the study began the MMT in the early phases, from November 2007 to September 2008. Those differences of time may cause the difference of the results obtained.

### **Summary**

Our study has gained important information that higher dosage of methadone and older age of the patients would be favorable factors for MMT retention in Taiwan. Furthermore, dramatic changes in dosage could lead to patients' withdrawal from the MMT. Education for patients and clinicians about dosage of methadone is necessary for better outcome of retention rate of MMT patients.

### **Acknowledgment**

All authors declare no potential competing conflicts of interest in writing this report.

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