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FACTORS AFFECTING NON-RETENTION IN METHADONE MAINTENANCE TREATMENT: A RETROSPECTIVE STUDY IN CURE AND CARE CENTRE CHOW KIT, MALAYSIA

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Keywords:

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ABSTRACT: Methadone Maintenance Treatment (MMT) is a national harm reduction program in Malaysia that prevents opioids withdrawal, reduces cravings, and aids in the drug abuser's recovery. Treatment retention is used as a measure of MMT effectiveness. However, it is often associated with many factors that cause premature termination. Our study aimed to analyze the percentage of loss to follow-up patients receiving MMT in the Cure and Care Service Centre (Chow Kit, Malaysia) and identify the factors that affected treatment non-retention. Data collection was obtained from 335 medical profiles of patients to assess the percentage of non-retention and analyze the factors associated with involuntary and voluntary termination. Data analysis was carried out using SSPS version 24 and Microsoft Excel 2011. Majority of the patients were male (n=141), aged between 41 and 60 years old (n = 93) and Malay (n=112). Our findings demonstrated a high percentage of non-retention among MMT patients, where 50.7% and 48% of the factors had caused involuntary and voluntary premature termination, respectively. Involuntary termination from treatment was mainly due to patients getting imprisoned because of recidivism (n=49, 32.2%). Furthermore, there were patients who opted for terminating methadone early due to lack of commitment towards the program (n=35, 23%) and continuing to take opioids 17.8% (n=27, 17.8%). Many other patients were either deceased or expelled from the program due to aggressive behavior. It was shown that non-retention could be affected by many factors and our findings could pave the way towards making improvements to current practice.

INTRODUCTION: In many countries, opioid dependence and abuse cause significant health and social burden. Individuals who are chronically exposed to opioids either for medical or social reasons response are prone to opioid addiction and dependence. Opioid dependence is a chronic relapsing disorder that can lead to health hazards such as respiratory depression and cognitive impairment [1-4]. In Malaysia, statistical data reported by the Agensi Antidadah Kebangsaan (AADK) showed that in 2018, a total of 17,474 and 7,793 new and relapse cases, respectively, were identified. Of these, 7,746 people in Malaysia are currently addicted to opiates, mainly heroin and morphine [5]. A combination of a long term pharmacological treatment and psychosocial approaches is vital to reduce opioid dependence, and aid in a patient's recovery and social functioning [6].

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Methadone is an opiate receptor agonist approved as a pain killer by the United State Food and Drug Administration in 1947. Also, methadone has been proven beneficial for substitution therapy for opioid-dependent individuals to stabilize and decrease illicit opiate abuse [7]. Primary prevention, overdose prevention programs and treatment of existing opioid use disorder can play a major part in reducing demand for opioids and mortality due to opiates overdose. Oral methadone therapy has exhibited an appropriate safety profile when it is correctly prescribed and used. Appropriate dosing could result in relatively better treatment outcomes such as better treatment retention among patients and decreased illegal drug use [8-10]. In October 2005, the Ministry of Health Malaysia introduced the Methadone Maintenance Treatment (MMT) program for opioid-dependent patients to alleviate the growing problems associated with opioid abuse in Malaysia. A total of 18 MMT centers were initiated to provide the MMT program in Malaysia and aid in the prevention of 1,597 new human immunodeficiency virus (HIV) infections from 2006 until 2013, which could have otherwise cost the government RM 3.85 million. The prevalence of HIV-infected patients was found to decrease from 22.1% in 2009 to 16.3% in 2014 [11].

