PROSPECTIVE COHORT STUDY OF FACTORS ASSOCIATED WITH RETENTION OF METHADONE MAINTENANCE THERAPY AMONG PATIENTS AT THE CENTER FOR MENTAL HEALTH AND DRUG DEPENDENCE IN CAMBODIA

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AUTHOR'S DECLARATION OF ORIGINALITY

I certify that "Prospective Cohort Study of Factor Associated with Retention of Methadone Maintenance Therapy among Patients at the Center for Mental Health and Drug Dependence in Cambodia" is my own work. It has not been published elsewhere or submitted for a higher degree to any other University or Institution.

All the relevant information and data that I have used or quoted have been acknowledged and recognized properly.

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ABSTRACT

Drug abuse is a main concern for the Royal Government of Cambodia. In response to the emerging issues of drug use and related HIV risk, harm reduction services have been authorized by the Government. As part of its commitment to Universal Access to HIV/AIDS prevention, treatment and care, the Government collaborated with NGO's to pilot a Methadone Maintenance Therapy programme (MMT). It was established in July 2010 in a public health facility.

Many studies have shown that treatment retention is one of the key elements to the success of a MMT programme. That means if we can keep the patients in treatment longer, the patients can get more benefits from the programme such as a reduction in, or cessation of, heroin use and improvement in their health status, financial issues and their quality of life. Therefore, retention in MMT Treatment is very important to prevent the patients from harm related to opiate use.

The purpose of this study is to explore the level of compliance (Retention) among the clients enrolled in Methadone Maintenance Therapy (MMT) at the Center for Mental Health and Drug Dependence (CMHDD) in Cambodia and to determine the associated factors.

Concerning the future scale-up of MMT services, the Ministry of Health has also advised that a study on the success of MMT at CMHDD should be conducted before the MMT programme can be rolled out throughout the country.

Having found the associated factors toward retention in MMT, the MMT programme can be improved for future replication.

Method

This study used a prospective cohort study design. The subject of study were injecting and non-injecting opiate users treated at the Center for Mental Health and Drug Dependence ***since 1 July 2010*** and the last clients enrolled ***on 30 June 2011***. All the enrolled clients were followed up through to the end of this study ***on 30*** **September 2011** (15 month cohort study).

This study is to explore factors associated with methadone maintenance compliance (retention) in a group of patients on methadone maintenance therapy at the Center for Mental Health and Drug Dependence in Cambodia.

SPSS version 16 (PASW statistics 16) was used for analysis. The independent variables in this study were used and the clinical records of all methadone patients in which demographic data is taken to describe the association between Retention in MMT treatment and other associated factors. Independent variables are Gender, Age, Marital Status, Level of Education, Job Status, Patterns and Types of Drug Use, Past History of Drug Use, Duration of Methadone Treatment and Methadone Dose. The dependent variable is Compliance Pattern (Retention) to methadone treatment and the variables were explored in the analyses.

Results

During this period of study (from 1 July 2010 to 30 June 2011), there were 107 patients enrolled in treatment and followed up until 30 September 2011. Of 107, 4 patients died due to other diseases and were not included in this study. Overall retention within this study was 82.5% (N = 85) among 103 patients. 3 months, 6 months, 9 months, 12 months and 15 months retention rates were 92.2%, 80.3%, 72.4%, 70.7% and 70.7% respectively. Most of non-retention patients quitted the treatment at an early stage of this cohort. During the 15 months, there were 18 patients who were not retained in treatment. Of them, 44.4% (N = 8), 33.3% (N = 6), 16.7% (N = 3), 5.6% (N = 1) quit MMT respectively in 3 months, 6 months, 9 months and 12 months.

In this study, female, higher educated, married, single opiates use, injecting opiates use, using opiates equal to or more than 4 times a day, and living farther than 4 km's from the clinic, had higher retention rates. But there was no significant association with retention in Treatment.

There was a significant association between homeless and higher retention ($p = 0.0001$). It may be due to the fact that they were vulnerable groups and got more support from NGOs to facilitate their access to MMT. Methadone dose is another predictor variable where it was found that a methadone dose equal to, or higher than, 60 mg's/day/person had a significant association with retention in MMT ($p = 0.03$).

Conclusions

Based on WHO recommendations, one year retention over 60% is considered as an effective programme in the reduction of daily opiate use, and an average methadone dose of over 60 mg's/day/person is an effective dose to retain the patients in MMT. In this regard, this study found that the 15 month retention rate was 70.7% and the average daily dose of methadone was 70 mg's. Therefore, the MMT programme in Cambodia is considered as an effective programme in terms of reduction of harm related to opiate use and daily opiate use, and these findings should be used as a baseline for rolling out MMT services to other areas.

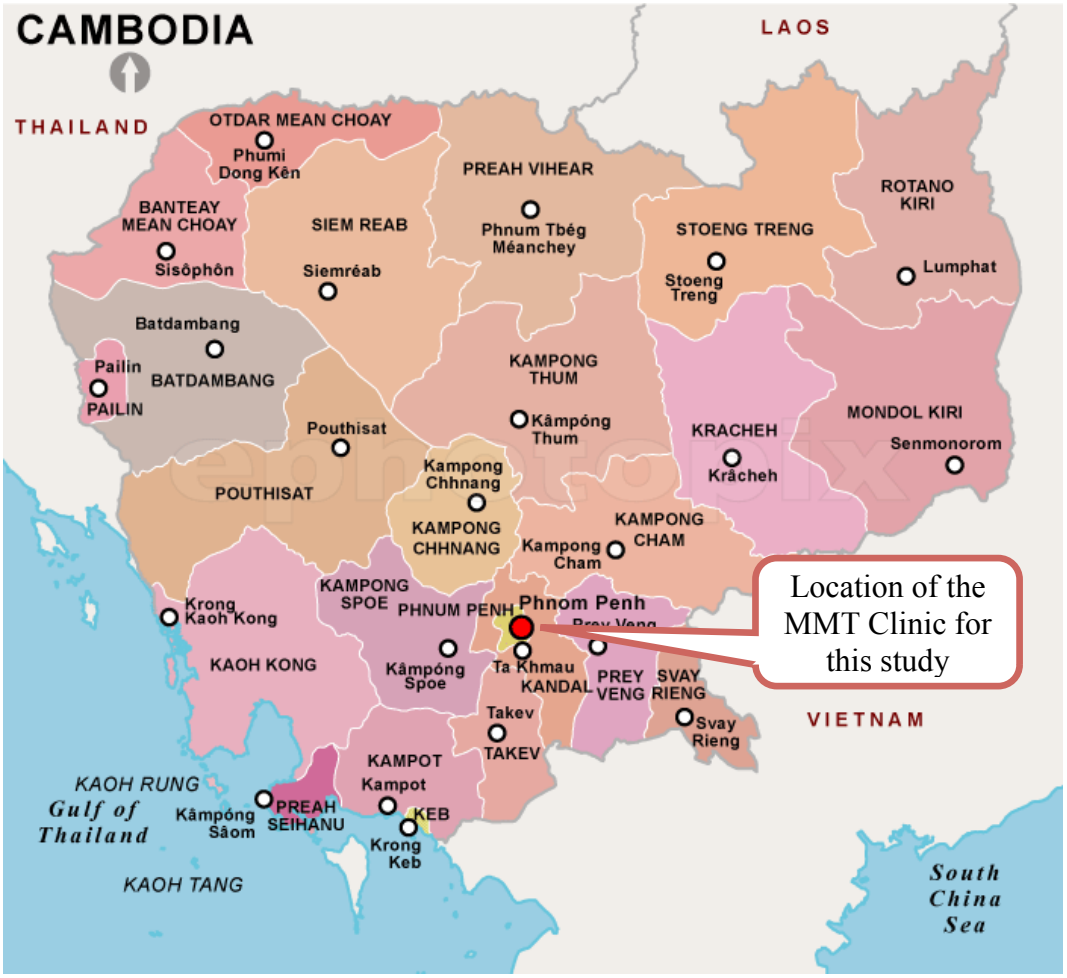
To keep the patient better retained in treatment in the early stage, NGO partners and the MMT service should provide more orientation to MMT clients before starting the methadone dose to make MMT patients understand better about MMT treatment and to make better decisions.

The findings also show that the role of NGOs is also very important to improve treatment retention among MMT patients. It should also be recommended to build up capacity among MMT service providers in treatment, dosing, and counseling to ensure the quality of the MMT service. For future development of MMT, collaboration with NGOs working in the community is needed and the development of treatment guidelines to ensure compliance of the patients and methadone dosing. Other recommendations are that non-medication interventions are also predictive factors associated with retention in MMT.

LISTOF ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ATS	Amphetamine Type Stimulants
AusAid	Australian Agency for International Development
CBT	Cognitive - Behavioural Therapies
CMHDD	Center for Mental Health and Drug Dependence
DU	Drug User
FHI	Family Health International
HIV	Human Immunodeficiency Virus
IDUs	Injecting Drug Users
I-RARE	International Rapid Assessment Response and Evaluation
Laos PDR	Lao People's Democratic Republic
MMT	Methadone Maintenance Therapy
MOH	Ministry of Health
NGO	Non Government Organization
OST	Opioids Substitution Therapy
SG-NACD	Secretariat General of the National Authority for Combating Drug
WHO	World Health Organization
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNODC	United Nations Office on Drugs and Crime

Figure 1: Map of Cambodia and Location of the MMT Service



Source: Ephotopix (Internet Source)

CHAPTER I

1- INTRODUCTION

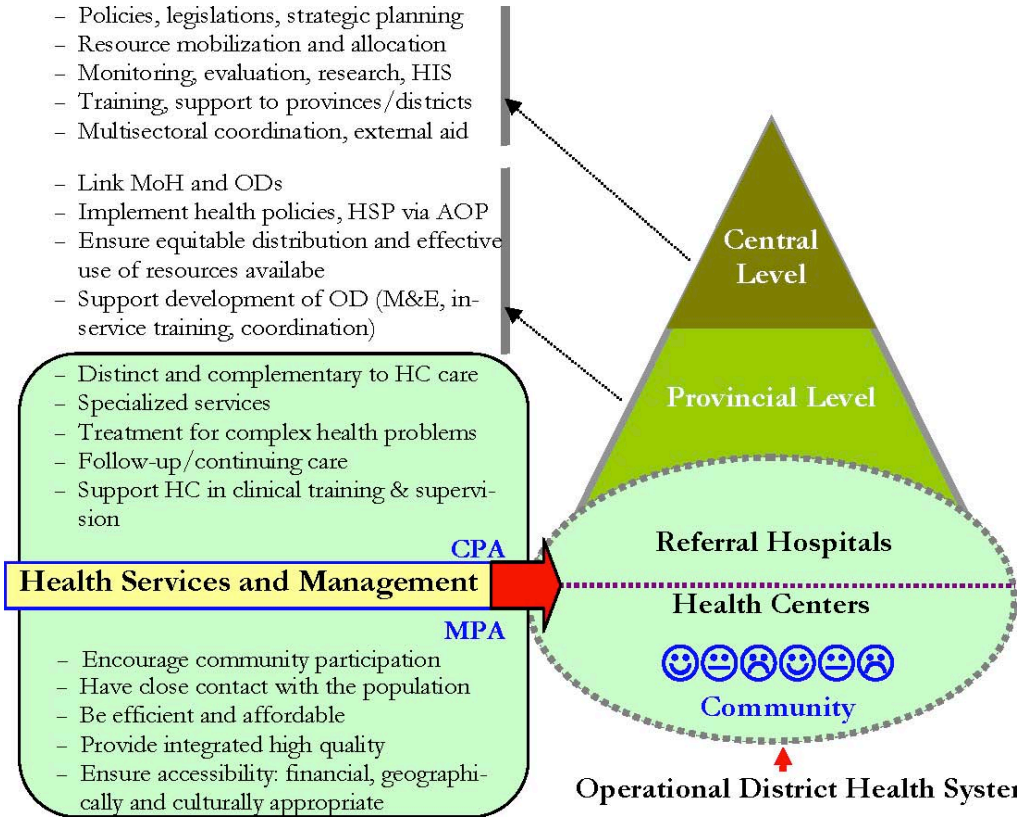
1.1 About the health system in Cambodia

The Kingdom of Cambodia is a South East Asian country that is located in the southern portion of the Indochina peninsula. It is bordered by Vietnam to the East, Thailand to the Northwest, the Lao PDR to the Northeast and the Gulf of Thailand to the Southwest. With a total landmass of 181,035-km's^2, Cambodia currently has a population of about 14,805,000 with an estimated rate of population growth of 1.7 percent. The life expectancy of Cambodian people is 65 years for women and 57 years for men. 95 percent of Cambodian people follow and practice Buddhism. The capital city of Cambodia is Phnom Penh, which is the nation's political, cultural, social and economic center. 20 percent of Cambodian people are living in urban areas (Ministry of Health, 2008).

During the Pol Pot Regime, from 1974 to 1979, the country's health system and structure were decimated by the Khmer Rouge. After gaining liberation, Cambodia had only 50 medical doctors who had survived and escaped from that dark regime. Meanwhile, medical schools and nursing schools appeared, and they provided medical training to people. Also, health services were re-established to provide treatment and healthcare to the people from the whole country down to the community level (Ministry of Health, 1999).

Cambodia has 24 provinces and municipalities. According to the national health coverage plan, health service delivery is provided by eighty-eight referral hospitals and nine hundred health centers, which are based at the commune level. These referral hospitals and health centers function and serve as commune health centers (Ministry of Health, 2008). The health service provision has been vertically integrated from the national to peripheral level.

Figure 1. 1: Health System Organization



Source: Ministry of Health, Cambodia, 2008

As a post conflict country, Cambodia, which has been at full peace from the early 1990s, faces challenges with many health problems. Those problems are

HIV/AIDS, malaria, maternal-child health, tuberculosis, high maternal mortality rates, high child mortality rates, non-communicable diseases, and other health-related-problems. In recent times, illicit drug use has become the nation's major concern for communities and for the Royal Government of Cambodia. In the public sector, substance abuse has been put in the non-communicable disease programme strategy by the Ministry of Health. The non-communicable disease programme strategy has been integrated into the health strategic plan 2008—2015 (Ministry of Health, 2008).

