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EFFECTIVENESS EVALUATION OF THE PILOT PROGRAM FOR TREATMENT OF OPIOID DEPENDENCE WITH METHADONE

IN HAI PHONG AND HO CHI MINH CITIES, VIETNAM

The objective of this evaluation study is to monitor and demonstrate the outcomes of methadone maintenance treatment overtime by repeatedly measuring the following:

- Changes in drug use status, including needle sharing behavior;
- Changes in sexual behaviors, including type of partners and prevalence of condom use;
- Improvement in social behaviors/interactions including reduced engagement in crime and success in re-integrating within society;
- Patients' physical and mental health; and
- Quality of life.

The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the United States Agency for International Development (USAID) has provided financial support that make this study "Effectiveness Evaluation of the pilot program for the treatment of opioid dependence by methadone in Hai Phong and Ho Chi Minh Cities" possible. The contents are the responsibility of FHI 360 and do not necessarily reflect the views of USAID or the United States Government.

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ABREVIATIONS

ART	Antiretroviral Therapy
ARV	Antiretroviral drug
DOLISA	Department of Labor, Invalids, and Social Affairs
ENV	Environmental health
FSW(s)	Female Sex Worker(s)
HBV	Hepatitis B Virus
HCMC PAC	Ho Chi Minh City Provincial HIV/AIDS Committee
HCMC	Ho Chi Minh City
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IDU(s)	Injecting Drug User(s)
ITT	Intent-to-treat
LTFU	Loss to follow up
MMT	Methadone Maintenance Treatment
MoH	Ministry of Health
MSM	Men who have sex with men
NGO	Non-Governmental Organization
PLHIV	People living with HIV
PYR	Person Year
PHS	Physical health
PSY	Psychological health
QoL	Quality of life
SOC	Social health
STDs	Sexually Transmitted Disease(s)
STI	Sexually Transmitted Infection
UNAIDS	The Joint United Nations Program on HIV/AIDS
VAAC	Viet Nam Authority of HIV/AIDS Control
VND	Viet Nam Dong
WHO	World Health Organization

EXECUTIVE SUMMARY

Background: It is estimated that there are 170,000 injecting drug users (IDUs) in Vietnam. The HIV prevalence among IDUs is as high as 56% in some provinces. In 2008, a Methadone Maintenance Therapy (MMT) pilot service program was initiated in two urban areas, Hai Phong and Ho Chi Minh City (HCMC). The goals of the pilot were to reduce high-risk behaviors and HIV transmission among heroin dependent individuals and to inform the scale-up of MMT in Vietnam. This study aimed to evaluate the effectiveness of the MMT pilot in: (1) reducing drug use, (2) decreasing the practice of risk behaviors for HIV transmission, and (3) improving the quality of life (QoL) of IDUs.

Methods: A 24-month prospective cohort study was undertaken. Each member of the cohort of 965 patients in Hai Phong and HCMC was interviewed and completed questionnaires during the baseline assessment and then in follow-up visits at 3, 6, 9, 12, 18, and 24 months. The questionnaire collected information on demographics, location, QoL, drug use and sexual behaviors, involvement in criminal activity and physical health status. Blood samples were taken and tested for HIV at the beginning of the study and then after 6, 12, 18 and 24 months of treatment. Urine specimens were also taken and tested for opiates at the end of each visit.

Key findings:

- **High retention and compliance:** The majority of participants were retained in the study and complied with treatment during the two-year study period. After 2 years of follow-up, 171 patients (17.7%) stopped MMT and left the program. Dropout rates ranged from 7 to 10.8 cases per 1000 patient-months. The main reasons for dropouts were being arrested (40%); loss to follow up (32%); death, mostly due to AIDS, (8.2%); and hospitalization leading to discontinuation of methadone treatment (3%).
- **Reduced drug use:** MMT was associated with a dramatic reduction in percentage of participants using drugs, from 100% of participants using drugs at program enrollment to 34- 36% after 3 months and 19%-26% of participants after 6 months of treatment. This low prevalence of drug use then persisted in both cities till the end of the study.
- **Improved quality of life:** The percentage of patients reporting a good or very good QoL increased from approximately 16% at baseline to 55% after 3 months. The percentage of patients “satisfied” or “very satisfied” with their health also increased from 31.5% at baseline to around 50-55% following 24 months of treatment.

- **Reduced risk behaviors for HIV transmission:** Among patients who reported using drugs, the percentage of patients self-reporting injecting drug use reduced from 87% at baseline to about 50% between month 6 and 12. The rate of needle sharing also decreased from 2% to 0% for the same time period. Condom use increased among study participants, particularly in sex with sex workers.
- **Improved employment status:** Patients in full-time employment increased from 42% at baseline to 54% of patients after 24 months. These increases were particularly observed among clients who had been on treatment for longer periods of time.

Recommendations:

Results of this 24-month study support the effectiveness of MMT in dramatically reducing illicit drug use and risk of HIV transmission. Findings also suggest that MMT reduces criminal activity and improves quality of life. The data support expansion of the MMT program in Vietnam.

To further improve effectiveness of therapy, local authorities should consider offering and strengthening community-based initiatives, such as vocational training and support in securing employment, stigma-reduction interventions, and risk-reduction education that support MMT clients and help achieve the program's goals.

I. Introduction

According to estimates of the Joint United Nations Program on HIV/AIDS (UNAIDS), there were about 33 million people living with HIV (PLHIV) and approximately 2 million deaths from HIV-related causes worldwide in 2007 [1]. HIV epidemics vary significantly from region to region, both in scale and scope. While practice of risky sexual behaviors fuels epidemics in African countries, injecting drug use is the main mode of HIV transmission in Asia. The latter characteristic holds true for Vietnam, where injecting drug users (IDUs) account for approximately 45% of the total 190,000 HIV cases in the country [2-4].

According to the 2007 – 2012 HIV/AIDS Estimates and Projections for Vietnam, the HIV epidemic in the country remains concentrated, with high prevalence rates among high risk populations – namely IDUs, female sex workers (FSWs) and men who have sex with men (MSM) [5]. Of these populations, IDUs are most severely affected by HIV epidemic. The Ministry of Public Security estimates that there were about 170,000 registered IDUs in Vietnam at the end of 2008 [2], of whom 30% were living with or potentially infected with HIV.

Sharing of injection equipment is a well-known route of HIV transmission. In Vietnam, it is the primary mode of HIV transmission among IDUs. In addition, IDUs engage in high-risk sexual behaviors, especially with partners who do not inject drugs, making them a potential bridge for HIV transmission to low-risk populations.

Since the mid-1990s, Vietnam has implemented various prevention programs to reduce and control HIV transmission among IDUs and other populations at risk. These have included peer education, community outreach, information, education and communication activities and needle and syringe exchange programs. In 2006, the Vietnam Administration of HIV/AIDS Control (VAAC), under the Ministry of Health (MoH), initiated development of an opioid substitution treatment pilot program using methadone.

Methadone, a synthetic opioid, is the most widely used pharmacologic treatment for opioid dependence. When integrated with counselling and support services, methadone maintenance treatment (MMT) has been associated with reduced rates of illicit drug use, needle sharing and HIV incidence. After 6 to 18 months of follow up, studies have found that the prevalence of frequent drug use and needle sharing is significantly lower among IDUs on methadone treatment compared to those not on treatment [6-16]. A study undertaken by Moss and colleagues reported a reduction in illicit drug use from 33% to 15% and a decrease in drug injection from 19% to 6% of IDUs sampled after 5 years of MMT [17].

Metzger DS et al. conducted a similar study among HIV-negative IDUs in a methadone program and those not in a program. Results showed that after 18 months, HIV prevalence was 3.5% among the group on methadone and 22%

among the group not on methadone [6]. And in Hong Kong, where methadone treatment is widely accessible, low HIV prevalence (0.3%) was reported among MMT clients [18].

Evidence shows that methadone treatment also improves treatment adherence among IDUs on anti-retroviral therapy (ART) and enhances overall quality of life [6, 7, 15, 16, 19-25].

Since 2006, VAAC has been working with international organizations and other stakeholders to pilot MMT in Hai Phong and Ho Chi Minh City (HCMC) – two cities where IDU populations are heavily affected by HIV. The program adheres to the Ministry of Health's *Guidelines on Methadone Substitution Therapy for the Treatment of Opium Substance Dependence* [26, 27]. Approximately 1,500 individuals were enrolled into the pilot. The objectives of the pilot program are to: (1) reduce the transmission of HIV and related infections among opiate users; (2) improve the health status and quality of life of IDUs; and (3) increase reintegration of IDUs within communities.

This study followed a cohort of patients who were on methadone treatment between 2009 and 2011. Outcomes of interest were measured at program enrollment, and subsequently at 3, 6, 9, 12, 18 and 24 months after initiation of treatment. This study was a core component of a program evaluation, which also included a process evaluation study focusing on infrastructure, human resources, operations, service quality and cost analysis (i.e. estimating the costs of establishing and operating an MMT clinic including fixed costs, operating costs, management and administration costs) of the MMT pilot. The program evaluation served as a foundation for the scale-up of MMT in other cities and provinces.

II. Objective

The objective of this evaluation study is to monitor and demonstrate the outcomes of methadone maintenance treatment overtime by repeatedly measuring the following:

- Changes in drug use status, including needle sharing behavior;
- Changes in sexual behaviors, including type of partners and prevalence of condom use;
- Improvement in social behaviors/interactions including reduced engagement in crime and success in re-integrating within society;
- Patients' physical and mental health; and
- Quality of life.