The Cure and Care Service Centre (CCSC) Chow Kit was established by AADK in 2011 as a drop-in center for drug abusers around Kuala Lumpur who are seeking medical treatment and rehabilitation. The MMT program is one of the services being offered at the CCSC to improve the quality of life of the clients, in addition to providing an outpatient aftercare program following drug rehabilitation such as individual counseling, education and group meetings and social activities as part of the drug addiction recovery. Treatment retention is a commonly used parameter to measure the effectiveness of MMT [12]. Duration of treatment is correlated with a variety of positive outcomes that include reduced risk of relapse and associated high-risk behaviors such as sharing of syringes, enhanced social functioning such as employment and reduced criminal activity. The optimal duration of the maintenance period usually varies between patients. However, long-term maintenance treatments, some of which were up to 20 years, are predominantly more successful in assisting opiate users to rehabilitate and lead to a healthy lifestyle with an improved quality of life when compared with short-term or abstinence-oriented programs. Thus, retention is one of the most crucial aims in any methadone program [13, 14]. Factors of retention in MMT programs have been investigated by many researchers and commonly in situations of heroin abuse. Several factors such as physical condition, concurrent medications, high tolerance to opioids, mental status or prior use of high-purity heroin, were found to cause many patients to need a substantial increase in the daily methadone doses for treatment success [15]. Patients who are sustained on inadequately low doses of methadone are more likely to abuse illicit opioids and respond poorly to the therapy. To date, there have been only a few studies of MMT retention among drug abusers in Malaysia and patients' adherence was rarely evaluated until the end of the treatment. The purpose of this study was to assess MMT users who failed to adhere to the program and factors affecting the non-retention of treatment.

MATERIALS AND METHODS:

Study Setting: The CCSC offers a range of services, especially for homeless individuals, where they provide half-day accommodation for clients which begin in the morning until afternoon without permanent residency. Patients are eligible for methadone treatment if they; 1) are confirmed opioid abusers, 2) have been addicts for more than two years, 3) have no detrimental effects due to methadone, and 4) do not have any medication complications or mental health problems. Patients can voluntarily refer themselves to the service.

Most of the clients are active drug users or those who have attempted to withdraw from opioid addiction. Each patient signs a treatment contract and undergoes a medical evaluation. Upon admission to the program, patients are asked to provide demographic information and a brief drug-use history. Patients receive methadone treatment daily as a witnessed ingestion and are under the supervision of a pharmacist. Prior to receiving methadone, the physician must assess each patient and prescribe methadone according to the suitable individualized dose. Patients are assessed weekly for methadone titration to treat opioid withdrawal symptoms and randomly *via* a urine test, at least two to four times monthly at the start of the program.

Study Design: This is a retrospective analytical study of a fixed cohort of 335 patients who were enrolled in the CCSC Chow Kit, Malaysia from January 2012 to December 2016. Patients either voluntarily joined the program were referred by other CCSC centers. The study participants consisted of 152 methadone patients who met the inclusion criteria: 1) enrolled into the program during the study period and; 2) did not complete the MMT program (loss to follow-up). Those who defaulted from treatment due to uncertain reasons and whose treatment was interrupted more than twice were excluded from the study.

Data Collection and Statistical Analysis: The data were collected from the patient's medical profile and methadone chart which were obtained from the methadone clinic at the CCSC Chow Kit. Patient demographic data such as gender, age and ethnicity were collected. The independent variables studied were categorized under two classifications - involuntary termination factors *i.e.* when the patient involuntarily defaulted from the treatment and; voluntary termination factors *i.e.* when the patient willingly stopped the methadone therapy for more than 5 days. Patients were considered involuntarily terminated if they were either imprisoned, aggressive towards the staff, deceased, admitted into other rehabilitation centers or warded. On the other hand, patients were considered voluntarily terminated if they decided not to stay in the program. The data analysis was done using SPSS version 24 *via* descriptive statistical analysis and Microsoft Excel 2011. Chi-squared tests were performed to measure variations in variables of interest between the voluntarily and involuntarily terminated patients. A p-value of less than 0.05 was considered statistically significant.