Traditionally, drug abuse had not been of any concern in Cambodia. Some Cambodian families used drugs as a tradition (Addiction in Sub Mekong Region, 1998) such as chewing tobacco, and betel especially by women. Usually, betel is served to visitors and guests, especially in rural area. In the past some people used Cannabis in making soup or by smoking. Heroin use is also reported especially among business families. And some traditional healers used Heroin to treat diarrhea.

So far there is no reliable national estimates of the number of drug users in Cambodia. Based on experts consensus led by UNAIDS in 2007, illicit drug users were accountable for 46,300. Of them about 23,150 (50%) are ATS users, and 2,900 (6.3%) others are heroin users and 80% of heroin users are Injecting Drug Users (National Authority for Combating Drugs, 2008).

Illicit drug user is the term used to describe a person who is reported by a data provider as having used an illicit drug as defined by Cambodian law. The term

includes persons sniffing glue or solvents. The term “Drug Use” is used instead of “ Drug Abuse” or “ Drug Dependence” because these terms suggest a higher standard of assessment, which is generally unavailable in Cambodia. The term ‘illicit’ is included to emphasize the legal aspect of the description rather than a clinical or behavioral confirmation of drug use (National Authority for Combating Drugs, 2008).

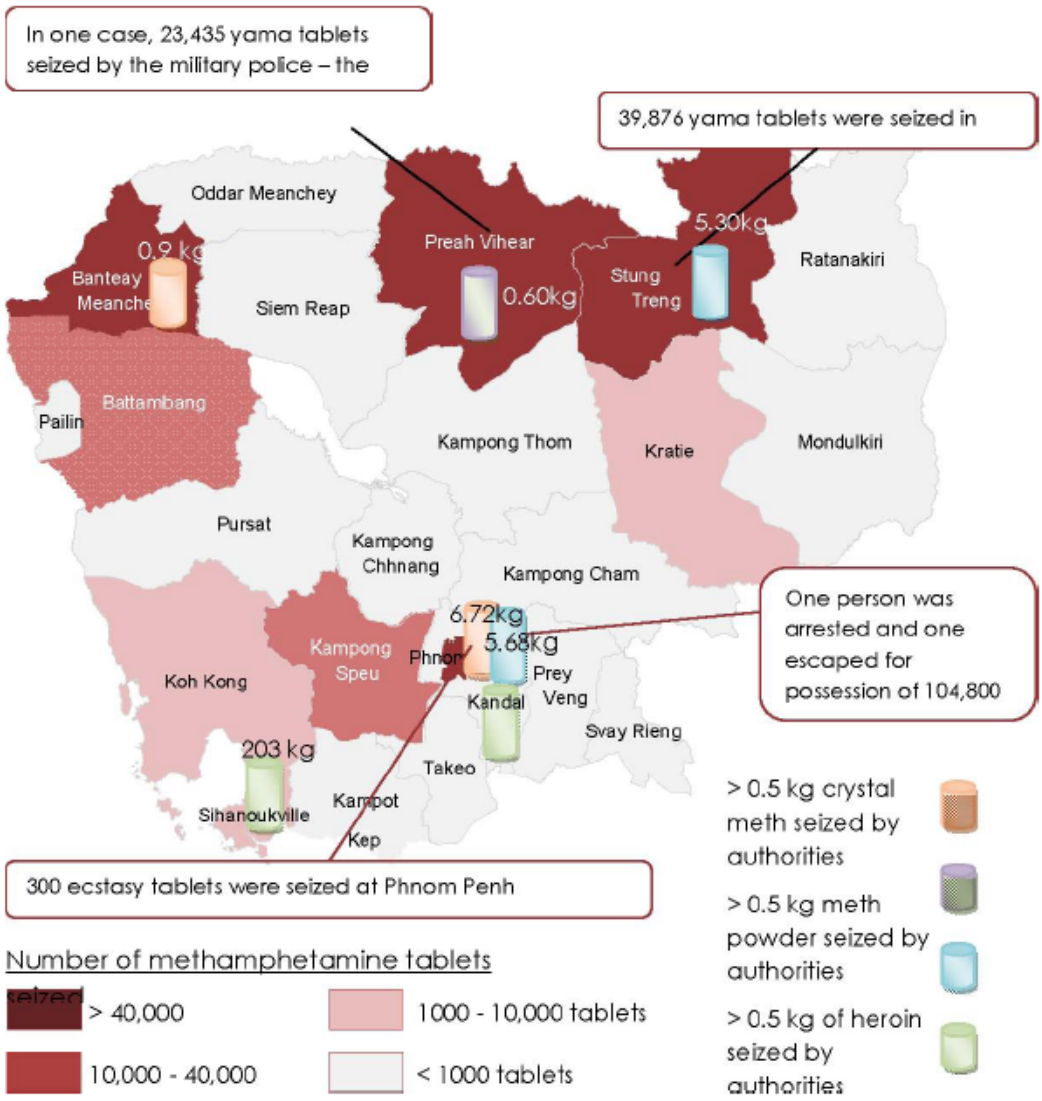
Transmission of HIV has a strong connection with injecting drug use. According to many studies, in several parts of the world, general healthcare and welfare services including the development of community-based health and social services, and drug dependence treatment programmes are needed due to the extent of HIV/AIDS epidemics amongst injecting drug users (WHO/UNAIDS/UNODC, 2004).

Using injecting equipment and drug solutions with other people, having sexual contact with IDUs, and sexual activity with people at high risk of HIV make those users vulnerable to infection with HIV and other blood-borne viruses. Female drug users are prone to HIV as they tend to utilize injecting equipment of their partners and find it hard to discuss sexual practice with low risk and condom usage as compared to their male counterparts even though they are the majority of injecting drug users. Thus, presumably, IDUs engage in the sex industry. Transmission of hepatitis C, leading to at least 50-85% of cases of chronic infection dominantly occurs through injection drug use. Chronic infection advances to liver cirrhosis among almost 7-15% of persons who are infected,

while at the same time some advance to liver cancer. More than 70% of HIV infections in some countries of Asia and Europe is caused by injection drug use compared with only 5 to 10% worldwide. Generally, the use of opioids is found in both regions of Asia and Europe (WHO/UNODC/UNAIDS Possition Paper, 2004).

Transformation of the pattern from non-injecting to injecting drug use has been recorded. WHO, in collaboration with many Government and NGO agencies, carried out an International Rapid Assessment Response and Evaluation (I-RARE) in 2005 in two urban areas of Phnom Penh and North West Cambodia, including Poipet, to inspect drug use and sexual risk patterns that, allow an increased risk of contracting HIV by the DU and IDU. Accessibility of sterile needles and syringes cost and availability, and a low level of understanding of injecting drug use leading to HIV, were ascribed to reuse of needles or syringes by the surveyed IDU (WHO/UNODC/UNAIDS Position Paper, 2004).

Figure 1. 2: Methamphetamine, Heroin and Cannabis Seizures in Cambodia, 2007



Source: National Authority for Combating Drugs, 2008

1.3 Different Interventions in Responding to Opiate Dependence

Methadone belongs to the opioid family of drugs, which includes morphine, codeine and heroin. Opioids are classified under depressant drugs as they work by slowing down the functions of the central nervous system. Methadone was

developed in Germany in 1941 for pain relief. It was then used as a treatment for heroin dependence in New York, USA, in 1964 and it is now recognized internationally as an effective method for treating opioid dependence (WHO, 2008).

Methadone is a synthetic opioid that is typically administered orally as a liquid and is a medication most commonly used for substitution therapy of opioid dependence. Methadone maintenance treatment is also an extensively researched treatment modality. There is strong evidence from research and monitoring of service delivery, that substitution maintenance therapy with methadone (MMT) is an effective intervention in reducing illicit drug use, reducing mortality, reducing the risk of spread of HIV, improving physical and mental health, improving social functioning and reducing criminality. Higher doses of methadone are generally associated with greater reductions in heroin use than either moderate or low doses (WHO/UNODC/UNAIDS Position Paper, 2004).

Literally, Methadone has been used to detoxify opioid users but it has not been effective due to high relapse rates. Traditional abstinence-based approaches to drug dependence aim to stop drug use permanently. Few clients achieve abstinence, at least in the short term, as many abstinence-based services have acknowledged more recently. It is just as important to provide harm reduction services to clients who may relapse soon after leaving treatment (WHO, 2006).

Relapse following detoxification alone is extremely common, and, therefore, detoxification rarely constitutes an adequate treatment for substance dependence

on its own. Simple detoxification or stopping opioid use is often insufficient; therefore, a therapeutic process is required. Detoxification, however, is a first step for many forms of longer-term abstinence-based treatments (WHO/UNODC/ UNAIDS Position Paper, 2004).

There are many interventions to reduce harm related to injection drug use. In this regard the Government of Cambodia has adopted a Harm Reduction Strategy in which there are two main programmes, that of a Needle/-Syringe Programme and Opioid Substitution Therapy (OST). Globally, there are two types of medication used in Opioid Substitution Therapy, one is Methadone and the other one is Buprenorphine. But as Buprenorphine is more expensive than Methadone, Cambodia has chosen Methadone even though Buprenorphine is as effective as Methadone. Figure 1.3 shows comprehensive services for Drug Users.

Figure 1. 3: Drug-Specific Support Services

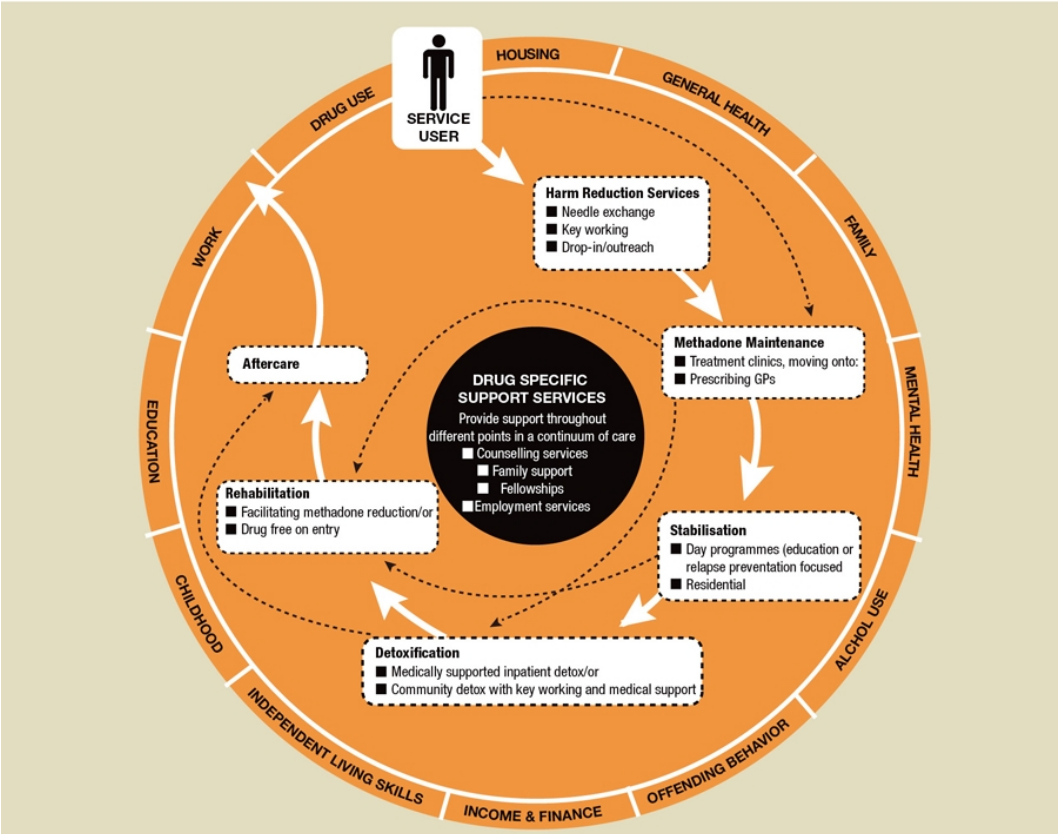


Figure 1 Example of the continuum of care within drug services
Source: Homeless Agency Partnership (2010: 82)

Source: Lyons, 2010

Methadone Maintenance Therapy (MMT) is an effective treatment for opiate dependence and was initiated in 1964 in the United Sates by Dr. Vincent Dole, Dr. Marie Nyswander, and Dr. Mary Jeanne Kreek, at the Rockefeller Institute for Medical Research, which is known now as Rockefeller University and Rockefeller Hospital. After several studies, it was found to be a safe and effective

intervention for opiate addiction. Then, MMT was recommended and integrated into multi-modality treatment systems in New York, Illinois, Connecticut, Massachusetts, Pennsylvania, and Washington D.C. Since the 1970's, MMT has been more widely disseminated within a national network of addiction treatment programmes in the United States (William, 2010).

1.4 Rationale

Recently Cambodia has made a great achievement in combating HIV transmission. As a result, the prevalence of HIV tested sero—positives has decreased from 1.2 % in 2003 to 0.9 % in 2006 among people aged from 15 to 49 years, although the prevalence of HIV among IDUs is 24.4% (National AIDS Authority, 2010). This figure has shown an emerging concern that the spread of HIV transmission would occur if there is no proper harm reduction intervention.