III. Methods

1. Study design

A prospective cohort study of 965 MMT patients was undertaken in Hai Phong and HCMC. Patients were followed for two years (Jan 2009 – Nov 2011) and outcomes of interest measured at baseline, 3, 6, 9, 12, 18 and 24 months. The following data were collected from four sources:

- Data on patient behaviors were collected from personal interviews,
- Clinical data, including on MMT therapeutic doses and changes in dosage during treatment, clinical features, and withdrawal symptoms, were extracted from medical records every three months.
- Kessler scores (which measure the level of psychological distress during the 4 weeks prior to patient interview) and data on MMT side effects were extracted from counseling records.
- Biological markers of heroin use and viral infections causing blood-borne diseases (such as HIV, Hepatitis B and Hepatitis C) were measured through urine test and blood tests.

2. Study sites

Hai Phong

Hai Phong is a port city on the Red River Delta in northern Vietnam, with a population of approximately 1,900,000 people (General Statistics Office of Vietnam, 2011). HIV infection began spreading in the mid-1990s, mostly among IDUs. By the late 1990s, about 60% of IDUs in Hai Phong were HIV-positive. This figure starting decreasing in 2006, and has since leveled at around 40-50% of IDUs [28].

Statistics from the Hai Phong Department of Labor, Invalids, and Social Affairs (DOLISA) indicate that in 2007, there were 9,500 drug users in Hai Phong (75% were IDUs). An important HIV risk factor among IDUs is their frequent sharing of needles and injection equipment [4, 28]. Some commercial sex workers are also injection drug users which further increases their risk of HIV above that already posed by unprotected sex.

In 2007, the government selected Hai Phong as a site for the methadone pilot, to be carried out in three out-patient clinics in Le Chan District, Thuy Nguyen (by April 2008) and Ngo Quyen District (by August 2008).

Ho Chi Minh City

Ho Chi Minh City is Vietnam’s largest city, with over 7,500,000 residents (General Statistics Office of Vietnam, 2011). The Ministry of Labor, Invalids, and Social Affairs (MOLISA) estimated that there were 45,000 opiate users in HCMC in 2004, 99% of whom used heroin. The majority of these users started using heroin in their youth mainly in the late 1990s, and primarily injected the drug [28, 29].

HIV/AIDS in HCMC is closely associated with a population of older IDUs, who initiated drug use in the early 1990s, as well as a younger group of IDUs, who started use in the mid to late 1990s [30]. The first case of HIV among IDUs was detected in 1994, following which infection rates peaked in 1996 when 40% of all drug users in the city were infected. Though rates subsequently decreased, a new influx of IDUs has driven the percentage of users infected back up to 65%.

Similar to Hai Phong, government and non-government stakeholders have implemented interventions to address the epidemic including: harm reduction, counseling and support for prevention and treatment of addiction, and HIV/AIDS care and treatment. An MMT pilot program was initiated in three clinics in District 4, District 6, and Binh Thanh District in May 2008.

3. Study participants

The Vietnam MoH outlined the following eligibility criteria for admission into the MMT program: (1) medical diagnosis with opioid dependence; (2) no contraindications for methadone use; (3) age of at least 18 years; (4) written voluntary consent for participation in the program; (5) possession of a referral document from the commune-level people’s committee; (6) stable housing arrangements in the district where the MMT clinic is located; and (7) not prosecuted for or charged with a criminal offence. As the program was a pilot, patients were carefully selected by district patient-selection committees which at that time required the following criteria for admission: (1) use of drugs by injection; (2) opioid addiction for at least three years; (3) several unsuccessful drug rehabilitation attempts; and (4) previous active participation in HIV/AIDS control and prevention activities. In addition to these admission criteria, the following exclusion criteria were applied: (1) refusal or inability to provide informed consent and (2) presence of a serious medical condition that requires hospitalization or extensive medical care.

4. Study samples

All patients admitted to the six MMT clinics during the period from January to September 2009 were invited to participate, of whom 965 patients were enrolled in this study. Of 477 patients approached in Hai Phong, 10 refused to participate in the study. In HCMC, of 502 patients invited, only three refused participation and one died a day after the baseline patient interview.

Table 1: Number of patients enrolled by study site

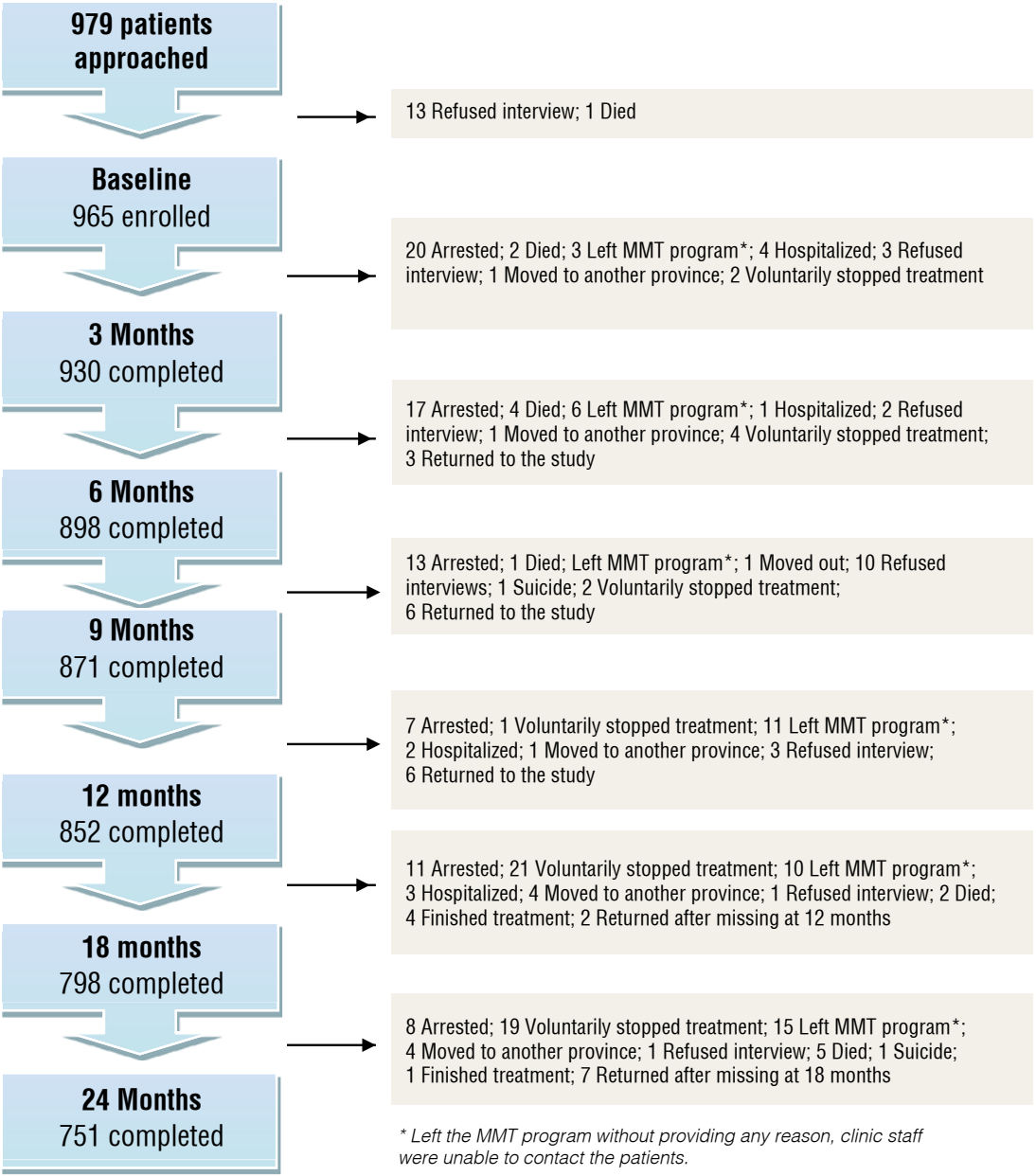
Hai Phong	Number of patients	HCMC	Number of patients
Le Chan	126	District 4	167
Ngo Quyen	128	District 6	181
Thuy Nguyen	213	Binh Thanh	150
Total	467	Total	498

All patients were invited to join the study before initiation of MMT treatment. Study investigators explained the purpose of the study, participant eligibility requirements and the voluntary nature of the study. If participants agreed to participation and provided consent, they were recruited into the study.

Over the 24-month period of the study, 214 patients dropped out - of whom 16 died. Reasons for drop out and deaths are described in detail in the Results section of this report. The final numbers of participants for whom data are available are: 965 patients at baseline, 930 at 3 months, 898 at 6 months, 871 at 9 months, 852 at 12 months, 798 at 18 months and 751 patients at 24 months.

Figure 1 provides an overview of participant follow-up in this study, with details on the number of patients who dropped out and reasons for drop out at 3, 6, 9, 12, 18 and 24 months.