Ethical Consideration: The approval for data collection was acquired from AADK on 9th March 2017 [reference number: AADK 900-9/2 (1)] and ethical approval was obtained from the Universiti Teknologi MARA Research Ethics Committee (UiTM REC) on 26th May 2017 [reference number: 600-IRMI (5/1/6)].

RESULTS: The demographic characteristics of the patients included in the study are shown in **Table 1**. In both groups, the majority of the patients were male (n=141), aged between 41 and 60 years old (n=93) and Malay (n=112). There was no significant difference between the groups with respect to the demographic data (p>0.05).

TABLE 1: DEMOGRAPHIC CHARACTERISTICS OF MMT PATIENTS

	Voluntary termination		Involuntary termination		Total, n	P value*
	n	Percentage %	n	Percentage %		
Gender						0.793
Male	69	45.4	72	47.4	141	
Female	4	2.6	5	3.3	9	
Age						0.776
20-40	20	13.2	19	12.5	39	
41-60	46	30.3	47	30.9	93	
60-80	7	4.6	10	6.6	17	
Ethnicity						0.335
Malay	56	36.8	56	36.8	112	
Chinese	11	7.2	18	11.8	29	
Indian	4	2.6	1	0.7	5	
Others	2	1.3	2	1.3	4	

*Pearson Chi square test, $p < 0.05$ is significant

The youngest and oldest patients whose treatments were defaulted for MMT in CCSC Chow Kit were 24 and 75 years old, respectively. Unsurprisingly there were only 4 female patients recruited at the center, which is consistent with the low prevalence of female drug abusers in Malaysia [15]. A total of 335 patient records were analyzed and only 79 (23.6%) patients continued the treatment at the time of data collection **Table 2**. The number of defaulters or patients whose treatment was interrupted were 256 (76.4%), demonstrating a high occurrence of loss to follow-up at the center. Involuntary and voluntary termination factors contributed to 50.7% and 48% of the total factors discovered, respectively. Involuntary termination from treatment was mainly caused by patients getting imprisoned due to recidivism (n=49, 32.2%).

Patients with aggressive behavior (n=10, 6.6%) either towards the physician, pharmacist, administrative staff or even other patients, were also forcibly terminated from the program. About 16 patients were reported deceased (n=16, 10.5%) with the oldest patient aged 75 years old dying due to age-related health complications. There was only 1 patient (0.7%) who was admitted to another rehabilitation center or hospital ward. Most of the patients had no commitment towards the program and continued to take opioids, contributing to 23% (n=35) and 17.8% (n=27) of the total voluntary termination factors, respectively. Some patients thought that the psychologically did not need MMT and this contributed to 3.9% (n=6) of the total factors that led to voluntary non-retention.

About 5 patients (3.3%) felt the lack of support from family or partner made them highly demotivated to undertake the program, and thus voluntarily defaulted from the therapy.

TABLE 2: INVOLUNTARY AND VOLUNTARY TERMINATION FACTORS AFFECTING NON-RETENTION AMONG MMT PATIENTS

	n	Percentage (%)
Total MMT patients	335	100
Defaulters	256	76.4
Retaining patients	79	23.6
Involuntary termination factors	79	51.9
Imprisoned	49	32.2
Deceased	16	10.5
Aggressive behavior	10	6.6
Detained at another rehabilitation center	1	0.7
Warded	1	0.7
Missing	2	1.3
Voluntary termination factors	73	48
Lack of commitment	35	23
Continued to take opioids	27	17.8
Felt did not need MMT	6	3.9
Lack of support	5	3.3

DISCUSSION:

Involuntary Termination Factors: Patients who were involuntarily terminated were usually caught for possessing illegal drugs (regardless of whether it was the first or a re-offense case) although they were taking methadone at the same time. Serious toxicity such as fatal polymorphic ventricular fibrillation might occur if they continued taking other opioids while consuming methadone due to an accumulation of opioids in the body [16].