In Cambodia, MMT is the most recent programme and was approved by the Ministry of Health (MOH) on 31st March 2010 (Ministry of Health, 2010) through an Agreement signed with the Secretariat—General of the National Authority for Combating Drug (SG-NACD), the Australian Agency for International Development (AusAID), the World Health Organization (WHO) and Family Health International (FHI). Referring to the clinical guidelines of MMT in Cambodia, the main purposes of MMT in Cambodia are:

MMT OBJECTIVES IN CAMBODIA

- Reduce the patient's drug use
- Improve the patient's health and well-being
- Reduce transmission of blood-borne infectious diseases (e.g. HIV and hepatitis)
- Reduce death
- Reduce crime committed by patients
- Facilitate an improvement in the patient's social functioning
- Improve the economic status of patients and their family

MMT Clinic in Cambodia is a MoH-run demonstration using evidence-based international good practices. As planned MMT clinic aimed to provide up to 100 opiate-dependent people with methadone on a daily basis for up to 12 months. The clinic linked MMT clients with other key health programmes, e.g. HIV/AIDS, TB, and socio-economic rehabilitation services. A final evaluation was also recommended after 12 months of MMT demonstration. If it had success outcomes, the Government's approval would be sought to establish MMT as a standard programme in the health system and possibly scale-up to other places in the country.

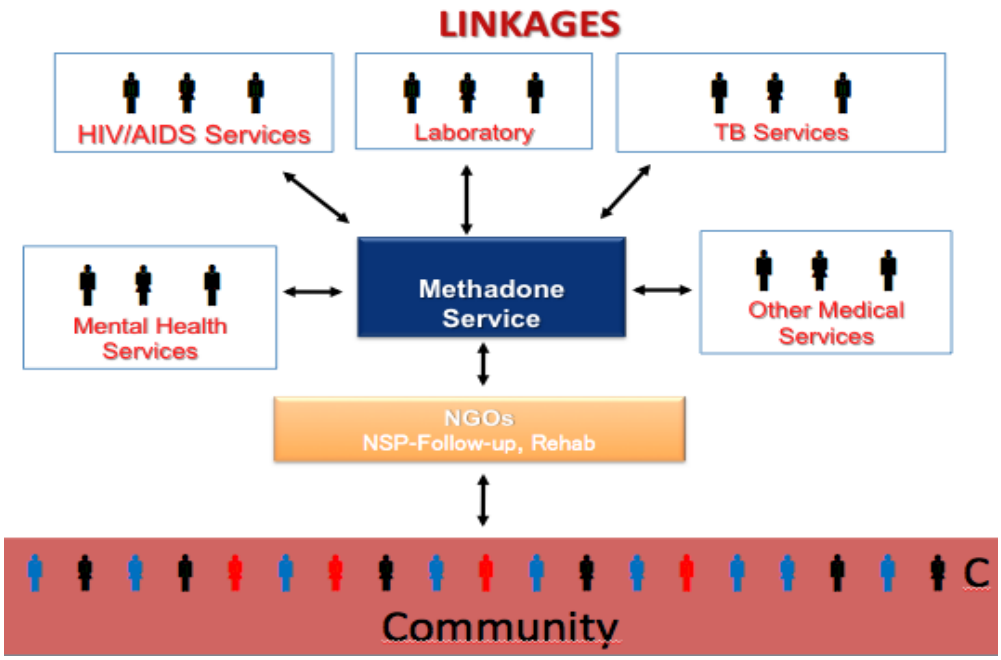
In order to achieve the above purposes, commitments should be made by clients and MMT staff to retain the clients in the treatment as long as possible. In MMT programme, Treatment Retention is a key leading to success of the programme in

term of harm reduction related to opiates use. It is also vital for this pilot project of MMT in Cambodia for the future scale up of MMT services in Cambodia.

The purpose of this study is to explore the level of compliance (Retention) among the clients enrolled in Methadone Maintenance Therapy (MMT) at the Center for Mental Health and Drug Dependence (CMHDD) in Cambodia and to determine its associated factors.

MMT programme in Cambodia is collaborated by the Ministry of Health (MoH) and non-government organizations (NGOs). The Ministry of Health manages the MMT service while NGOs are in charge of referring MMT clients to MMT service and follow up with MMT clients in each community. Having found the associated factors toward retention in MMT, it would be good evidence for MMT programme to improve MMT service for future replication. Figure 1.4 shows linkage between MMT and other services.

Figure 1. 4: Service Linkage between MMT and other Services



It is recommended to encourage the patients to remain in treatment for at least 12 months to achieve enduring lifestyle changes (Henry, 2003). A Cochrane Review also revealed that methadone is an effective maintenance therapy intervention for the treatment of heroin dependence because it retains patients in treatment and decreases heroin use better than treatments that do not utilize opioid replacement therapy (WHO, 2005). A review of methadone maintenance therapy in Australia (1995) found that the patients who had premature termination of MMT tend to return to drug use (Commonwealth Department of Human Services and Health, 1995).

More recent studies have shown that although MMT does not always result in abstinence from drug use, it can improve attendee life including drug use, productivity, criminality and HIV risk behaviors. In this regard, it was found that

it resulted in the improvement of productivity and less illegal income among MMT participants, which may indicate, reduced criminality. So methadone maintenance therapy has positive outcomes for opiate injection drug users (Corsi, 2009).

Haynes et al., defined that Compliance is the most accepted and one important element to show the success of any control and therapeutic programme. However, other studies also showed that Compliance to MMT could be associated with multiple factors (Ezat, 2009).

1.5 Aims of the study

The main hypothesis of this study is to investigate factors associated with retention in Methadone Maintenance Therapy. The outcome variable of this study is Treatment Retention. That means the patients remained in MMT Treatment programme during this study. The predictor variables include gender, age, marital status, level of education, living situation, job, history of opiates use, patterns and types of drug use, distance to clinic, duration of retention in MMT programme, and methadone dose.

The research questions of this study are:

- What is the retention rate among the patients attending in MMT programme in Cambodia?
- What are predicting factors significantly associated with retention in MMT programme in Cambodia?

The aim of this study is to explore factors associated with treatment retention among methadone patients in general and to find which predicator variable were associated with retention in MMT programme in Cambodia during the period of this study.

The findings of this study would be helpful for evaluation of the MMT programme and to gain lessons to improve MMT service in Cambodia.

CHAPTER II

2- LITERATURE REVIEW

2.1 Opioid Use

Opioid or Opiate are referred to as either a natural or synthetic drug. Its properties or main ingredient are similar to Opium or Morphine. Opium is one type of poppy, Papaver Somniferum. It was used as long ago as 4000 B.C. by the Sumerians and Assyrians. The use of Opium spread from the Middle East when the Islamic religion was expanded. Europeans became aware of opium in the early 1500's (Clark, 2008).

Like other dug use, Opiates are used through many ways such as smoking or snorting or injection. The most dangerous route of administration is Opiate injection because it can be a cause of transmission of blood borne diseases such as HIV and Hepatitis.

A UNAIDS report (2008) showed that over previous decades in many countries, injecting drug users were at high risk of exposure to HIV. Users of drugs were at increased risk of premature mortality and blood borne infections. There had been several causes of death due to illicit drug use; the most common causes of death among such individuals were infection, overdose, suicide, violence and accident (Langendam, 2001). The nature of addiction varies from one individual to another. Usually individuals who are addicted to drug experience withdrawal

symptoms; the severity of the symptoms varies from one individual to another – even people who have been using the same amount. Some people experience it more easily than others (Getting Through Heroin Withdrawal, 2004).

The spread of HIV is still a concern regionally as well as globally especially among injecting drug users. For instance, the South East Asia and Western Pacific regions have been facing major challenges associated with HIV prevalence and its preventive measures. WHO released a report on the Practices and Context of Pharmacotherapy of Opioid Dependence in the South-East Asian and Western Pacific Regions (WHO, 2002). According to reports from China, the prevalence of HIV sero-positive is high among of injecting drugs users. Sixty-two percent of them were reported to be infected by HIV by the end of 2000, which is equal to 20,711 cases of injecting drug users infected by HIV. Similar experiences also exist in Yunnan Province of China, where 8,317 cases of HIV were reported in September 2000, and 70% of those who got a positive result were confirmed to be injecting drug users. The result from a three-year study on this issue in a locality in Yunnan Province indicated that HIV positivity was sharply rising from 10 to 70 percent over the study period (WHO, 2002).

In Indonesia, WHO (2002) reported an increase in HIV prevalence among injectors. The results showed that 73% of all new HIV positive tests and 37% of new AIDS cases were both among injecting drug users. In Bogor, in West Java province, the report showed that one-in-four injectors got a positive HIV

test/result, and a study among prisoners in Bali found that 53% of injectors were HIV positive.

Drug injection has also recently been indicated as the main cause of HIV spread in such countries as Malaysia, Myanmar, Vietnam and Thailand. In Malaysia, even though there is no report of the exact number of injecting drug uses, 85% of HIV transmission, equivalent to 65,893 HIV detected cases, is estimated to be caused through the injecting of drugs. The situation is even more serious in Myanmar and Thailand as more than 50% of the drug injectors in these two countries are estimated to be infected with HIV. Similarly, it was reported that approximately 60% of the injectors in Vietnam are HIV infected and that they accounted for the majority of the positive results of HIV tests.

2.2 Methadone Maintenance Therapy

Methadone Maintenance Therapy is a part of Harm Reduction Programme. To reduce harm related to drug use, there are two main programmes; one is Opioid Substitution Therapy (OST), which uses Methadone or Buprenorphine, and the other is the Needle/Syringe Programme (NSP), which provides sterile needles and syringes for injection drug users.

Methadone Maintenance Therapy has been considered as an effective approach to prevent harm related to opioid use. In 2004, the World Health Organization, United Nations Office on Drugs and Crime, and the Joint United Nations Programme on HIV/AIDS disseminated a position paper

(WHO/UNODC/UNAIDS Position Paper, 2004) on "Substitution Maintenance Therapy in the management of opioid dependence and HIV/AIDS prevention". There is strong evidence to prove that methadone maintenance therapy is an effective method to reduce illicit drug use, reducing mortality, reducing the spread of HIV, improving physical and mental health, improving social functioning and reducing criminality (WHO/UNODC/ UNAIDS Position Paper, 2004).

However, MMT is a maintenance therapy and needs long-term treatment for opioid users. MMT patients need to remain in the treatment because retention can prevent the patient from harm related to opioid use and is key for a successful MMT programme. Thus, retention has been accepted as a measure of the success of a MMT programme (Liu, 2009), and to retain the patients in treatment is a challenge.

Evidence shows that treatment compliance in MMT has many different associated factors based on different studies (Liu, 2009).

Based on WHO recommendations, an adequate methadone dose is an important factor to retain MMT patients in treatment. In addition, it has been revealed that effective methadone maintenance therapy needs to provide adequate doses of medication and access to counseling as well as medical and psychiatric care as needed (WHO, 2005).

It was also found that within one year, when 60% to 80% of patients are retained in MMT treatment, there will be a reduction of daily illicit opioid use from one

hundred percent at the time of starting treatment to less than twenty percent one year after MMT treatment is adopted. WHO's report has shown that Methadone maintenance cannot completely eliminate heroin use among clients, but it does substantially reduce opioid use. In maintenance treatment, methadone "doses of 60 mg/day or more have been identified as being most effective in terms of retention in treatment and reductions in illicit drug use and criminal behavior" (WHO, 2005).

Similarly, the Department of Mental Health and Substance Abuse (2004) has shown that methadone doses in excess of 60 mg/day are most clearly associated with better retention in treatment and maximal suppression of heroin use. Methadone doses for effective MMT are typically 60-100 mg/day (NIDA, 2006).

Based on the 10 years of experience of a MMT clinic, a study in Israel found that high doses of methadone were associated with retention on MMT. It showed that a daily methadone dose of 100 mg or higher is a predicting factor associated with retention on MMT (Peles, 2005).

Riest Dan et al., 2010, also revealed that Methadone dose was a key factor to retain MMT patients on treatment. It was stated that episodes with daily doses over 100 mg had the highest probability of being retained on treatment at every time point. Episodes with a daily dose below 60 mg discontinued earliest (Reist, 2010). However, WHO/UNODC/UNAIDS (2004) has recommended that the maximum daily dose of methadone should be left to the practitioner to judge and decide based on the assessment of the individual patient.

Some studies (Ezat et al., 2009) found that age is associated with compliance and that socio-demographic factors influence compliance. That means the older the age, the better the retention. The model revealed that increments of one year of age lead to a 6% increment in compliance. Other socio-demographic factors such as full time job status and distance to a methadone clinic were also found significantly associated with good compliance with therapy, and a history of shorter duration of addiction was found to be related to good compliant clients (Ezat, 2009).

Similarly, Carol et al., 2008, found that the odds of remaining in treatment for 730 days or more increased with age. At retention rates of 20% and lower at 17 weeks, and of 85% and higher at 40 weeks, 50% of patients remained in treatment for 730 days or more.

Miguel et al., 1997, found that Patient characteristics such as age, race, gender, employment, criminal history, severity of addiction, and psychological status, have been studied as predictors of retention.

Among the most important factors are socio-demographic factors; factors related to previous history of addiction, factors related to the therapy process, and factors related to impact of therapy (Ezat, 2009).

The illicit use of drugs tremendously impacts on society and brings about many serious social issues such as marital and relationship breakup, joblessness, homelessness, and child neglect, which often leads to children being brought into

the care system. Illicit drug use is also obviously associated with crime. Some opioid dependent people commit crimes so that they can afford to use drugs. Drug-related crime is estimated to account for half of all crime recorded in the UK and incurred annual costs of about £1 billion to the criminal justice system in 1996 (National Institute for Health and Clinical Excellence, 2007).

CHAPTER III

3- METHODOLOGY

3.1 Design

This study used a prospective cohort study design to follow a group of Opiate Users enrolled in MMT. Injecting and non-injecting opiate users who were enrolled and treated at the Center for Mental Health and Drug Dependence since 1 July 2010 until 30 June 2011were recruited in this study. All MMT clients were recruited and followed up through the end of this study in 30 September 2011. It is an analysis of risk factors and follows a group of people who received treatment at CMHDD, and uses correlations to identify associated factors of retention.

- Retention is an outcome variable of this study. It is a pattern of patient receiving regular methadone dose, having or missed methadone dose equal or less than 5 consecutive days any time in the period of study; considered **as Retention.** In this regard the patients still are retained in treatment.
- The pattern of patient receiving methadone is not regular and having missed dose or missed methadone dose more than 5 consecutive days at anytime of treatment during the study time is considered as **Non Retention or Dropout.** In this regard, the patient has terminated treatment and a new dose must be started if the patient returns to CMHDD.