Figure 1: Participant flow



5. Key indicators

Study indicators:

- Patient characteristics at baseline: demographic and socio-economic characteristics, previous experience with substance abuse treatment.
- Treatment retention
- Methadone dosage, treatment adherence and side-effects
- Illicit drug use evaluated through urine tests and self-reporting.
- Biological indicators including infection with HIV, Hepatitis B, and Hepatitis C.
- Injecting and sexual behaviors
- Physical health and mental health
- Quality of life
- Criminal behaviors
- Employment status
- Usage of health and other social support services.

6. Data collection

Data collection was initiated in January 2009 and completed in September 2011. For each patient enrolled in the study, data was collected at baseline (the period between consent for participation and treatment initiation), and at 3, 6, 9, 12, 18 and 24 months after treatment initiation. At each stage, the study team collected the required data from: face-to-face interviews with participants, review and extraction of information from medical and counseling records, and biological samples (urine and blood specimens) (see Table 2).

For patients' convenience, interview appointments were made when they visited clinics for methadone treatment. The same procedures were followed at each visit: participant interview, urine test for opiate use, and collection of a blood sample to test for HIV, HBV and HCV infection at baseline and at subsequent stages of follow-up for those who had negative result in the previous round.

Standardized and structured questionnaires were developed, translated and tested before being used in the study. Questionnaires collected information on social characteristics, marital status, addiction history, injecting and sexual behaviors, health status, and engagement in criminal activities.

Questions on risk behaviors were adopted from the Vietnam HIV/STI behavioral and biological surveillance survey used widely since 2005. Questions about addiction and related issues (such as family relations, legal status) were taken from the Addiction Severity Index- Lite [31].

Patient's quality of life was evaluated using the WHOQOL-BREF questionnaire [32]. This includes 26 items measuring 4 domains of health-related quality of life: physical, psychological, social and environment health The WHOQOL-BREF questionnaire has previously been validated and used in a population of ART patients in HCMC, Vietnam.

In addition to clinical data such as MMT dose or side effects, data was also extracted on a number of standardized measures used at MMT clinics. Patient’s level of psychological distress was evaluated by MMT staff using the Kessler 10 item scale (K-10) [33]. Mental health status was evaluated by clinic counselors based on 10 signs/symptoms.

Table 2: Study indicators and data sources

	Before treatment (baseline)		Follow-up at 3, 6, 9, 12, 18 and 24 months of treatment	
	Interview	Medical records / counseling forms	Interview	Medical records / counseling forms
Behavioral indicators				
Risk behaviors related to the transmission of HIV, HBV, HCV, and STDs	✓		✓	
Drug use behaviors	✓	✓	✓	✓
Health indicators				
Physical health: clinical and laboratory indicators		✓		✓
Mental health: Kessler scale or administration of a minimum mental test		✓		✓
History of opiate addiction, and previous cessation measures		✓		
Drug use- related issues: withdrawal, neurological toxicity, related physical disorders		✓		✓
Other co-morbidities: infection with HIV, Hepatitis B and C, TB, and other acute or chronic conditions		✓		✓
Progression of treatment: therapeutic dosages, side effects, toxicity		√		√

	Before treatment (baseline)		Follow-up at 3, 6, 9, 12, 18 and 24 months of treatment	
	Interview	Medical records / counseling forms	Interview	Medical records / counseling forms
Social indicators				
Social characteristics: education, marital status, job, income	✓		✓	
Incidence of criminal activities at home and other places	✓		✓	
Quality of life	✓		✓	
Biological indicators				
Infection with HIV, Hepatitis B and C	✓*		✓*	
Positive urine tests and other tests used to determine drug use	✓**		✓**	

* Blood Test before treatment, at 6, 12, 18 and 24 months
** Urine test before treatment, at 3, 6, 9, 12, 18 and 24 months

Interviews were conducted by study staff from Hai Phong Medical University and the HCMC Public Health Association. Enrolled patients were interviewed by study in a separate room. The study coordinator made appointments with participating patients based on their identification information. This identifying information however, was not recorded in study questionnaires. Instead, each patient was assigned a unique ID code at the beginning of the study. Confidentiality of their information was stressed during each patient interview.

Data on patients’ drug use practices were collected from two sources. On the interview day, each patient was asked to provide a urine specimen for opiate testing. In addition, results of routine opiate tests performed by clinic staff were collected. HIV, HBV and HCV infection status was assessed through blood tests at baseline, and at the 6-month, 12-month, 18-month and 24- month follow-up visits. Blood tests were performed at the HCMC Center for Preventive Medicine and Hai Phong PAC, based on testing algorithms of the Vietnam Ministry of Health testing.

All data collection activities were monitored and supervised by independent teams to ensure compliance with the study protocol and guidelines.

7. Management and analysis of data

7.1. Data management:

All completed data collection forms were sent to data management centers in the two cities. Before being stored and processed, all data were checked for completeness and validity by data managers and study monitors. Accepted forms were kept in study participant files. For each visit, patient files included an interview questionnaire, a medical record data extraction form, a counseling data extraction form, a biological test result form, and a study retention note.

Interview and data extraction records were converted into electronic versions using entry forms developed in Microsoft Access. Twenty percent of all data collection forms were randomly selected and re-entered (double data entry) for quality control.

Data on daily methadone dosage were generated from clinic dispensing databases, maintained as MS excel spreadsheets. After being cleaned and verified, the data was coded with study IDs based on patient clinic IDs. Once coding was completed, patient clinic IDs were omitted from the dataset.

For each round of follow-up in the study, the final datasets include interview, clinical, methadone dispensing, counseling, and biological data. Participant study IDs were always only used.

7.2. Data analysis:

Descriptive analysis

Descriptive analysis was undertaken based on calculating means, medians and standard deviations for continuous measurements, and frequencies and proportions for categorical variables.

For analysis of quality of life, QoL items were scored, and domain average scores calculated based on the WHOQOL-BREF instrument manual. Mean scores were estimated for physical health, psychological health, environmental and social health.

Estimates of MMT program dropouts (and retention): a patient was confirmed as a dropout of the program in the following cases: police arrest, voluntary termination of MMT treatment, exit from the program without providing a reason (MMT staff are unable to contact patient), death or hospitalization preventing return to the program.

Estimates of concurrent heroin use: current (in the 30 days prior to the visit) heroin use among patients was determined through the following: 1) self-reported drug use; 2) positive opiate urine test undertaken by clinicians; and 3) positive opiate

urine test at study visit. Over the two-year study period, a significant number of patients were arrested because of drug use, especially in HCMC. These patients, if opiate test positive, were counted as heroin use cases in the analysis.

Methadone dosage and adherence: Methadone dose was defined as the last dose taken by the patient - which was normally the dose taken on the interview day. Methadone adherence was defined as: 'good' if a patient did not miss any treatment day over the 24 month study period, 'moderate' if a patient missed doses for 1- 4 days, and 'poor' if a patient missed doses for 5 continuous days or more.

Special analysis for program outcomes

We used survival analysis to assess retention in the program during the 24 months of follow-up. The number of person-months a patient received treatment was 24 if the patient was successfully retained in the program until the end of the study. Time between the methadone initiation date and the date of dropout was used to calculate the duration that the patient remained in the program, if date of dropout was available. If the date of dropout was not available, the midpoint between two rounds of interviews was used as the approximate date of dropout. For example, if a patient left the program on an unspecified day during the first three months, the patient was considered as contributing a month and half to the total time all patients spent in the program.

Simple regression was initially performed using the Cox Hazard Proportional Model with dropout status as a dependent variable and others as independent variables. Independent variables included socio-demographic and relationship status, injecting behaviors, and treatment characteristics. Variables found to be potentially associated with the outcome of interest (p-value<0.3 in simple regression analysis), were entered into a final Multivariate Cox Proportional Hazards Model. Prior to performing the analysis, every eligible variable was checked for compliance with the assumption of proportionality.

In addition to the common regression model that was built on data from all participants (in both Hai Phong and HCMC), a separate model was developed for each city. However, we found model outputs were very similar for the two cities. Therefore, only results from the common model were used and reported in this report.

8. Ethics

The study proposal and other study materials were reviewed and approved by the Protection of Human Subject Committee of FHI360 (PHSC approval letter dated Jan 7, 2009) and by the Ethics Committee at the Hanoi School of Public Health (Approval # 065/2008/YTCC-HD3 dated Nov 28, 2008).

IV. Results

1. Baseline characteristics

Median age of the study population was 30 years (range: 16.6 to 58 years), and the majority of participants were males (95%). HCMC participants differed from Hai Phong participants in a number of ways. A higher proportion of participants in HCMC were female (8% versus 1.9% in Hai Phong) and single (61% versus 43.5% in Hai Phong). Participants were also younger than in Hai Phong (29.3 years versus 33.8 years), with a significantly lower percentage of patients older than the age of 30 years (37.4% in HCMC compared to 68% in Hai Phong).

The overall level of education within the sample was low: 56% of participants completed secondary education or lower while less than 5% had finished college or university studies. Close to half of the study sample, 48.3%, had completed some form of vocational training. At the time of initiation of treatment, the majority of participants, 84.3%, were living with their parents or siblings, while significantly lower numbers were living with their wife and kids (36.8%) and relatives or friends (less than 10%). Nearly 7% of participants reported sharing a house with other drug users. On average, patients had resided in their current district of residence for about 28 years (median 30 years).

In Hai Phong, 66.6% of study participants had either full-time or part-time jobs, compared to 61.7% in HCMC. In both cities, over 27% of participants were day laborers performing basic tasks, and only 11.3% were steadily employed, usually within a family business.