Although, patients had been advised about the reasons for forced termination before joining the program, some of them continued to be aggressive while still in the treatment. These defaulters were blacklisted in the CCSC registry and could never join any MMT program throughout the country. Malaysia is among six countries which have half the global population of people who inject drugs (PWID) and have an elevated prevalence of HIV [17]. It is not uncommon that death among opioid abusers is caused by HIV or acquired immune deficiency syndrome (AIDS) complications from unsafe injection of drugs, needle sharing, and unplanned or unprotected sex. Psychiatric and medical comorbidities with high prevalence such as diabetes [18, 19], hyperlipidemia [20-22] and osteoporosis [23, 24] had also become the risk factors that can result in an interaction that worsens the health problems and reduces quality of lives among PWID.

Unlike CCSC, the method for abstinence was largely in the form of cold turkey or other similar approaches under a controlled environment at another rehabilitation centre. Thus, the person could no longer depend on methadone to correct his addiction to opioid drugs. For the patient who was warded, it was unknown whether methadone was given during his stay at the hospital. In general, patients were responsible for informing the attending physician or nurses about their participation in the MMT program so that they could continue taking methadone when staying at the ward. Nonetheless, when the patient failed to take methadone for more than 5 days without prior notice, he was considered involuntarily defaulted from the program at the center.

Voluntary Termination Factors: For most patients who voluntarily terminated the treatment, in some conditions, they opted to not come to take the methadone for a period not exceeding more than five days to prevent being expelled from the program. Insufficient doses could lead to premature termination, which is one of the greatest challenges to a successful MMT program. Usually, the physician would prescribe an initial low dose of methadone to avoid an accumulation of opioids in the body system that can lead to toxicity. These patients might not understand why the doctor prescribed them with a low dose and feel that the dose is not adequate as they can still get the

withdrawal symptoms in the early stage even when taking methadone. As a result, they may be taking the illicit opioid drug when the symptoms become excruciatingly difficult to bear. A study carried out in China revealed that the cue-induced cravings were least severe in long-term MMT participants, in contrast with that observed in short-term post-methadone participants [25]. Patients who were maintained on inadequately small doses were more likely to resume the illicit opioids, hence responding poorly to the treatment.

Eventually, they no longer felt that methadone is helping them, so they continued to take the illicit drug. Furthermore, findings from another study have revealed that the best retention rates were discovered among clients who were treated with methadone doses between 60 mg to 100 mg or more daily. The tendency for these patients to re-inject themselves with opioids also decreased when given large methadone doses [26]. Social and family support are very important for drug addicts to achieve abstinence from opioid addiction. It was reported that patients who had relatives on methadone treatment had a higher retention rate, thus indicating that family ties have a huge influence on individuals' drug use behaviors [27]. The MMT program in CCSC incorporated psychosocial interventions such as group and family counseling to improve the retention rate among opioid abusers.

These abusers are usually accompanied by concurrent anxiety disorders, low self-esteem as well as depression [28]. Hence, it is very crucial to introduce psychotherapy and counseling sessions in addition to the methadone treatment. Additional measures that include motivational enhancement therapy, spiritual improvement, and job placement could be carried out to obtain successful outcomes especially among clients with unfavorable predictive characteristics.

CONCLUSION: Although there were many clients in CCSC who failed to adhere to the methadone maintenance therapies shown by the high percentage of non-retention demonstrated in this study, CCSC has effectively served to promote and use evidence-based practice in the treatment and health care of drug users. The reasons for non-retention vary according to whether they were voluntarily or involuntarily defaulted. Most clients were involuntarily defaulted due to imprisonment or voluntarily opting-out from the treatment due to a lack of commitment towards the program. The duration for methadone treatment is crucial to achieve positive outcomes and promote continuous positive behavioral transformation among the opioid abusers.

Prolonged daily attendance or completion of the program reduces the possibility of relapse. Clients who remain in treatment for a longer duration also express better emotional well-being, increased productivity, improved physical health, less depression, and a more positive outlook towards their future.

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