Other important predictor variables are defined as the following:

- Gender is a predictor variable classified into two categories as male and female;
- Age is a continuous variable in year. It was classified by age group as categorical variable for analysis;
- Marital Status is a categorical variable classified as single, married, widowed, separated, co-habiting;
- Level of education is defined as no education, primary school, secondary school, university and Post University;
- Living Situation is categorized as homeless, living with partner, living with parent and living with NGO partner;
- Job was defined as categorical variable as no job, part time work, full time work that the patients had at entry point when they enrolled in the treatment;
- History of opiates use is a continuous variable and referred to the past history of opiates use when the patients started to use opiates until the time of admission in MMT;
- Frequency of Opiates use per week before enrolled in the treatment was a continuous variable and converted to categorical variables for analysis;
- Pattern of drug use was categorized as Only Opiates Use, or Use Opiates with other illicit drug, smoking use or injecting use;

- Distance to clinic is a continuous variable and determined a distance from their living location to MT clinic. It was categorized into categorical variable for analysis;
- Duration in MMT programme was referred to the duration of the patients enrolled in MMT during the period of this study and categorized in different groups of duration as categorical variables for analysis,
- Methadone dose was referred to the maximum dose of methadone that the patients received during the period of the study.

3.2 Methods

3.2.1 Study Site

The study was conducted at the Center for Mental Health and Drug Dependence in Phnom Penh, Cambodia. This center is the first center in Cambodia where the MMT has been established to provide treatment for Opiates Dependents.

3.2.2 Selection (inclusion) Criteria

- Must be adult patient
- Can give consent
- Patient needs to fulfill ICD-10 criteria (International Classification of Disease version 10). A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

- A strong desire or sense of compulsion to take the substance; difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;
- A physiological withdrawal state when substance use has ceased or been reduced, as evidenced by the characteristic withdrawal syndrome for the substance; or the use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
- Evidence of tolerance, such that increased doses of the psychoactive substances are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non-tolerant users);
- Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
- Persisting substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be aware of the nature and extent of the harm.

3.2.3 Exclusion Criteria

- Psychotic patient;
- Negative Urine Test for Heroin Use;
- Cannot communicate in Khmer;
- Foreigner.
- Severely sick because of other physical illness.
- Without NGOs' referral

3.2.4 Data Collection Procedure

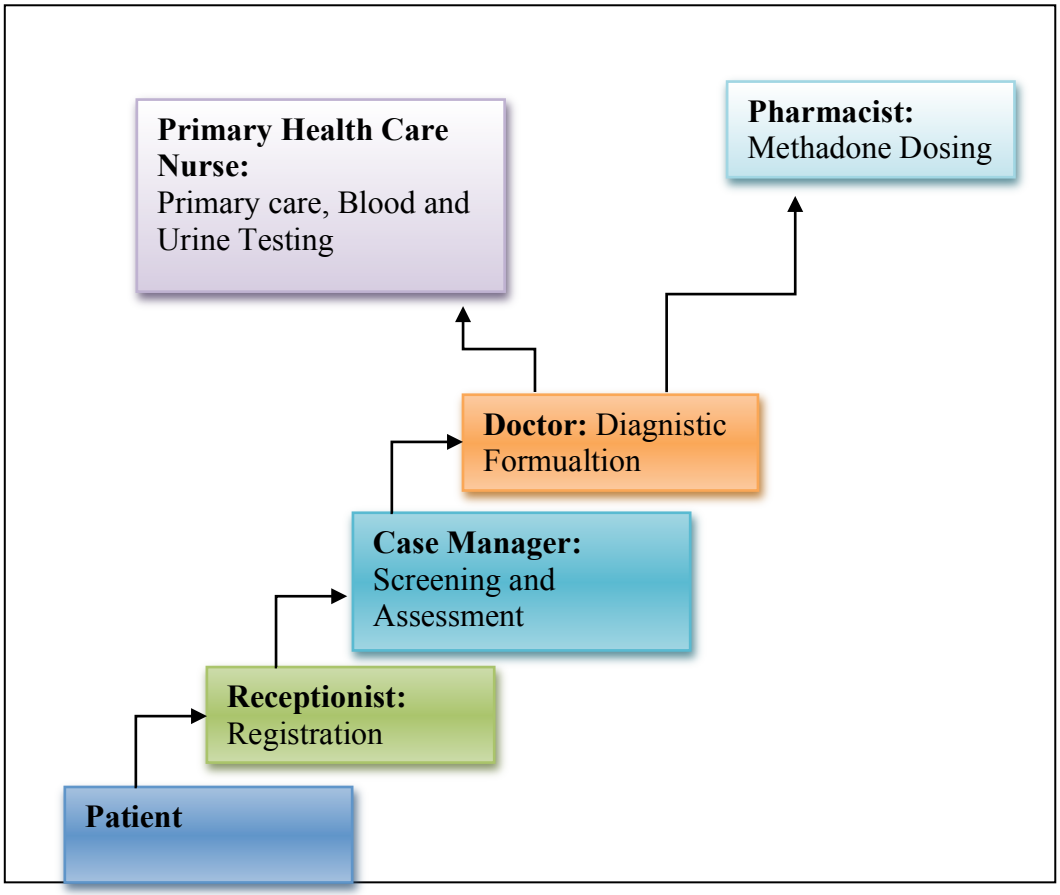
A-Patient Enrollment and Treatment Process

First, the patients need to meet a receptionist for registration and completing an informed consent form. Then they were referred to case managers and gave an interview for screening and assessment of psychosocial and substance abuse problems. After that the case managers were referred to doctors for final assessment. After seeing doctors, the patients were referred to primary health care nurses for blood and urine test. Finally the patients can get methadone dose at the pharmacy.

All information given by the patients, and the results from screening, assessment and medical examination were recorded in MMT data management system. The patients were tracked from the enrollment until they dropped out of the treatment.

In case of dropout, the interviewers contacted NGOs partners or traced the patients in community to find out other information related to dropout.

Figure 3.2.4. 1: Flow of the patients and treatment process



B- Materials

The study used the data recorded in the MMT data management system that was completed by receptionist, case managers, doctors and pharmacists. There were a number of information items that were extracted for this study, such as:

- Socio demographic information;
- Patterns and types of Opiates Use;

- History of drug use;
- Length of retention in MMT;
- Distance to MMT clinic
- Retention or non retention in Treatment;
- Methadone dose for each patient

3.2.5 Data Analysis

The data was extracted from the MMT data management system of CMHDD and analyzed by using the SPSS version 16. The socio-demographic characteristics such as age, gender, educational level, marital status, job status, and living arrangement were described to identify the minimum, median, mean, maximum and percentage. The association between Independent variables (Sex, Age, Level of Education, Job Status, Age, Past history of Drug Use, Duration of methadone treatment and Methadone dose and Dependent variables (Retention or Non retention) was tested by using the chi-square test; T-student test; regression and p value of less than or equal to 0.05, to find out statistical significance. In application of statistical tests, 2 by 2 tables were made, then continuous variables were categorized as Yes/No or in categories:

- Age is a continuous variable, converted to

	Variable	Recode
Age Group	18 – 23 Years old	0
	24 – 29 Years old	1
	30 – 35 Years old	2
	36 – 41 Years old	3
	Over 42 Years old	4

- Length in treatment is a continuous variable, converted to

Variable	Recode
Less than 1 year	0
More than 1 year	1

- Methadone dose is a continuous variable, converted to

Variable	Recode
Methadone dose equal or lower than 60 mg/day	0
Methadone dose over 60 mg/day	1

- Distance to MMT clinic is a continuous variable, converted to

Variable	Recode
Equal or shorter than 4 km	0
More than 4 km	1

- Past history of Opiates use before MMT is a continuous variable, converted to

Variable	Recode
Less than or equal to 3 years	0
From 4 to 6 years	1
From 7 to 9 years	2
More than 9 years	3

CHAPTER IV

4- RESULTS

The enrollment of the patients started from 1 July 2010 to 30 June 2011. There was an interruption to the enrollment between October 2010 and February 2011 due to a lack of incentive supports for MMT staff. Totally there were 107 patients enrolled in the treatment. All of them were referred by NGOs partners such as Korsang Organization and Kalyan Mitt organization. All the enrolled patients were followed until 30 September 2011. The patients enrolled in this study had different duration of treatment in MMT due to different times of enrollment. The groups of cohort varied from 4 months to 15 months. It was noted that 4 patients were dead so, they were excluded from this study. Therefore, 103 patients were included in the analysis, where 83 patients were male and 20 were female. Table 5.0.1 summarizes the number of MMT patients who enrolled in the study by month.

Table 4.0. 1: Number of MMT patients enrolled by month

Time of enrollment	Number of Patients	Cohort time
July 2010	22	15 Months
August 2010	27	14 Months
September 2010	12	13 Months
October 2010	0	

November 2010	0	
December 2010	0	
January 2011	0	
February 2011	0	
Mach 2011	14	7 Months
April 2011	05	6 Months
May 2011	19	5 Months
June 2011	08	4 Months

The table 4.0.1 shows that 22 patients were followed up for 15 months and 107 patients had 4 months of follow up.

Figure 4.0. 1: Cumulative new patients enrolled in MMT during the period of 12 months

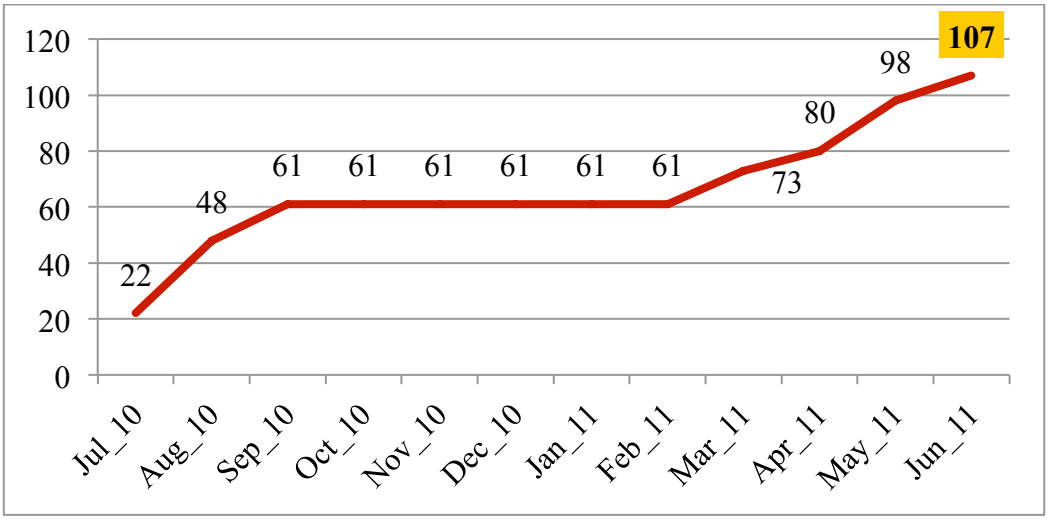
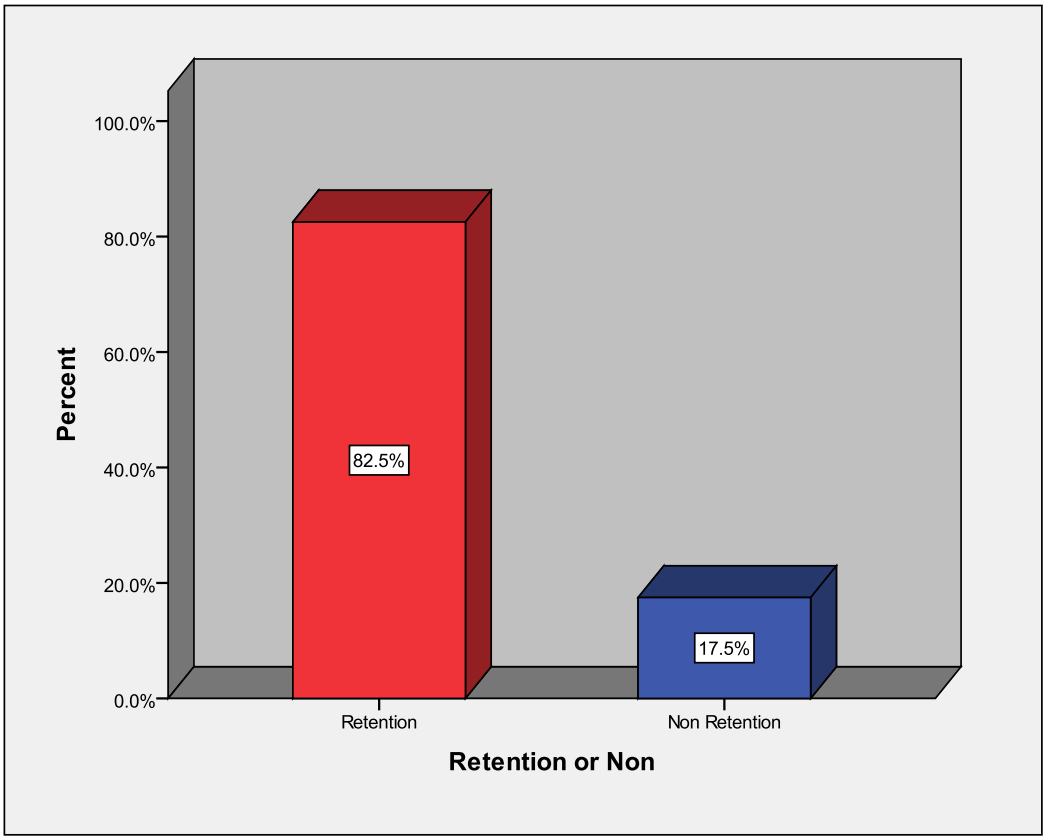


Figure 4.0. 2: Percentage of Overall Retention



In this cohort study, it is shown that the retention rate is high compared to other studies. However, originally 103 patients were enrolled in this analysis in the treatment in different times over the period of this cohort. Looking at the retention rate within up to 3 months in treatment, there were 92.2% (N = 95). Up to 6 months, 9 months, 12 months, and 15 months, the retention rates were respectively 80.2% (N = 57), 72.4% (N = 42) and 70.7% (N = 41) and 70.7% (N = 41). The table 4.0.3 shows a comparison of Retention in MMT done by other studies.