Approximately 98% of study participants in Hai Phong and 79% in HCMC earned an income. The average monthly income in the sample was about VND 6.9 million (\$365). Monthly income was earned from various sources. Although more than 55% of participants earned an income from stable sources (either from full-time or part-time jobs), this stable income only accounted for an average of VND 3.36 million per month (\$180). The majority of patients, 74.4%, received a substantial amount of financial support from family, at an average of VND 5.11 million per month (\$268). Only 7.4% of all study patients reported that they received an income from “other sources”, which totaled to about VND 5.75 million per month on average (\$302). Thirty-two patients reported a regular income from gambling, theft or drug selling. This number however is likely to be lower in reality, as participants are less likely to report income from illegal sources. All participants stated that they used their income to buy drugs, cost of which averaged at VND 6.6 million per month (\$349) (compared to a total average income of \$365 per month). Only a few IDUs reported that monthly expenses incurred were for personal needs or to support their family (1.3% and 2.4% of IDUs respectively).

Table 3: Socio-demographic characteristic of participants

	Hai Phong (n, %) (N= 467)	HCMC (n, %) (N=498)	Total (n, %) (N= 965)
Gender			
● Male	458 (98.1)	458 (92.0)	916 (94.9)
● Female	9 (1.9)	40 (8.0)	49 (5.1)
Age			
● Mean (years)	33.8	29.3	31.4
● Median (years)	33.1	28.7	30.3
Age groups			
● Under 20 years	8 (1.7)	5 (1.0)	13 (1.4)
● 20 to 25 years	46 (10. 0)	78 (15.7)	124 (13.0)
● 25 to 29 years	93 (20. 2)	228 (45.9)	321 (33.5)
● 30 years or more	313 (68.0)	186 (37.4)	499 (52.1)
Marital status			
● Single (never married)	203 (43.5)	304 (61.0)	507 (52.5)
● Currently Married	195 (41.8)	113 (22.7)	308 (31.9)
● Living with partners	2 (0,4)	38 (7,6)	40 (4,2)
● Separated/ Divorced/ Windowed	67 (14.4)	43 (8.6)	110 (11.4)

	Hai Phong (n, %) (N= 467)	HCMC (n, %) (N=498)	Total (n, %) (N= 965)
Education level			
● No schooling	2 (0.4)	4 (0.8)	6 (0.62)
● Completed primary	41 (8.8)	53 (10.6)	94 (9.75)
● Completed secondary	206 (44.2)	233 (46.8)	439 (45.54)
● Tertiary	197 (42.3)	189 (38.0)	386 (40.04)
● Completed University/ colleges	20 (4.3)	19 (3.8)	39 (4.05)
Previously had vocational training	220 (47.11)	246 (49.5)	466 (48.3)
Currently employed	311 (66.6)	307 (61.7)	618 (64.0)
Earns an income	456 (97.9)	391 (78.5)	847 (87.9)
Average monthly income (millions VND)	6.1	7.8	6.9

HIV, HBV and HCV prevalence in patients at baseline were 28.3%, 11.8% and 55.2% respectively. Biological testing detected one new HIV case, 27 new HBV infections, and 141 new HCV infections over the 24-month period.

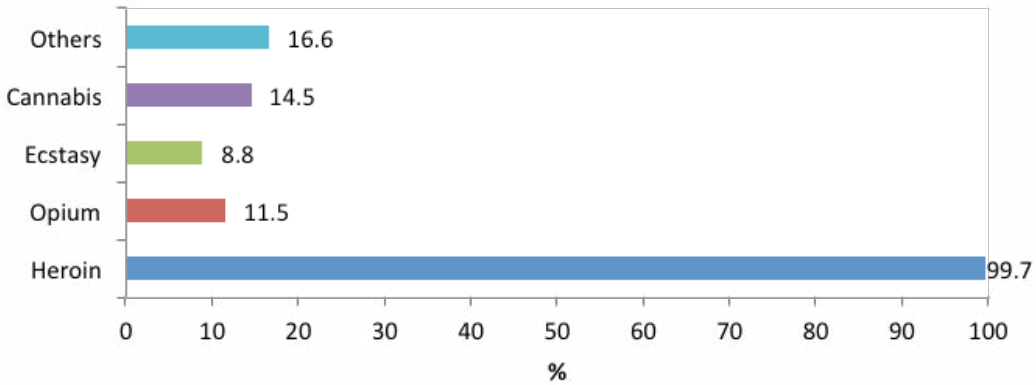
Mean duration of drug use of participants was about 10 years. Heroin was most commonly used (see Figure 2), with almost all IDUs having used heroin during the 30 days prior to initiation of MMT treatment. An estimated 11.5%, 8.5% and 14.5% of participants had also used opium, ecstasy and cannabis respectively, before enrollment into the study. In addition, sixteen percent of patients reported using sleeping aids and other types of pharmaceutical drugs during the same period. Twenty-nine participants used a combination of two drugs, while four patients reported use of three different drugs during the 30 days before MMT initiation.

Almost all participants used heroin 2 times a day or more, spending a daily amount of 12 US dollars (USD), with very few patients reporting heroin use only once a day. Injecting was the main method of heroin use, as reported by 84% of participants. An estimated 34% patients in HCMC reported ever sharing needle/ syringes, while a lower percentage, 13%, did so in Hai Phong. Needle sharing in the 30 days prior to the baseline interview was low in both cities: 0.8% in Hai Phong and 4.2% in HCMC (see Table 4).

Table 4: Participants' history of drug use

	Hai Phong (%) (n= 467)	HCMC (%) (n= 498)	Total (%) (n= 965)
Mean duration of drug use (years) (SE)	9.7 (0.2)	9.6 (0.2)	9.7 (0.1)
Frequency of heroin use in the last 30 days prior to the baseline interview			
● Once per day	5 (1.1)	12 (2.4)	17 (1.8)
● 2 to 3 times/day	291 (62.9)	316 (63.6)	607 (63.2)
● 4 times or more per day	167 (36.1)	169 (34.0)	336 (35.0)
Method of drug administration in the last 30 days prior to the baseline interview			
● Injecting	379 (81.2)	433 (87.0)	812 (84.2)
● Inhaling/ Sniffing/ Ingesting	104 (22.3)	99 (19.9)	203 (21.0)
Ever shared needle/syringes	61 (13.2)	169 (34.0)	230 (23.8)
Needle sharing in the last 30 days prior to the baseline interview	4 (0.8)	21 (4.15)	25 (2.6)
Attempted cessation at least once	451 (96.6)	494 (99.2)	945 (97.9)
Average number of cessation attempts	6.2	6.6	6.4

Figure 2: Type of drugs used among participants



2. Program retention

Over the 24-month period of the study, a total of 171 patients (17.7%) stopped MMT treatment and left the program. Dropout rates ranged from 7 to 10.8 cases per 1000 patient-months (i.e. 7 to 11 cases left the program per 1,000 patients treated in a month). As shown in Table 5, dropout rates remained relatively stable over the course of the study.

Table 5: Dropout rates from the program at each stage of follow-up

Round	Person-month	# Dropout	Incidence rate /1,000 person-month	95% CI	
0 – 3 months	2865.20	25	8.7	5.90	12.91
3 – 6 months	2767.59	30	10.8	7.58	15.50
6 – 9 months	2680.32	25	9.3	6.30	13.80
9 – 12 months	2589.18	18	7.0	4.38	11.03
12 – 18 months	4980.41	38	7.6	5.55	10.45
18 – 24 months	4666.82	35	7.5	5.38	10.45
Total	20549.52	171	8.3	7.16	9.67

Of those who dropped out, 73 (40%) were arrested; 54 (32%) left the program without providing any notification to their clinic and clinic staff were unable to contact them; 14 (8.2%) died, among those, 10 were due to HIV related illness; and 5 (3%) patients were hospitalized and could not continue methadone treatment. It is important to note that for three patients, treatment termination can be considered as a positive outcome as these patients voluntarily and gradually reduced methadone doses before finally stopping treatment (Table 6).

Table 6: Reasons for patient dropout from the MMT program

Reason	Number	Percentage
Under arrest	73	42.69
Voluntarily dropped out	20	11.7
Death	14	8.19
Hospitalization	5	2.92
Loss to follow up	54	31.58
Suicide	2	1.17
Finished treatment (*)	3	1.75
Total	171	100

* Voluntarily and gradually reduced methadone dosage before stopping treatment

In survival analysis, two factors were associated with patient dropout: heroin use during MMT treatment and methadone dosage. Participants who continued to use heroin while undergoing MMT were 26 times more likely to stop and leave the MMT program (HR: 26.7). On the other hand, every 10 mg increase in the methadone dose reduced the hazard of dropout by 6% (HR: 0.94) (see Table 7).

Table 7: Hazard Ratio (HR) for factors associated with retention based on Multivariate Cox Proportional Hazards Modeling

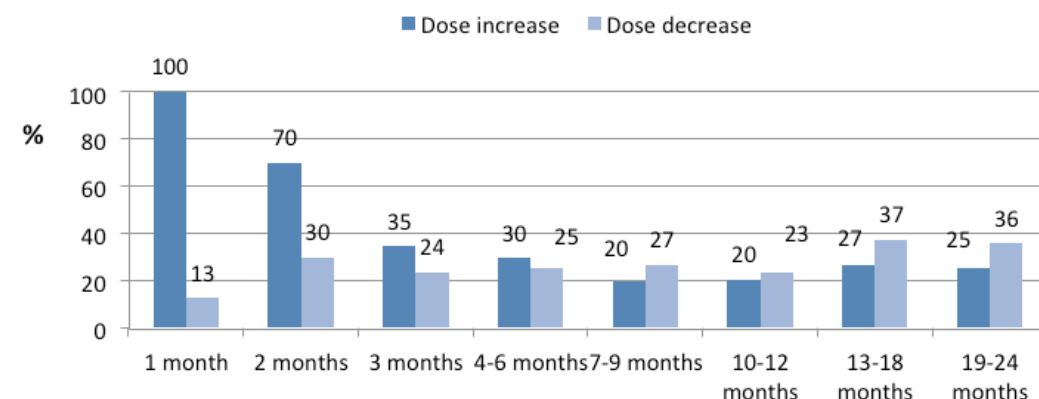
	Hazard Ratio* (95% CI)	P Value
Had serious problems with the community	1.69 (1.02 – 2.82)	0.043
Heroin use	26.72 (16.01 - 44.60)	0.000
Methadone dose	0.94 (0.92 - 0.97)	0.000
Drug use	1.97 (1.35 – 2.86)	0.000
Stopped treatment for 5 days or more	2.81 (1.49 – 5.30)	0.001

*Adjusted for province, sex, criminal activity, negative relationships with family, had serious problems with the community, ARV treatment, and methadone adherence

3. Methadone dosing and related side effects, and treatment compliance

Methadone dosage for study participants was adjusted frequently. All patients required increases in dosage during the first three months, followed by 30% of patients at six months, 20.4% after one year, and 25.4% of patients after two years on treatment. The need for decreases in dosage remained constant at around 20-30% of patients from months 4 to 24 (see Figure 3). Methadone doses were lowered for a range of reasons, including risk of overdose (clients become lethargic) and treatment side effects. These symptoms were observed in about 60% to 75% patients, leading to decreases in dosage.

Figure 3: Methadone dose adjustments over the course of the study

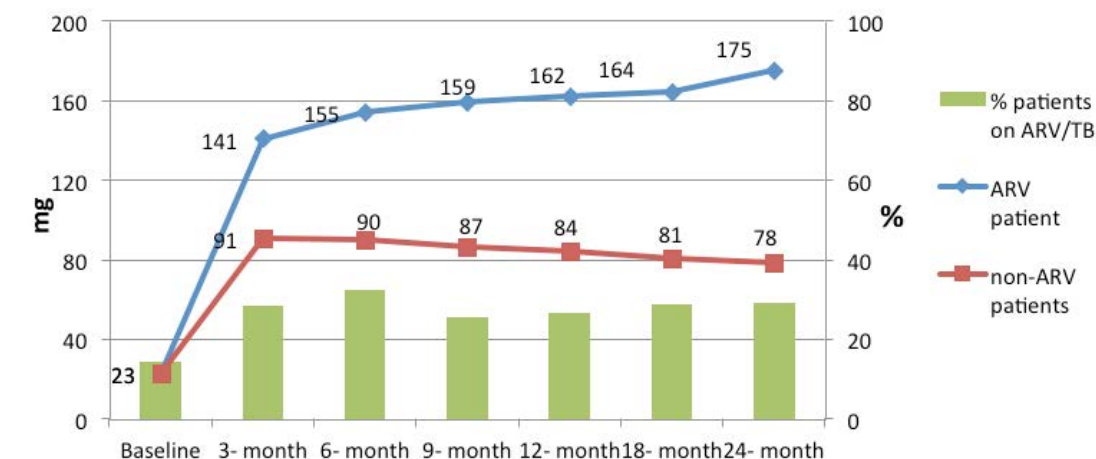


Methadone dosage for patients on ARV treatment was significantly higher than for those not on treatments. After 2 years of treatment, average methadone dosage was 175.4 mg and 78.3 mg for patients on ART and not on ART respectively (see Figure 4). Data also suggests that methadone dosage for patients on ARV treatment was adjusted more frequently than for patients who were not.

Patients' methadone doses were usually increased when they suffered from withdrawal symptoms, as observed by clinicians or reported by patients. During the first 3 months, dosage was often increased when concurrent heroin use was identified (either from reports by the patient or when urine samples tested positive for opiates) - as this is an indication of insufficient methadone dosage. Indeed, concurrent heroin use was observed among 95% of the patients for whom dosage was subsequently increased.

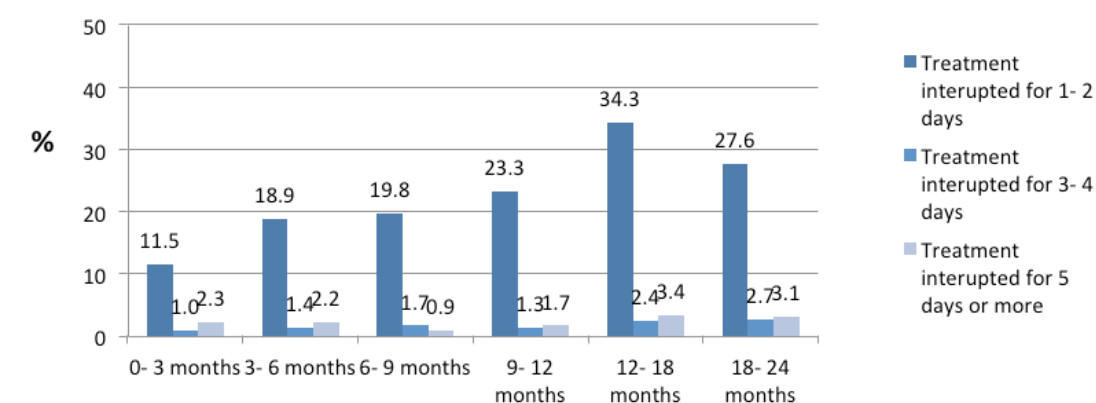
The percentage of patients requiring increases in methadone dosage due to being on ARV or TB treatment was 9% in the three months, 23.4% at 9 – 12 months, and 17.3% in the last three months of follow-up (months 21 – 24). These findings highlight the complexity of providing methadone therapy for populations of drug users with a high prevalence of HIV and TB infection, and the need for close coordination and information exchange between HIV/TB out-patient clinics and MMT clinics.

Figure 4: Mean methadone dose by ARV treatment status



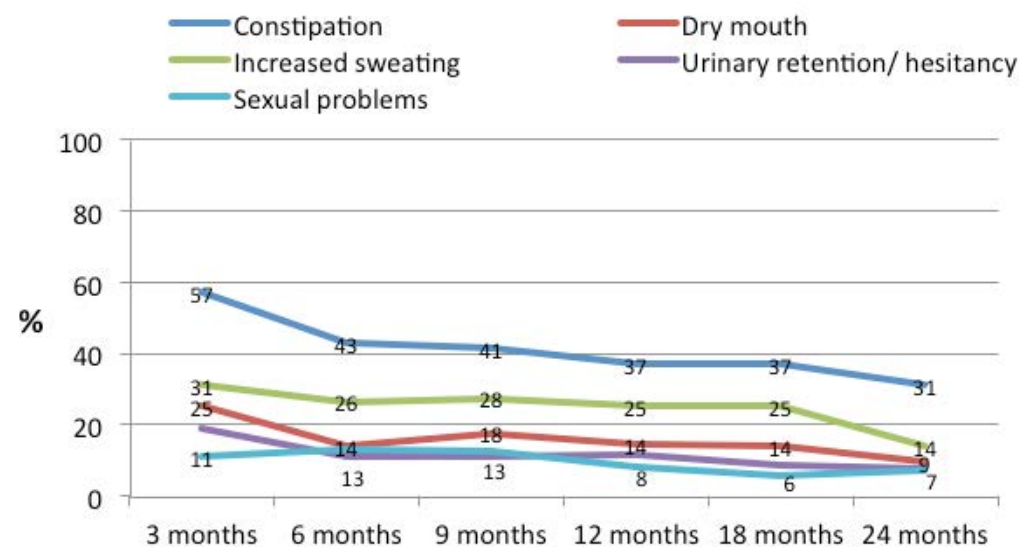
In the first three months of the study, only 11.5% of MMT participants missed their dose for 1 or 2 days (no adjustment was required to their doses). This percentage however, gradually increased - peaking at 34.4% between 12 to 18 months. In the final period of follow up (month 18 to month 24), 27.6% of patients missed their MMT dose for 1 or 2 days. A very low percentage of participants interrupted treatment for 3- 4 days (1-2%), as well as for 5 days and more (1 - 3%).

Figure 5: Treatment interruption (missed doses) over the course of the study



Side effects of MMT, such as constipation or a dry mouth, were also a concern in the program. Overall, about 75.2% of patients experienced at least one treatment side effect in the first three months, but reported side effects dropped to around 60.6% by the end of 12 months and continued to decline to 46.3% after 24 months (see Figure 6). Constipation, increased sweating and a dry mouth were the three most commonly reported side effects. Sexual dysfunction particularly, a chief concern for participants, was uncommon: in the second year, the percentage of patients reporting issues related to their sexual activity was under 10%.