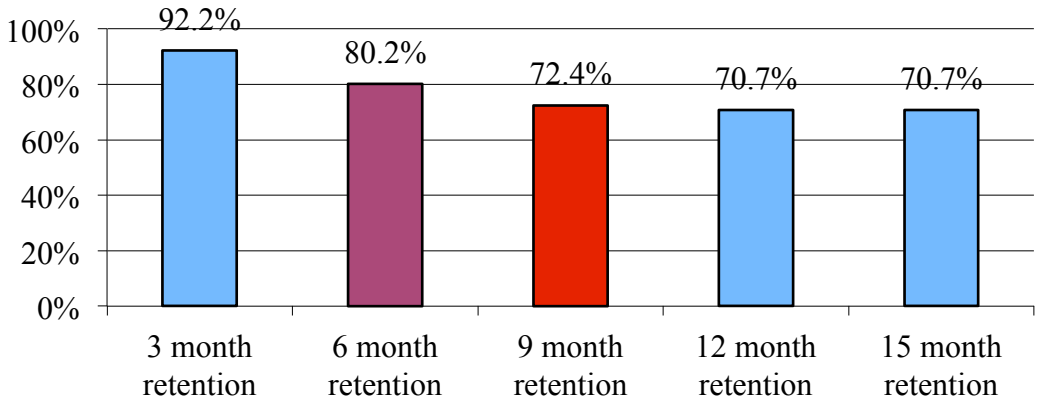
Table 4.0. 2: Number of patients in different cohort time

Cohort time	Number of patients enrolled in cohort	Retention in Cohort
3 months	103	95
6 months	71	57
9 months	58	42
12 months	58	41
15 months	58	41

Table 4.0. 3: Comparison of Retention Rate with other Studies

	Einat et al.	**Peymaneh et al.**	**Sharifa W.P et al.**	**Enwu Liu et al.**	**Mohamad Nasir et al.**
Duration	10 years	6 months	3 months	14 months	6 months
Design	Cohort	Cohort	Cross sectional	Cohort	Cohort
Sample	492	282	288	1003	64
Country	Israel	Iran	Malaysia	China	Malaysia
Retention	**74.4%**	**22.7%**	**86.1%**	**56.2%**	**54.6%**
	1 year retention	6 month retention	3 month retention	14 month retention	6 month retention

Figure 4.0. 3: Retention at different lengths in treatment in the cohort



4.1 Demographic Characteristics

There were 103 patients enrolled in the treatment from 1 July 2010 to 30 June 2011. The majority of participants were males (N: 83), which were accountable for 81%, and 19% were females (N: 20).

Table 4.1. 1: Demographic Characteristics

Variables	Number	Percentage
Sex		
Male	83	80.6
Female	20	19.4
Age (Mean: 30, Median: 30)		
18 - 23 Years	15	14.6
24 - 29 Years	43	41.7

30 - 35 Years	30	29.1
36 – 41 Years	07	06.8
Over 42	08	07.8
Marital Status		
Single	42	40.8
Married	39	37.9
Divorced	12	11.7
Widowed	03	02.9
Separated	02	01.9
Cohabiting	05	04.9
Education		
No education	20	19.4
Primary School	37	35.9
Secondary School	45	43.7
University and Higher	01	01.0

Among the male (N = 83) and female patients (N = 20), 81.9% and 85% were retained to do the treatment, respectively. It was shown that female patients had higher retention rate compared to male (85% vs. 82%) but there was no statistical significance (Chi = 0.105, df = 1, p = 0.74).

Table 4.1.2: Gender and Retention

Variables	Retention	Non retention
Male	68 (82.0%)	15 (18.0%)
Female	17 (85%)	03 (15.0%)
Chi = 0.105, df = 1, p = 0.74		

The age group varied from 18 years old to 52 years old (Total mean of age: 30 years, median: 29 years). The mean of age among females is higher than male (Age Mean of male: 29 years, median age of male: 28.5 years, Age Mean of female: 32 years, median age of female: 29 years). The results also showed that the younger age and older age had lower retention rate. In this study, retention rate of groups of patients aged lower than 23 years (73%) or higher than 36 years (71%, 63%) was lower compared with retention rates of groups of patients aged between 24 years to 35 years (87%, 88%). However, statistically there was no significant association between retention and age group. Compared with studies done by Sharifa WP et al., (2009) and Carol J. et al., (2005), this study found different results. In their studies, older age was associated with higher retention rates.

Figure 4.1. 1: Histogram of Age (in Years)

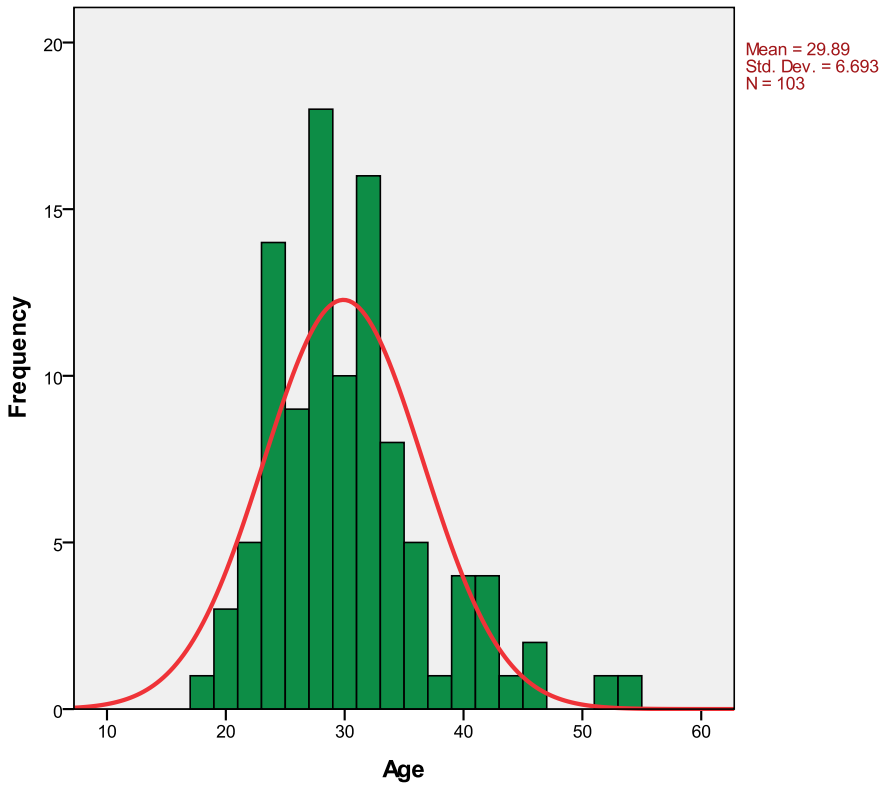


Table 4.1. 3: Age and Retention

	Variables	Retention	Non retention
Age	From 18 to 23 Years	11	4
	From 24 to 29 Years	38	5
	From 30 to 35 Years	26	4
	From 36 to 41 Years	5	2
	Over 42 Years old	5	3
	Chi = 5.7,df = 4, p = 0.27		

Most of them were single (N = 42, 40.8%) and married (N = 39, 37.9%), divorced (N = 12, 11.7%), widowed (N = 3, 2.9%), separated (N = 2, 1.9%) and cohabiting (N = 5, 4.9%). The group of patients who were married (N = 39) had high retention (90%) compared to other variables such as single, widowed, and divorced who had 81%, 75%, and 33% retention, respectively. However, there was no significant association between marital status and retention (Chi = 7.43, df = 5, p = 0.19).

Table 4.1.4: Marital Status and Retention

Variables	**Retention**	**Non retention**
Single	34	08
Married	35	04
Divorced	09	03
Widowed	01	02
Separated	02	00
Co-habiting	04	01
Chi = 7.43, df = 5, p = 0.19		

According to this study, the majority of patients had low education, where 19.4 % of them had no education (N = 20) and 35.9% were at primary school (N = 37);

Junior High school, High School and University were respectively accountable for 26.2% (N = 27), 17.5% (N = 18) and 1% (N = 1).

The group of patients with primary school or lower education (N = 57) had a lower retention rate (81%) compared to higher education (85%). However, in this study there was no significant association (Chi = 0.294, df = 1, P = 0.59).

Table 4.1.5: Education and Retention

Variables	Retention	Non retention
Primary school or Lower education	46	11
Higher than Primary school education	39	07
Chi = 0.294, df = 1, p = 0.59		

4.2 Social Characteristics

Table 4.2. 1: Social Characteristics

Variables	Number of enrolled patients	Percentage
Job Status		
Currently not work	67	65.0
Currently Self-employed	17	16.5
Currently work part time	08	10.7
Currently work full time	11	10.7

Living Arrangement		
Homeless	08	07.8
Living with partner	13	12.6
Living with parent	27	26.2
Living in NGO facility	42	40.8
Others	13	12.6
Distance to Clinic		
Up to 4 Km	71	68.9
From 5 to 15 Km	32	31.1

Most of the enrolled patients (65.0%) had no job (N = 67); the self-employed, and those with part-time, and full-time job were respectively 16.5% (N = 17), 7.8% (N = 08), and 10.7% (N = 11). Compared with other variables, No job had higher retention rate (N = 56, 83.5%) than other groups (N = 29, 80.6%) such as any job either self employed or part-time or full time job. However, in this study there was no significant association between job and treatment retention (Chi = 0.149, df = 1, P = 0.7).

Table 4.2. 2: Job and Retention

Variables	Retention	Non retention
No Job	56	11
Any Job	29	07
Chi = 0.149, df = 1, p = 0.7		

According to the study done by Yanhua Che et al. (2011), this study is shown up differently. Patients who were unemployed tend to attend the clinic for treatment more frequently compared to employed patients. Similar studies, Jose et al. (1977) revealed that the patients who were employed at the time of admission have consistently been more successful than unemployed. Pam Franscis et al. reported in an evaluation of Methadone Maintenance Treatment Services that Clients with poor employment records have had poor retention rates in methadone treatment programmes compared to clients with more successful employment records. However, Mitchell et al. (2005) revealed that employment has no significant relation with retention. There is only an indication that the employed, full-time / part-time, tend to stay longer than the unemployed.

Regarding to housing situation, the majority of MMT patients had no stable housing. That means about 7.8% (N = 08) were homeless, 26.2% (N = 27) were living with parents, and about 40.8% (N = 42) with NGO facilities, 12.6% (N = 16) with partners. This study has shown that the patients who lived with

partners (N = 13) had lower retention rate (54%) compared to other groups. Statistically, it revealed that there was a significant association between retention and living situation. It is also shown that the Group of homeless, living in NGOs facility and living with parents have higher retention rates whereas a group of patients who lived with partners had a lower retention rate (Chi = 13.83, df = 4, p = 0.008).

This finding appeared differently with Lundgren Lena M. (2007), who found that Homeless patients had lower retention rates compared to a group of patients who were not homeless. However, this is probably because the group of homeless patients in this study got more support from outreach NGOs working in Community.

Table 4.2. 3: Living Situation and Retention

Variables	Retention	Non retention
Homeless	8	0
Living with partners	7	6
Living with parent	22	5
Living in NGOs facility	39	3
Others	9	4
Chi = 13.83, df = 4, p = 0.008		

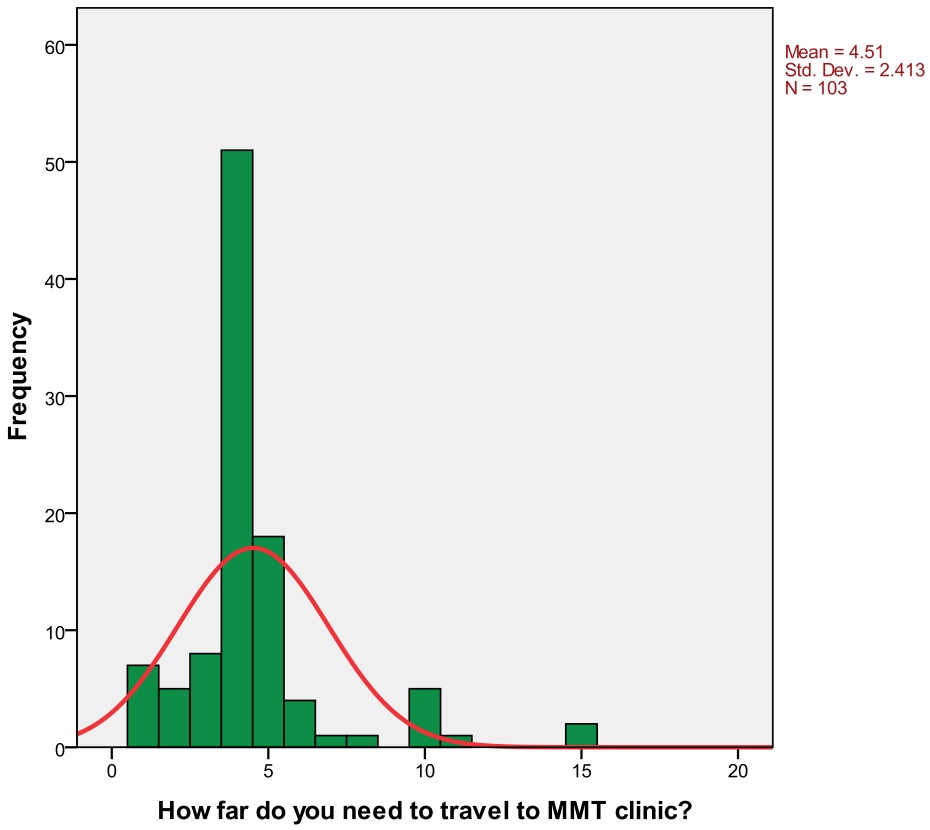
The distance from their living locations to MMT clinic varies from less than 1 km to 15 km (mean = 4.45, median = 4, SD = 2). 71 patients (68.9 %) in this study lived within an equal distance to or less than 4 Km from the clinic, and 32 patients lived in locations further than 4 km.