Figure 6: Participant-reported side effects over time

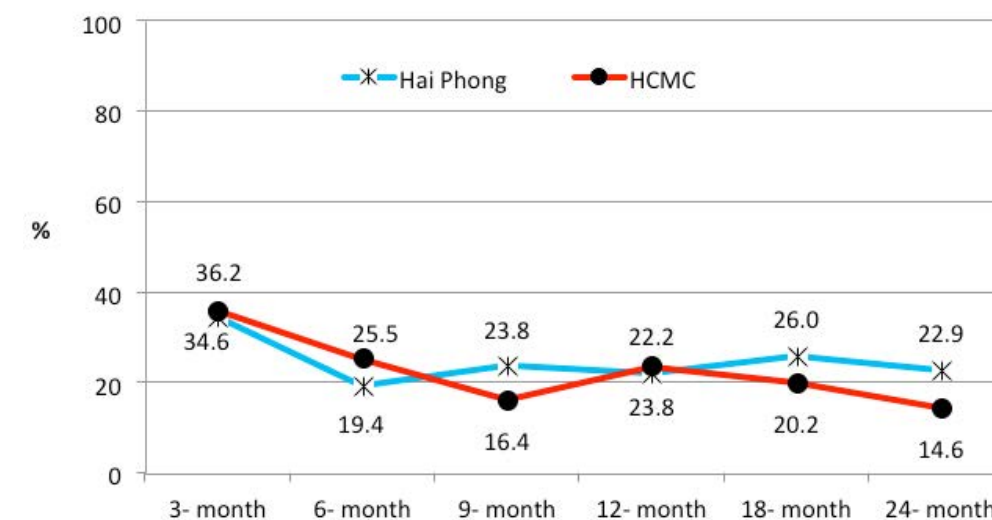


4. Changes in drug use and sexual behaviors

Figure 7 shows trends in heroin use among MMT patients during the 2-year period. Though all patients reported heroin use at program enrollment, the percentage of patients using the drug dropped to 34-36% after 3 months. This declining trend continued from months 3 to 6, following which it stabilized for the rest of the follow-up period. At the end of month 6, 19% of participants in Hai Phong and 26% of participants in HCMC were using heroin. Concurrent heroin use with MMT treatment was reported among 14.6% and 22.9% of MMT patients in HCMC and Hai Phong respectively at the end of the second year of the study. These findings however, should be interpreted with caution. Although participants arrested by police were most often arrested for crimes related to their personal drug use, they may have been heroin users, but this could not be verified. This is likely to result in an underestimation of the percentage of heroin users in the city, and may mean that findings are skewed towards showing that a higher number of patients continued heroin use in Hai Phong than in HCMC.

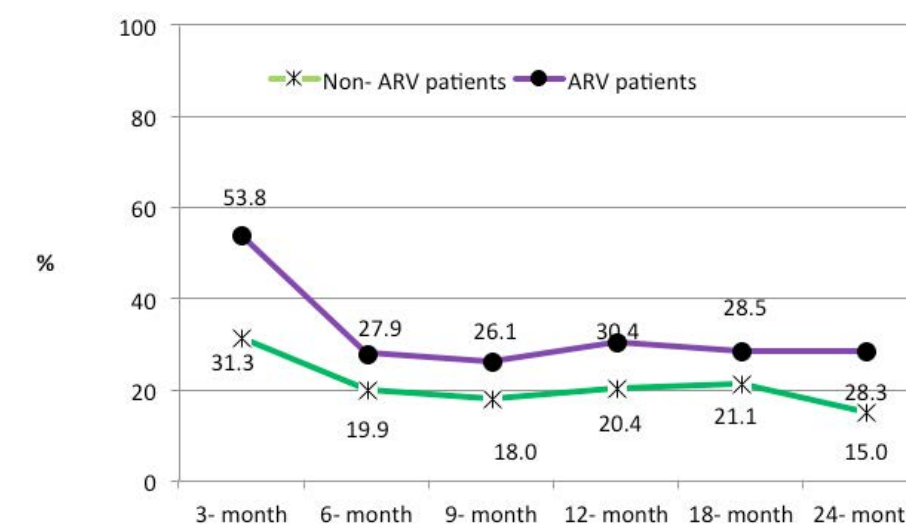
It is also worth noting that estimates of the percentage of participants who were still on heroin in this study were significantly higher than clinics' estimates, which were based on results from urine tests for opiates. During this period, clinics routinely only tested urine for participants suspected to be using drugs.

Figure 7: Percentage of participants who continued heroin use during methadone treatment



Participants on ARV treatment tended to use drugs more than those who were not on ARVs, even despite dosage increases and higher therapeutic doses for the former.

Figure 8: Percentage of patients concurrently using heroin by ARV treatment status

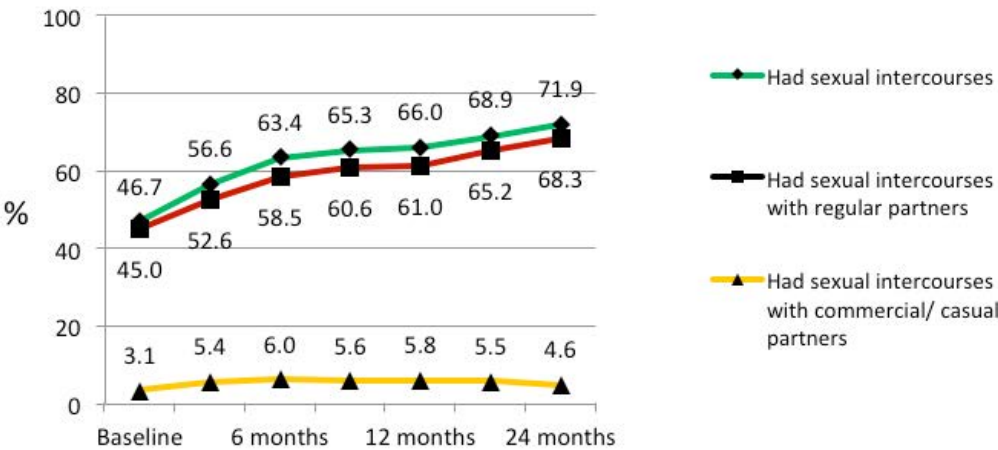


Sexual activity among patients on MMT treatment increased over time. While 47% of participants reported being sexually active in the three months prior to enrollment, 66% reported the same after 12 months of treatment. At 24 months, 71.9% participants reported sexual intercourse in the past 3 months. This increased sexual activity was with regular sex partners as well as commercial/casual partners. While sex with regular partners increased from 45% before

treatment to 68.3% after 2 years, sex with commercial/casual partners did not change significantly over time - starting at from 3.1% before treatment and fluctuating between 4-6% during treatment (see Figure 9). These results were consistent with the finding that a very low percentage of patients reported sex-related problems as a side effect of methadone treatment.

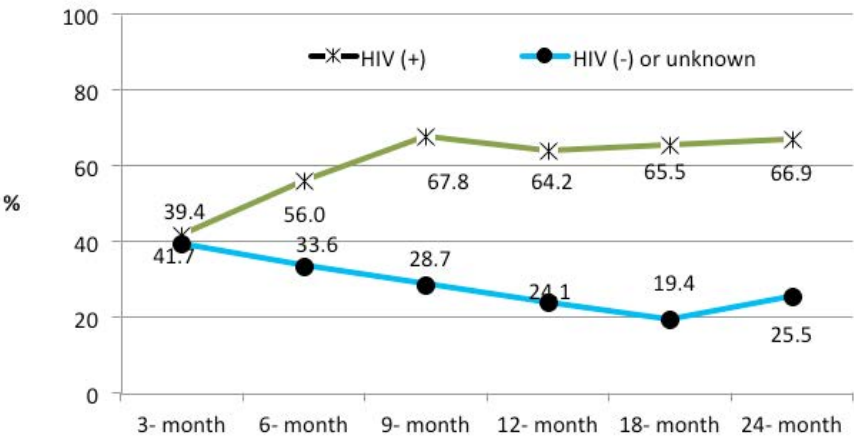
The percentage of patients reporting condom use with commercial partners remained consistent over time, at over 90%. Report of condom use with regular partners initially saw a marked increase from 36.6% of patients prior to treatment to a peak of 41.5% of patients at 9 months, but then gradually decreased between 12-24 months.

Figure 9: Participant's sexual behaviors



The data indicate an improvement in condom use among HIV-positive participants, but at the end of 24 months, there were still only about 66.9% of HIV-positive participants using condoms “consistently” with their spouse (see Figure 10).