In this study, it was shown that the further distance to MMT clinic, the higher retention rate. That means 78.8 % of a group of patients living within 4 km from the clinic retain in treatment, and the retention rate among a group of patients living further than 4 km was 90.6% (N = 29). But, there is no statistical significance. However, it shows contrast with some studies (Peymaneh, 2009; Riza, 2009), which showed that the shorter distance to MMT clinic, the better retention rate in MMT. This finding reflects the important roles of NGOs working in community which can help MMT programme in supporting the patients to access MMT clinic.

Table 4.2. 4: Distance to MMT Clinic and Retention

Variables	Retention	Non retention
Equal or shorter than 4 Km	56	15
More than 4 Km	29	03
Chi = 2.11, df = 1, p = 0.146		

Figure 4.2. 1: Histogram of Distance to Clinic (in Kilometers)



Among 103 patients in this study, 52 patients (50%) had partners who were not drug user, and the other 51 patients had a partner who was drug user. The patients whose partners were also drug users (N = 51) had lower retention rates (N = 41, 80.3%) compared to the patients whose partners were not drug users (N = 44, 84.6%). However, there was no significant association between the two variables (Chi = 3.18, df = 1, P = 0.57).

4.3 History, Patterns and Types of Drug Use

There were different histories of Opiates use; the history of opiates use varied from less than one year to 45 years (Mean: 9.8 and median: 8). However, few of

them had used Opiates more than 10 years before attending at MMT. Among the patients enrolled in this study, female patients had a longer history of heroin use compared to male patients (Mean of year for female: 13, median of year for female: 9 years; Mean of year for male: 9 years, median of year for male: 7.5 years). In this study no correlation was shown between history of opiates use and retention. Soyka et al., (2008) found that the duration of continuous opioid use and the age at onset of opiates dependence were found to have a predictive value for negative outcome.

Figure 4.3. 1: Histogram of Past History of Opiate Use (in Year)

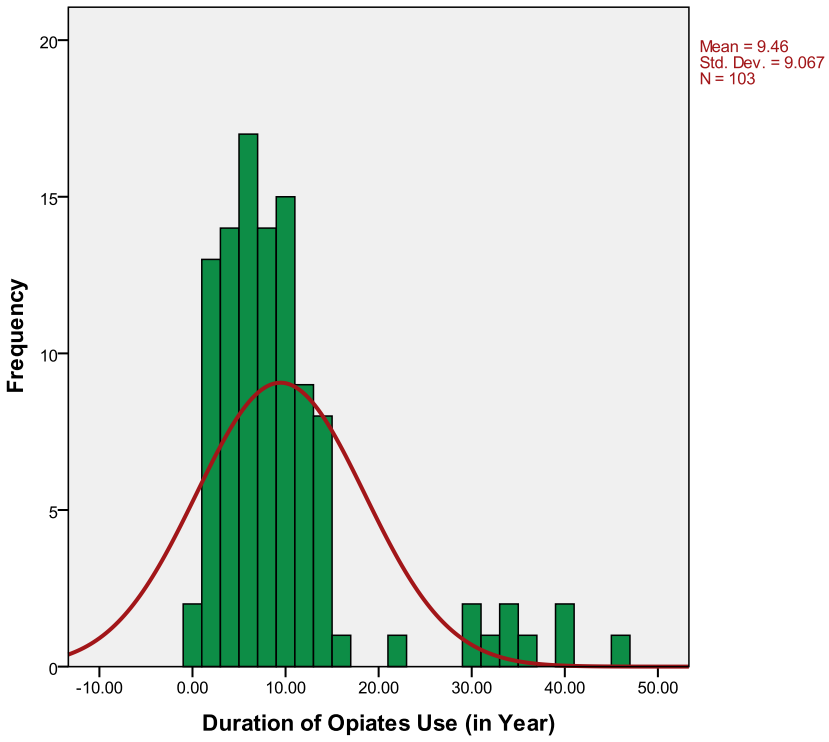


Table 4.3. 1: History of Opiate Use and Retention

Variables	Retention	Non Retention
Past History of Opiates Use before MMT		
Less than or equal to 3 years	20	03
From 4 to 6 years	18	05
From 7 to 9 years	19	03
More than 9 years	28	07
Chi = 0.93, df = 3, p = 0.82		

Table 4.3.2 shows patterns and types of drug use. 103 patients were Opiates users. Most of them used Opiates and other drugs (N = 94, 91.3%), only 9 patients were single opiate users (08.7%). This study showed that patients who used heroin and other drugs (N = 94) had lower retention rate (N = 76, 81%). Statistically, there was no significant association (Chi = 2, df = 1, p = 0.14).

Within this sample, the majority of the patients were Injecting Drug Users, which were accountable for 93.2% (N = 96), and only 07 patients were Opiates smokers (6.8 %). The group of patients who injected drug had higher retention rate (83%) compared with retention rate among a group who smoked drugs (71%). In this study, there was no significant association between patterns of opiates use and treatment retention.

Table 4.3. 2: Patterns and Types of Drug Use

Variables	Number	Percentage
Main Route of Opiates use		
Injection	96	93.2
Smoke	07	6.8
Types of Drugs Use		
Opiates Use Only	09	8.7
Opiates and Others	94	91.3

Table 4.3. 3: Main Route of Opiate Use and Retention

Variables	Retention	Non Retention
Main route of opiate use		
Injection	80	16
Smoke	05	02
(Chi = 0.6, df = 1, p = 0.42)		

Of 103 patients, the frequency of opiates use varied from 7 to 56 times per week (Mean: 26, Median = 28. SD = 9.8). That means in average, they used opiates more than 3 times a day. 52.4 % of them used opiates more than 4 times a day. Retention rate among patients who used opiates less than 4 times a day (78%) was

lower than those who used drug more than 4 times a day (87%). Table 4.3.5 shows the frequency of opiates use per day and retention.

Table 4.3.4: Frequency of Opiate Use

Variables	Number	Percentage
Used Opiates less than 4 times a day	49	47.6
Used Opiates more than 4 times a day	54	52.4
(Range: (7 - 56), Mean: 26, Median: 28, SD = 9.8)		

Figure 4.3. 2: Histogram of Frequency of Opiate Use

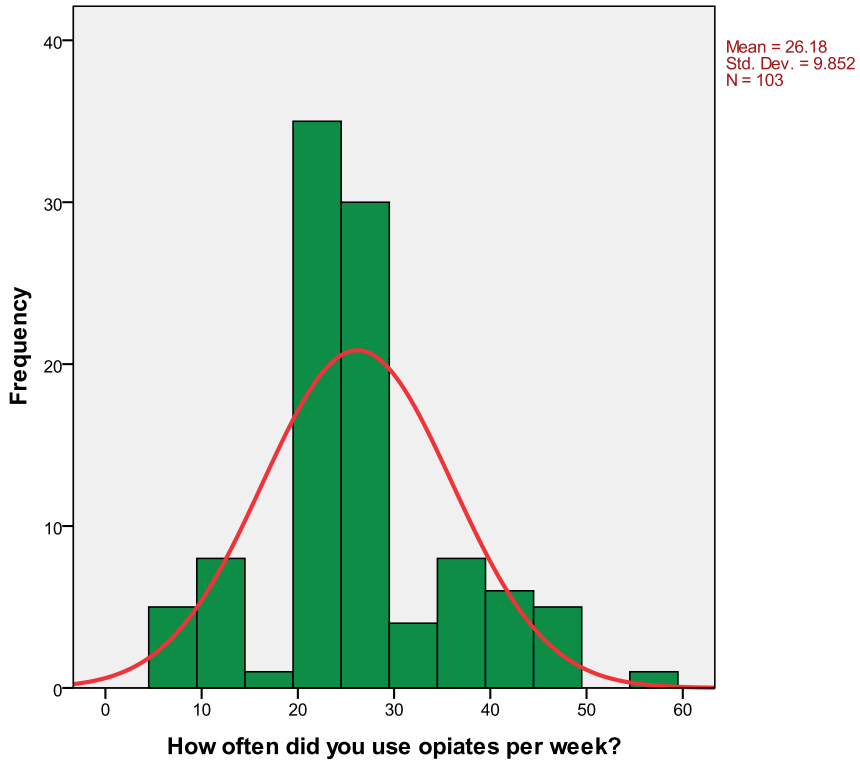


Table 4.3. 5: Frequency of Opiate Use and Retention

Variables	Retention	Non Retention
Frequency of opiate use		
Used Opiates Less than 4 times a day	38	11
Used Opiates from 4 times a day and more	47	07
(Chi = 1.6, df = 1, p = 0.2)		

4.4 Methadone Treatment and Retention

1. Length in MMT treatment

Among 103 patients, 57.3% (N = 59) had a length of stay in MMT less than one year, and 42.7% (N = 44) had more than one year. Retention rate among the patients who attended in MMT less than one year was 69.4% (N = 59). The retention rate among the patients who received MMT less than one year was lower than the rate among patients who retained in treatment more than one year. Table 4.4.1 shows the length in MMT and retention:

Table 4.4.1.1: Length in MMT

Variables	Number	Percentage
Length in MMT Treatment		
Less than one Year	59	57.3
More than one year	44	42.7

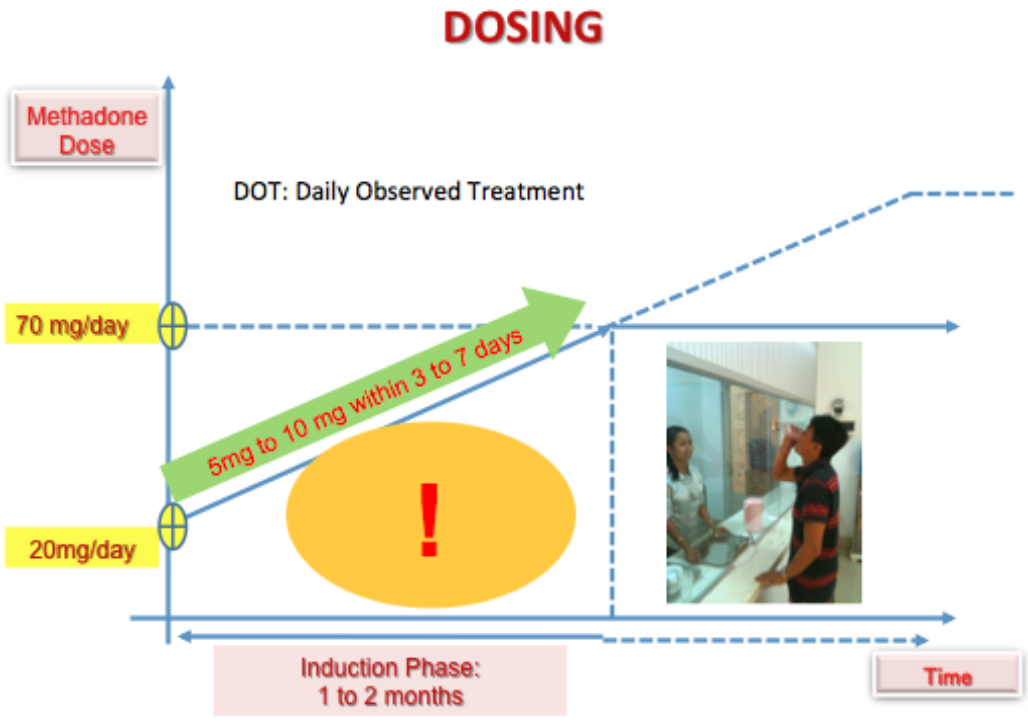
Table 4.4.1.2: Comparison between Length in MMT and Retention

Variables	Retention	Non Retention
Length in MMT		
Length in MMT less than one year	41	18
Length in MMT more than one year	44	00

2. Methadone dose

Usually the initial dose of methadone was 20mg. Every 3 or 5 days, 5mg of methadone was increased based on the judgment of a doctor. The increment of methadone gradually increased until the patients had no withdrawal symptoms. In this study, the maximum dose of methadone varied from 20mg to 120mg (Mean = 74.6, Median = 70, SD = 22).

Figure 4.4. 1: Gradually Methadone Dosing Process



Source: Center for Mental Health and Drug Dependence in Cambodia, 2010

However, the increment of methadone was dependent on the patients' compliance and therapist's judgment. That means, in principle, if the patients missed the methadone dose between 3 to 5 consecutive days, the methadone was reduced by half. So in some cases, they missed doses so often so that their doses could not be increased and remained low compared to others patients who regularly took methadone doses.

In this sample, it was found that 34% (N = 35) of the patients got a average daily methadone dose equal to or less than 60mg, and the other 66% (N = 68) received average daily methadone dose more than 60mg.

Figure 4.4. 2: Histogram of Methadone Dose (in Milligrams)

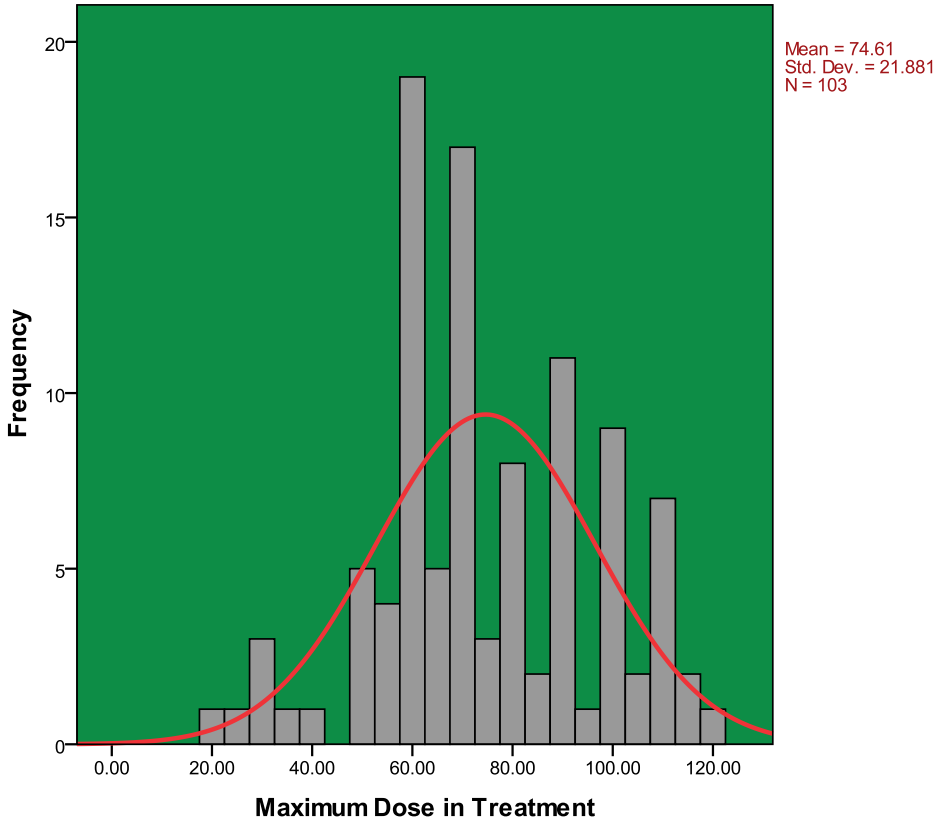


Table 4.4. 2.1: Methadone Dose Comparison

Variables	Number	Percentage
Average Daily Methadone Dose		
Less than or equal to 60mg	35	34.0
More than 60mg	68	66.0
(Chi = 4.52, df = 1, P = 0.03)		

Comparing between the patients who received over 60mg of methadone dose per day and those who received methadone dose equal or lower than 60mg per day, it

was found that the retention rate of the patients who got methadone dose more than 60 mg/day was higher. Statistically, there was a significant association (Chi = 4.52, df = 1, P = 0.03).

Table 4.4.2.2: Retention and Methadone Dose

Variables	Retention	Non Retention
Methadone dose equal or lower than 60 mg/day	25	10
Methadone dose Over 60 mg/day	60	08
Chi = 4.52, df = 1, P = 0.03		

CHAPTER V

5- DISCUSSION

This study tried to explore factors associated with Retention in MMT among the patients receiving a Methadone dose at the Center for Mental Health and Drug Dependence (CMHDD). In Cambodia there is only one center for treatment of Opiate dependents, which is located in the Capital where most of opiate dependents living. The capacity of the clinicis for about 250 to 300 patients only.

Based on Expert consensus, there are about 1,000 to 10,000 heroin users in Cambodia; it is seen that the MMT clinic cannot respond to the needs of Opiates users in Community. That means the supply side is not adequate for demand side. Moreover, as CMHDD is just newly established, the center could only get patients referred by NGOs partners. It is due to the fact that the center needs to assure follow up and linkage between MMT clinic and community within its limited capacity. In this regard, it is obvious that the operating system is limited and not with free access, that means only the patients who were referred by NGOs partners can access to MMT clinic. Usually NGOs work with vulnerable populations such as the homeless and jobless population. So the population in this study does not represent the general population of opiate users.

5-1 Retention in Methadone Maintenance Therapy

In this study, it was shown that the retention rates are different at different cohort

time. The retention rates were respectively 92.2% for 3 months retention, 80.2% for 6 months, 72.4% for 9 months and 70.7% for 12 months. These rates were high compared with other MMT programmes in the region. In Malaysia, Nasir Mohamad et al., (2010) found that 6 months retention was about 54.69%. In a 6 months cohort study in MMT programme conducted in Indonesia, they found that the 3- and 6-month retention rates were respectively 74.2% and 61.3% (Riza, 2009).

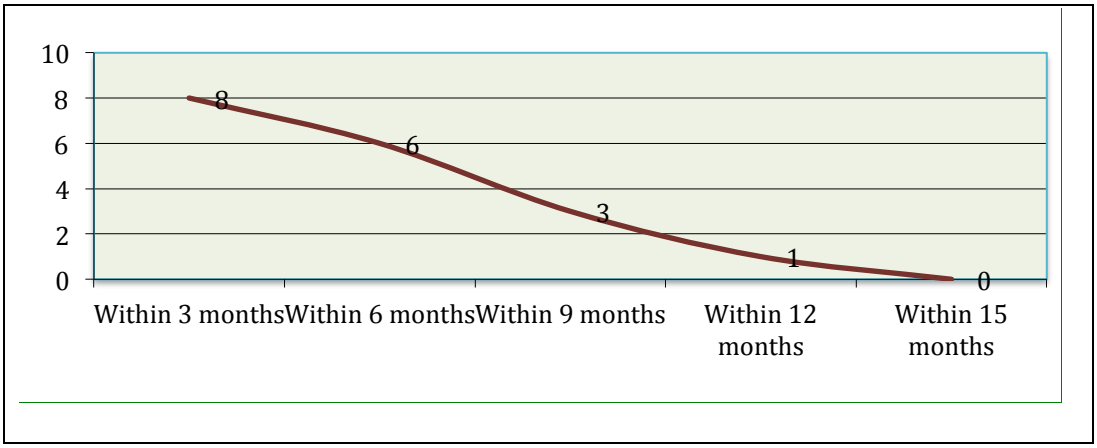
In China, Liang et al., (2009), in a 14 month cohort study in 8 locations, they revealed that the 6 month retention rate of the clients was 68.8%, and 57.4% at 12 month of the treatment programme. It is difficult to conclude about the different rates of retention comparing with those studies, because in different countries, there are different contexts in terms of socio-economic and political contexts and service arrangement and delivery system.

However, the diversity contexts of MMT service organization would be taken into consideration. In this regard current MMT service in Cambodia was free of charge and operated in collaboration with NGOs working community, which were the main supporters in referring and following up the patients in community.

Moreover, most of the participants in this sample were a marginalized population and could not represent the general population of opiates users. As they were a vulnerable population, usually they got more supports from NGOs working in community.

MMT is a long-term treatment. Very often the patients attending a long-term treatment could not retain in as long as the duration of treatment, and retention rate fell lower along the way. In this study, the retention rate is decreasing from 92.2% to 70.7% from 3 month retention to 15 month retention. However, in the group of non-retention patients most of them quitted the treatment at an earlier stage of treatment. Among 18 patients who did not retain in MMT, it was found that 44% (N = 8) quitted the treatment within the first 3 months. And respectively, there were 33% (N = 6), 17% (N = 3), and 6% (N = 1) within the period of 6 months, 9 months and 12 months. Miguel et al., (1997) found that the dropout rate among MMT patient was higher during the first and second year of treatment, compared to the subsequent year. This may be due to the early stage of treatment; the patients were difficult to cope with withdrawal symptoms while their methadone dose needs to be adjusted with their tolerance and withdrawal symptoms.

Figure 5.1. 1: Number of Non-Retention by Time



5-2 Retention and Socio-Demographics

This study found that predictive variables such as gender, age, marital status, job and level of education were not associated with retention in MMT treatment. In this study, gender was not associated with retention. Retention among males was lower than among females; 82% (N = 68) for males and 85% (N = 17) for females. In this regard, Female Drug Users were usually considered a vulnerable group; they could get support from NGOs more than males in terms of contact, reminding, and facilitation. However, Rizar (2009) stated that in many studies, there was no consistency association between gender and retention. Some studies show males had higher retention rate while other studies found a reverse situation.

Table 5.2.1: Chi-square test between Gender and Retention

Gender	Compliance		P-value (Chi square test)
	Retention (%)	Non Retention	
Male	68 (82%)	15 (18%)	0.745
Female	17 (85%)	3 (15%)	

In this study, there was no association between age and retention. In this sample, the mean and median of age were 29 years and 29.8 years. There was no difference between the mean and median of retention and non retention groups. In the results of this study, the younger group (aged from 18 to 23 years) and the

older group (aged from 36 years) had lower retention rates compared with a group aged from 24 to 35 years old. It was contradictory to other studies, which found that older age had longer retention in treatment.

Davis C. et al., (2006) found that Age over 40 years had a significant association with MMT retention. Similarly Einat et al., (2006) showed that Age equal to or over 40 years was associated with a cumulative longer retention in MMT treatment. Dannis et al., (2005) revealed that older patients had a higher retention rate in MMT. However, mean age of the sample in this study showed that the population of this study was younger (mean = 29 years) compared to population of those studies.

Table 5.2.2: Chi-square test between Age Group and Retention

Age	**Compliance**		**P-value (Chi square test)**
	Retention (%)	**Non Retention (%)**	
18 - 23 Years Old	11 (73.3%)	4 (26.7%)	0.279
24 - 29 Years Old	38 (88.4%)	5 (11.6%)	
30 - 35 Years Old	26 (86.7%)	4 (13.3%)	
36 - 42 Years Old	5 (71.4%)	2 (28.6%)	
Over 42 Years Old	5 (62.5%)	3 (37.5%)	

Many studies found that Job is associated with retention in MMT treatment (Herman et al., 2000) but it was not found in this study. This may be because most of respondents in this study had no sustainable job. It is due to the fact that they are marginalized population. In this regard, even though they have full time job, their jobs would not be a sustainable job, as well as low skill jobs. So there is still no difference between jobless and fulltime job because even in those with a full time job, it was not a sustainable job, and their incomes would not be a significant difference too. They still rely on NGOs supports to access to MMT clinic. In this study, among jobless patients the vulnerable group and got more supports from NGOs, so they could retain better in treatment.

Table 5.2.3: Chi square test between Job Status and Retention

Job Status	Compliance		P-value (Chi square test)
	Retention (%)	Non Retention (%)	
No Job	56 (83.6%)	11 (16.4%)	0.149
Any Job	29 (80.6%)	7 (19.4%)	

The overall duration of history of opiate use in this sample varied from 12 to 42 years with a mean of 22.6 and median of 29 years. There was a similarity between the mean and median of retention and Non-retention group (Retention, Mean: 22 years, Median: 22 years; Non retention, Mean: 23.8 years, Median: 22 years). In

this study, duration of history of opiate use was split into 4 categories such as up to 3 years, from 4 to 6 years, from 7 to 9 years, and over 9 years. Statistically there was no association between history of opiate use and treatment retention (p = 0.82). Miguel et al., 1997 revealed that the history of opioid use is a predictive factor of treatment retention that means shorter duration of opiates use had shorter rates of retention. Sharifa et al., (2009) found that the shorter duration of addiction showed a good compliance in MMT.

Table 5.2.4: Chi square test between Past History of Opiate Use and Retention

Past History of Opiates use	**Compliance**		**P-value (Chi square test)**
	Retention (%)	**Non Retention** (%)	
Less than or equal to 3 years	20 (87)	3 (13)	0.805
4-6 years	18 (78.3)	5 (21.7)	
7-9 years	19 (86.4)	3 (13.4)	
More than 9 years	28 (80)	7 (20)	

Distance to clinic is also a factor of accessibility; in this study, the distance varied

from 1 to 15 km with a mean of 4.45 km and median of 4 km. Comparing between a group of patients living equal to or less than 4 km and over 4 km, there was no significant association between distance to clinic and treatment retention p = 0.146). Peymaneh Shirinbayan, 2009 and Riza Saravita 2009 found distance to clinic as a predictive factor of treatment retention; the shorter distance to clinic, the higher treatment retention. It was reflected that the patients in this study got transportation support from NGOs at least during the first 3 months of treatment especially during induction phase. After the induction phase, NGOs could support vulnerable groups who really needed transportation. This context may be different from other MMT services.

Table 5.2.5: Chi square test between Distance to MMT clinic and Retention

Distance to MMT Clinic	**Compliance**		**P-value (Chi square test)**
	Retention (%)	**Non Retention** (%)	
0-4 Km	56 (79)	15 (21)	0.146
Over 4 Km	29 (91)	3 (9)	

Many studies showed that the homeless were also associated with higher retention. Compared with non-homeless patients, a group of homeless patients had lower retention rate (Lundgren, 2007).

However, our study showed that homeless, living in NGOs facilities and living

with parents had significantly higher retention.

This is due to NGOs supports. It is due to the fact that those patients were a most at risk population and vulnerable groups so they got more support from NGOs than other groups.

Table 5.2.6: Chi square test between Living Situation and Retention

Living Situation	Compliance		P-value (Chi square test)
	Retention (%)	Non Retention (%)	
Homeless	8 (100)	0 (0)	0.008
Living with partner	7 (53.8)	6 (46.2)	
Living with parent	22 (81.5)	5 (18.5)	
Living in NGO facility	39 (93)	3 (7)	
Other	9 (69.2)	4 (30.8)	

5-3 Retention and Patterns of Opiate use

Patterns of Opiates use in this study were injecting and smoking use. Among 103 patients, 93.2 % of them (N = 96) were injecting drug users and 6.8% were smoking user (N = 7). It would highly increase the risk to be infected by blood

borne diseases when they shared needle and syringe. The injecting opiates users had higher retention rate compared to Smoking opiates user. In our study, there was no association between route of opiates use and retention (p = 0.42).

Table 5.2.7: Chi square test between Main Route of Opiate Use and Retention

Main Route of Opiates Use	Compliance		P-value (Chi square test)
	Retention (%)	Non Retention (%)	
Injection	80 (83.3)	16 (16.7)	0.423
Smoking	5 (71.4)	2 (28.6)	

Regarding types of drug use in our study, the majority of the patients (N = 94, 91.3 %) used opiates and other substances in addition. A group of patients who used more opiates had lower retention rate compared to a group of single opiates use.