Figure 10: Condom use with regular partners among MMT participants by HIV status



5. Improvements in health and quality of life

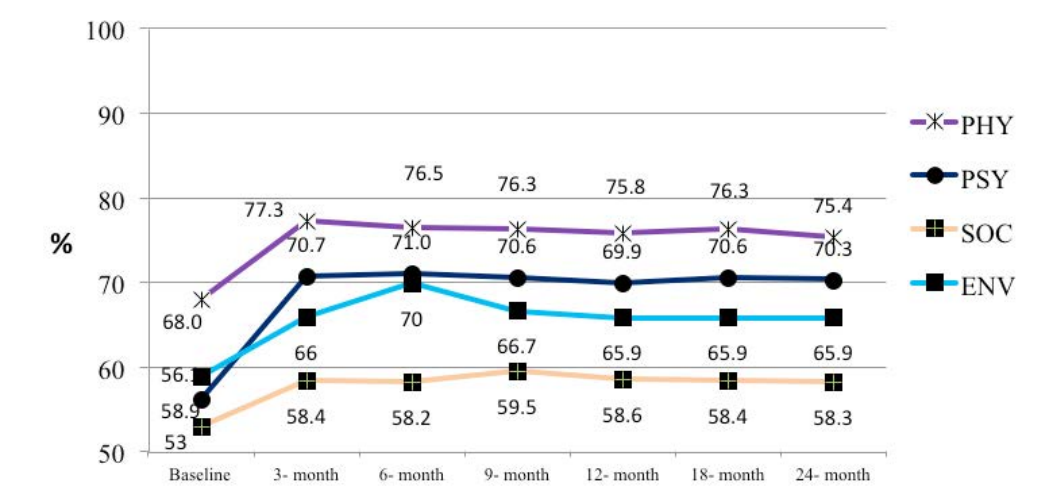
Based on results from the application of the WHOQOL-BREF questionnaire, overall quality of life improved considerably in the first 3 months following treatment initiation and remained high (as judged from scores) during treatment. While only close to 16% of participants said they had a “good” or “very good” quality of life before initiation of MMT, this percentage increased to 55% at 24 months. The percentage of participants “satisfied” or “very satisfied” with their health also increased from 31.5% before treatment to around 50-55% during treatment (see Table 8). Quality of life scores for specific domains also improved remarkably, particularly during the first three months (see Figure 11).

Table 8: Overall quality of life and health of MMT participants over time

	Baseline (n=965)	During treatment					
		3 months (n=930)	6 tháng (n=898)	9 tháng (n= 871)	12 tháng (n=852)	18 tháng (n= 798)	24 tháng (n=749)
Quality of life							
Very bad (%)	1.5	0.3	0.0	0.1	0.0	0.3	0.0
Bad (%)	10.9	1.2	1.6	0.8	0.8	0.5	1.1
Average(“-so-so”) (%)	71.8	46.9	45.8	46.7	48.7	44.3	43.9
Good (%)	15.0	48.6	49.1	48.8	46.8	51.2	51.7
Very good (%)	0.8	3.0	3.6	3.6	3.8	3.9	3.3
Client satisfaction with own health							
Very unsatis- factory (%)	0.3	0.1	0.2	0.0	0.4	0.3	0.3
Unsatisfactory (%)	18.1	5.2	6.0	5.9	5.9	5.0	5.6
Average (%)	50.1	34.0	36.8	35.9	38.5	39.5	41.4
Satisfactory (%)	29.6	57.0	53.1	54.3	52.6	52.6	49.7
Very satisfac- tory (%)	1.9	3.8	3.9	3.9	2.6	2.6	3.1

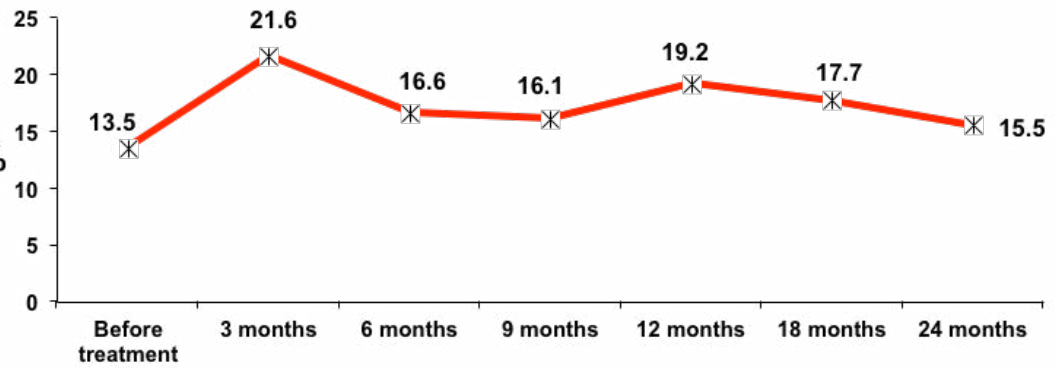
Physical and psychological health scores also increased, from 68 to 75.4 and 56 to 70 respectively. In addition, social and environmental health scores improved, but this improvement was mainly observed during the first 3 months after treatment initiation.

Figure 11: Patient's domain-specific quality of life (based on the WHOQOL-BREF questionnaire)



The percentages of participants reporting health-related problems in the 30 days prior to interview visits at each follow-up stage are shown in Figure 12. In this study, a “health problem” was defined to be any problem that affected the participant’s health “moderately” or “severely”. The percentage of participants with health problems was higher during treatment than before treatment. This is likely due to: (1) experience of common side effects of methadone such as constipation, and (2) the fact that some participants initiated ARV or TB treatment in conjunction with MMT and thus suffered from ARV/TB treatment side effects or immune reconstitution syndrome (IRS). The percentage of participants requiring hospital visits was just 2.2% in the first three months and 3.05% - 4.14% during the rest of the follow-up period.

Figure 12: Percentage of participants reporting health-related problems in the 30 days prior to interview visits.



At each visit, participants were asked about their perceptions of their own mental health. Patient-perceived mental health issues dropped significantly over the study duration. The percentage of patients having concentration or memory problems dropped from 51% to approximately 30-35%, experience of anxiety or severe tension decreased from 32% to nearly 6%, and report of hallucinations reduced from 11.5% to about 3%. A major finding is that the percentage of participants reporting thoughts of suicide declined from 15.3% at baseline to 0.5% after 24 months, while figures for attempts of suicide decreased from 5.3% to almost 0% for the same period (see Table 9).

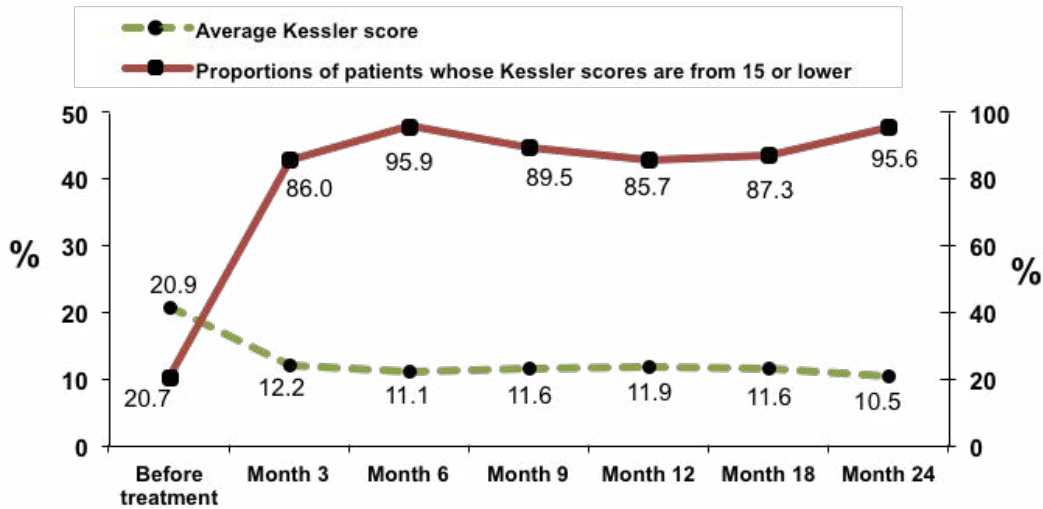
Table 9: Mental health status of MMT participants over time (from interviews)

	Before (%) (n=965)	After (%)					
		3 months (n= 930)	6 months (n=898)	9 months (n=871)	12 months (n=852)	18 months (n=798)	24 months (n=749)
Difficulty concentrating or remembering	51.19	30.86	34.86	31.61	32.22	35.09	35.25
Anxiety, severe tension	32.26	9.35	7.46	6.67	5.99	5.52	5.07
Depression/hopelessness	44.87	10.43	9.03	7.23	7.40	6.27	5.07
Severe loss of interest	28.91	8.71	7.47	7.00	7.16	5.01	5.07
Hallucinations, hearing things	11.50	3.33	3.45	3.21	3.40	3.13	2.94
Difficulty controlling violent behavior	18.46	6.88	7.68	5.28	5.63	5.01	4.94
Thoughts of suicide	15.34	1.08	1.22	0.46	0.23	0.25	0.53
Attempted suicide	5.29	0.32	0.11	0	0	0.25	0.13

Psychological distress, which was measured with the Kessler scale, among IDUs on MMT also dropped considerably. On average, the total Kessler score dropped from 20.9 (which is classified as “moderately or severely distressed”) to 12.2 (“not severe”) at the end of month 3, and then to 10.5 at the end of 24 months. Ultimately, the percentage of clients with no risk of distress (15 or below

on Kessler) increased from 21% before treatment to 95.9% at 6 months. Though this figure decreased between 9 to 18 months, it rose back to 95.6% at 24 months (see Figure 13).

Figure 13: Average Kessler score for MMT participants over time



6. Improvements in social life and relationships

Unemployment among participants decreased after two years on MMT. While 36% of drug users were unemployed at baseline, the figure decreased to 27% after one year and 24.1% after two years. The percentage of participants employed full time increased from 42% to 55.3% after 12 months of treatment, and then remained the same till the end of the study. Jobs held by MMT participants mainly consisted of running small household businesses or engaging in physical labor work.