Table 5.2.8: Chi square test between Types of Drug Use and Retention

Types of Drug Use	Compliance		P-value (Chi square test)
	Retention (%)	Non Retention (%)	
Only Opiates Use	9 (100)	0 (0)	0.148
Opiates use and Other	76 (81)	18 (9)	

Frequency of drug use was not found its association with retention in MMT treatment. This study found that a use opiates less than 4 times a day had lower retention rate.

Table 5.2.9: Chi square test between Frequency of Opiate Use and Retention

Frequency of Opiates Use	Compliance		P-value (Chi square test)
	Retention (%)	**Non Retention** (%)	
Less than 4 times a day	38 (77.6)	11 (22.4)	0.205
Use Opiates from 4 times a day or more	47 (87)	7 (13)	

5-4 Retention and Methadone Dose

Many studies found a significant association between Methadone Dose and treatment retention (Liu et al., 2008, WHO, 2004, Bao et al., 2009).

Looking at Methadone dose in this study, it was shown that the maximum daily individual dose of methadone varied from 20mg to 120mg and the average dose of methadone among the participants were 70 mg/person/day. But the average dose of retention group was from 30mg to 115mg (Mean = 76.3 mg, median = 70 mg, SD = 18.9); its mean was higher than the dose of non-retention group (Mean = 66.3 mg, median = 60 mg, SD = 31.7). This study found that the dose over 60 mg/person/day was significantly associated with treatment retention ($p = 0.03$). This finding is parallel with other findings, which indicated that higher methadone dose was associated with retention.

WHO, (2004) recommended that a dose of methadone over 60 mg/day/person had clear association with treatment retention and could suppress heroin use. Similarly it was found that Methadone doses from 60mg to 100 mg/day were considered as effective MMT (NIDA, 2003). An expert panel at the National Institute of Health also found that the dose of methadone at least 60mg was considered as the best practice in methadone maintenance therapy (Thomas et al., 2005).

Yanhua Che et al., (2010) found that there was no relationship between dose and probability of dropout in periods 1 and 3 months. However, after 3 month, there was lower a probability of dropout with higher average daily dose > 60 mg.

A study in China found that dose of methadone equal to and higher than 60 mg had higher retention rate compared to a group of patients who had methadone dose lower than 60 mg per day per individual (Bao et al., 2009).

Table 5.2.10: Chi square test between Methadone Dose and Retention

Average Daily Methadone Dose	Retention (%)	Non Retention (%)	P-Value Chi-square Test
Methadone Dose Less than or equal to 60 mg	25 (71.4)	10 (28.6)	0.033
Methadone Dose more than 60 mg	60 (88.2)	8 (11.8)	

CHAPTER VI

6- CONCLUSIONS AND LIMITATIONS

6.1 Conclusions

Methadone Maintenance Therapy has been established since 2010; it can attract many opiate users to treatment. Retention rate of MMT in Cambodia is very similar to other studies found in various MMT services. The overall retention rate were 82.5%. Looking at different times in the cohort, it was shown that the retention rate within the cohort of 3 months, 6 months, 9 months, 12 months and 15 months was 92.2%, 80.3%, 72.4%, 70.7% and 70.7%, respectively.

In this study, among demographic characteristics and social factors through methadone dosing within the 15 month cohort, it was found that gender, age, marital status, level of education, job, history of opiates use, and distance to clinic were not associated with retention in treatment.

Living situation and methadone were found association with retention in MMT. A group of patients who had unstable housing (homeless, living with parent, living in NGOs facility) had higher retention rate with statistical significance ($p = 0.0001$). However, the population in this study could not represent general population of MMT clients because the population in this sample was at risk group needing support from NGOs. Its higher retention may be due to the fact that

those groups of patient were vulnerable and got assistance from NGOs who facilitated their access to MMT clinic.

Methadone dose was also a predictor variable. In this clinic the mean of Methadone dose per day per individual was 70 mg. The dose of methadone equal to or over 60 mg/day was significantly associated with retention. This finding is supported by many studies and recommendations, which was showed that a dose of methadone over 60 mg/day is associated with treatment retention.

In addition, it was also found that most of non-retention patients quitted their treatment during the early stage of treatment within the period of 3 to 6 months. This would be concluded that it is related to the methadone dosing process, which the patients received. Methadone dose is usually started from 20 mg and increased every 3 to 7 days until the patients have no craving to use opiates again. That is a reason that the patients quitted their treatment more at an early stage because of withdrawal symptoms and craving. However, WHO (2004) has recommended methadone dose delivered based on therapist's judgment.

The retention rate varied from 92.2% within the first 3 months of treatment to 72.4% within 9 month cohort and 70.7% within 15 month cohort. It showed that the lower rate of patients quitted the treatment after 9 month in treatment.

However, these findings could not be generalized to all opiate users because the sample in this study is relatively small. However, it could be used as baseline for further study in the future to explore the effectiveness of MMT.

These results showed that the MMT programme in Cambodia could be considered as an effective programme concerning reduction of harm related to opiates use and daily opiate use. Possible scale up of the programme to other area in the country should be encouraged. However, there are other influenced factors that this study does not focus on to ensure holistic perspectives in regard to treatment retention in MMT.

A next study should explore other factors such as clients 'perceptions or attitudes to MMT services, organization of MMT service, quality of life, co-morbidity with opiates dependence, intervention modalities including counseling and psychosocial interventions, and ancillary services. Those factors would be influential to reinforce the quality assurance of MMT service.

Wang J. et al., (2007), in a study in China concluded that individual counseling could increase compliance rate among MMT patients in Urumqi. *Similarly, Canada Health 2002 reported that* Counseling could enhance MMT treatment retention and decrease opioid use (Canada's Drug Strategy Health Canada, 2002).

Perception of patients toward MMT is also important to retain the patients in MMT. In this regard, *Thesis's Liu (2009) found that* patients who committed to be treated at MMT service for life who intended to be treated in the methadone clinic for life seem to stay longer in the treatment.

Fischer Benedikt et al., (2006) has recommended that effective treatment must adjust to poly substance use and address the complex co-morbidity physically and mentally among the at risk population.

A national treatment agency for substance abuse in United Kingdom has reported that the effectiveness of methadone maintenance therapy depends more than just on methadone dose. A range of organizational management need to be arranged such as Counseling, other psychosocial interventions and ancillary services need to be provided to enhance outcome of methadone maintenance therapy (National Treatment Agency for Substance Misuse, 2004). WHO, UNODC, UNAIDS position paper 2004 showed that counseling and psychotherapy influence on the overall effectiveness of MMT.

6.2 Limitations

There are many limitations in this study. At this stage MMT service is not a free access service. The enrollment of MMT patients in the programme is strict. Most of the patients enrolled in this study were referred and supported by street based NGOs. Therefore, the sample of this study could not represent the general population of opiate users in a Community in which it was estimated that there are about 1.000 to 10.000 heroin users in Cambodia (NACD, 2007). Obviously, that this sample is relatively small compared with the estimated number. Moreover, the profiles of the patients enrolled in this study is low class population. There are patients from higher class population who do not disclose themselves for treatment.

Looking at predictive factors, there are other factors that this study did not focus on such as patients' perception to MMT, co-morbidity, quality of life and quality of counseling and treatment. Those factors may be confounding factor for these findings. In addition, this study did not include a qualitative method to control for these findings. Not using regression and survival analysis is a limitation of this conclusion.

It is also difficult to compare methadone maintenance therapy programme with other countries because the organization of methadone service considerably varies from one country to another.

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APPENDIX 1: CONSENT FORM

INFORMED CONSENT FOR VOLUNTARY METHADONE MAINTENANCE THERAPY

MY NAME IS: ……..…… GENDER: …..……

DATE OF BIRTH (OR APPROXIMATED AGE): ……...…

PLACE OF BIRTH (if known):

……..

ADDRESS:

…….....

REFERRED BY:

…….....

CONTACT PERSON IN CASE OF EMERGENCY:

…….....

PHONE NUMBER: ……..……..……..

ADDRESS:

……..…….....

After being informed about methadone treatment and about possible side effects that may occur during treatment, I understand the objectives of the treatment I shall receive. I confirm that I have read and understood the related important information which explains the objectives and risks of the treatment and have discussed it with a counselor / nurse at the clinic. I freely agree join the

methadone treatment programme and I therefore undertake:

1. To comply with the regulations of the methadone treatment clinic and to attend regularly to collect methadone and to participate in the treatment and counseling programmes.
2. To refrain as much as possible, from using any other substances of which may endanger and have serious consequences for my health during methadone treatment. I am fully aware of the risks of using alcohol and benzodiazepines, methamphetamines, heroin, morphine, opium while I am being prescribed methadone.
3. To keep health professionals informed of emerging health and social issues so facilitate timely actions by the clinic staff.

In case of any undesirable consequences that occur due to the failure to comply with the agreement I (and my family) shall bear full responsibility before the Center for Mental Health and Drug Dependence and the law.

Date: ……../……../……..

Patient's family representative or witness
(Signature or thumb-print, and full name)

Patient
(Signature or thumb-print, and full name)

APPENDIX 2: QUESTIONNAIRE

RESEARCH QUESTIONNAIRE

☐☐☐☐ **(Case Number)**

(Date of Registration): …… ……. ……. **DD MM YYY**

(Name)	**(Gender)**	**(Age)**
	(Male) 0 (Female) 1	(Age): .....(in Year)
Marital Status	**Nationality**	**Ethnicity**
(Single) 0 (Married) 1 (Divorced) 2 (Widowed) 3 (Separated) 4 (Co-habiting) 5	(Cambodian) 0 (Vietnamese) 1 (Others) 2 ***Q6- (Specify)*:**	(Khmer) 0 (Vietnamese) 1 (Chinese) 2 (Cham) 3 (Others) 4 ***Q8- (Specify)*:** .....

(Current address & Tel No.)	**(Permanent address – if different)**
(#) ..... (St.) ..... (Village/Group):..... (Commune):..... (District):..... (Province/City):..... (Tel.):.....	(#) ..... (St.)..... (Village/Group):Q14..... (Commune):..... (District):..... (Province/City):..... (Tel.):.....

Referred by:
(NGO) (0: No, 1: Yes) *(Specify NGO) :* .....
(Family) (0: No, 1: Yes)
(Police/Authority) (0: No, 1: Yes); *(Specify Police/Authority):*.....
(Self-referred) (0: No, 1: Yes)
(Others) (0: No, 1: Yes)*;*
(Specify Other):.....
(Name and contact information of NGO worker/Police/Authority/support person)
.....

(Education)		
(No education)	0	
(Primary School)	1	
(Junior High School)	2	
(Senior High School)	3	
(University)	4	
(Post University)	5	

(Date of Termination)	
..... / ..... / ..... DD MM YYYY	(Length in treatment – in days) ..... (N^{o} of days)

Social Information

(Current living arrangements)			
(Homeless)	0	(Sharing house with friends or others who are drug users)	4
(Living with partner)	1		5
(Living with parents)	2	(Sharing house with friends or others who are not drug users)	6
(Living in an NGO facility)	3	(Others) *(Specify):*	

(Is partner a drug user)**?**			
(Partner is a drug user)	1	(Partner does not use drug)	0
(Children)			
(No of children) ☐☐			
(Work)			
(Currently not working)	0	(Currently working full-time)	2
(Currently self-employed)	1	(Currently working part-time/ casual work)	3

Drug Use: History and Current Use

	(Age of first use)	**Current types of Drug Use**	**(Main route of use for current types of drug use)** (Injection) **0** (Smoke) **1** (Snort) **2** (Inhale) **3** (Oral) **4**
Opiates (Heroin, morphine, codeine, etc.)			
ATS (Amphetamine Type Stimulants)			
How often did you use Heroin per week? ……			

Diagnostic formulation based on ICD-10 (International Classification of Diseases, 10th Edition (Heroin Dependence) .....(Text)

Number of missed dose / month

Month	**Maximum Dose in the month (in mg)**	**Number of Missed Dose (in the month)**	**Retention (Tick the row of the month when patient drop out)**
1			
2			
3			
4			
5			
6			
7			
8			

9			
10			
11			
12			
13			
14			
15			

Do you satisfy with MMT Service?

□ Not at all (1)

□ Somewhat (2)

□ Satisfy (3)

□ Very satisfy (4)

Explain the reason: Why did you miss methadone dose?

□ Illness (1)

□ Busy at work/home (2)

□ No money for travel (3)

□ Arrested by Police/authority (4)

□ Other Reason (5)

(Specify)

……

……

……

……

……

Why do you drop the treatment? i.e after missing dose for more than 5 days.
(This question can be asked to NGO case managers or the patients if we can find him/her in community or s/he return for Methadone dose again)

□ Illness (1)

□ Busy at work/home (2)

□ No money for travel (3)

□ Arrested by Police/authority (4)

□ Other Reason (5)

(Specify)

……

……

……

……...……

……

How far do you need to travel to MMT clinic? ..... (In Km)

How did you come to MMT Clinic at the beginning?

(1) NGO Transportation

(2) Own Transpiration

==========

APPENDIX 3: LIST OF MONTHLY-ENROLLED PATIENTS

Month	Number
JUL 2010	22
AUG 2010	27
SEP 2010	12
MAR 2011	14
APR 2011	5
MAY 2011	19
JUN 2011	8
Total	**107**

APPENDIX 4: RECORD LIST OF PATIENTS RETAINED IN MMT

(The dead patients were removed from this list.)

Enrollment		Duration of Cohort (Retention / # of enrolled in the month)															
		M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15
Jul 2010				1							1					17/19
Aug 2010		2		1			1		1				1		21/27	
Sep 2010						2	3			1				6/12		
Oct 2010																
Nov 2010																
Dec 2010																
Jan 2011																
Feb 2011																
Mar 2011				1				12/13								
Apr 2011							5/5									
May 2011		1	1			17/19										
Jun 2011		1			7/8											
Non Retention	Retention	4	1	3	0	2	4	0	1	1	1	0	1	0	0	0
		99	94	73	71	56	52	52	51	50	49	46	18	18	18	18