Figure 14: Unemployment rate among participants

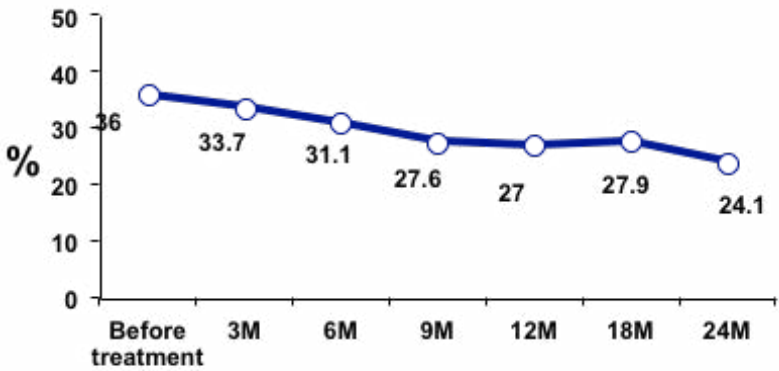
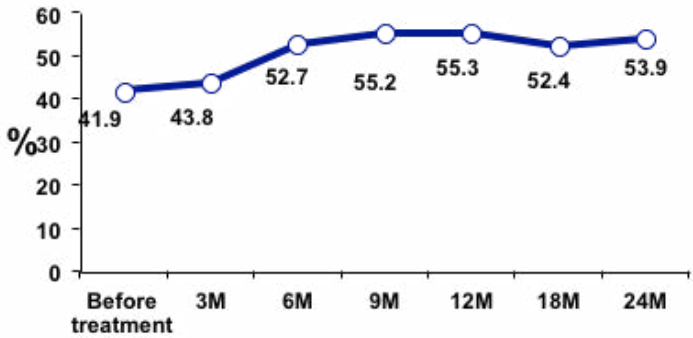
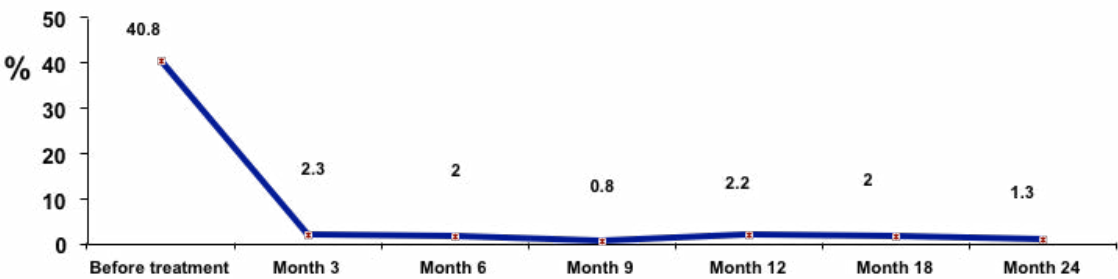


Figure 15: Rate of full-time employment with stable income among participants



Participants were also asked if they had been involved in criminal activities such as theft, fraud, or drug dealing. At baseline 40.8% stated that they had committed crime in the last 3 months. Over the two-year period of the study, the percentage of participants self-reporting criminal activity among those who remained in the cohort at each stage of follow-up was around 0.8-2.3%, or around 18-41 participants per interview round.

Figure 16: Percentage of participants reporting criminal activities



Findings show that MMT also helped participants to reintegrate into their families and society more broadly. The percentage of participants reporting problems in relationships with their family and friends dropped considerably, from 20% prior to treatment to 6.1% after three months and then 3.1% after 24 months. And while it is common for heroin users to pawn their family's possessions for drug money, or even force family members to give them money, such behaviors also declined sharply, in this case from 90% prior to treatment to 2.27% after 24 months of MMT. A significant decrease was particularly seen in the first 3 months following initiation of methadone treatment (see Figures 17 and 18).

Figure 17: Percentage of participants who experienced serious relationship problems with family or friends

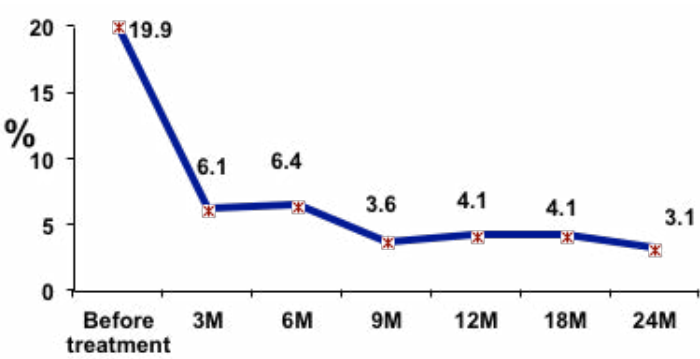
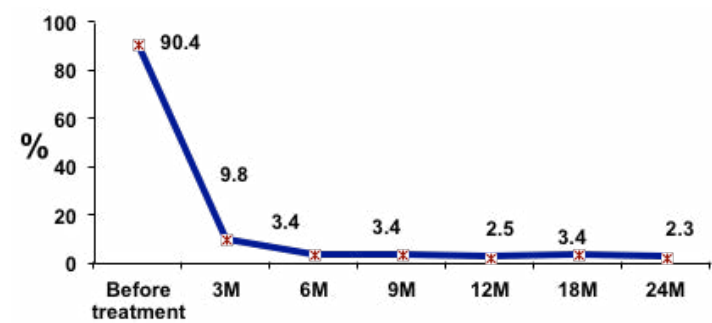


Figure 18: Percentage of participants who reported family conflicts (among those who reported negative relationships/behaviors with their family)



7. Access to health services and social support

“Other than increased access to HTC and ARVs, client access to health services remained fairly low. Perhaps once participants started methadone treatment, their need to inject heroin reduced and thus they felt less fear, anxiety and less risk for HIV, then they stopped seeking clean needles

It is important to note that this study only sought to measure the extent of services received in the last 30 days prior to the interview, and so findings do not reflect the availability of the services to participants. Therefore, numbers shown in Table 10 should not be interpreted as indicating the lack of or limited support services provided under the MMT program.

Table 10: Percentage of participants who received health and social support services in the month prior to interview

	Baseline % (n =964)	3 months % (n =930)	6 months % (n =898)	9 months % (n =871)	12 months % (n =852)	18 months % (n =798)	24 months % (n =749)
Health services							
VCT	64.5	62.7	34.5	36.4	27.1	38.4	44.3
ARV treatment	12.8	11.8	14.7	15.6	14.9	15.6	17.6
Opportunistic infection treatment	3.1	3.6	4.8	5.3	5.4	3.0	5.1
TB treatment	4.1	3.3	3.2	3.0	1.4	2.4	3.5
Treatment for mental health problems	0.1	0.5	0.2	0.1	0.1	0.0	0.1
Other	4.8	2.9	1.8	2.0	1.8	1.5	2.1
Social support							
Re-integration program for recovering drug users	3.2	3.8	4.6	3.2	4.2	4.6	6,3
Peer education	4.2	6.5	5.3	4.4	3.8	3.2	4.9
Clean needles and syringes	8.2	5.1	1.6	1.5	0.8	1.2	2,4
Free condoms	7.5	8.4	7.2	6.5	3.8	4.9	7.9
Social services	0.6	0.3	0.7	0.7	0.5	0.6	0.8
Legal services	0.2	0.4	0.1	0.3	0.5	0.1	0.5
Other	0.1	0.1	0.2	0.1	0.0	0.0	0.0

V. Discussion

In any treatment program, patient dropout is inevitable. In this MMT pilot, retention rates were notably high, 89.8% after one year and 82.3% after two years. Dropout rates in this study were lower than those experienced in other MMT studies, which report rates ranging from 17% after three months (Xiao et al 2010), 13%, 14% and 27% after six months ([34],[35], and 11% after 18 months (Metzger et al 1993).

Analysis of data showed that methadone dose was a positive predictor and concurrent heroin use a negative predictor of retention in the program. In reality, the high participant retention experienced in this study is likely to be the product of several factors including: (1) the community-based patient selection process which emphasized psychosocial stability, (2) enrollment in a highly desirable new program with limited treatment slots acting as an incentive to remain within the program, (3) the relatively high methadone dosage, (4) integrated individual and family counseling in the program, (5) fear of being sent to compulsory '06 Centers (upon leaving the program), (6) satisfaction with the program, (7) improvement in quality of life resulting from a reduction in illicit drug use and related criminal activity and (8) a positive health status over the course of treatment.

The data show that participants left the program due to a range of reasons – though these were likely to be largely related to concurrent drug use. For example, being arrested by local police was probably closely related to a participant's illicit drug use status. Similarly, the fact that many participants left the program without notifying, clinics suggests that other services and factors influence the success of a MMT program, as also outlined by other studies [36].

Global evidence shows that methadone treatment has a positive effect on drug use behavior. This study found that MMT significantly reduced drug use in participants, and even among those who continued using heroin, frequency of injection still decreased. Data on concurrent drug use is lower in this study when compared with international MMT data, though similar trends in a reduction of use have been reported internationally. It is expected to take several years before one can stop heroin use completely.

In addition, the practice of sharing needles also dropped among study participants, to the extent that after twelve months, only three cases of needle sharing were recorded. The level of needle sharing found in this study was significantly lower than that reported by the 2009 IBBS (3.3% in Hai Phong and 20% in HCMC) [37]. Our findings concur with those of other studies which also found lower frequencies of drug use and needle sharing among drug users on methadone treatment compared to those not on treatment after 6-18 months of follow up [6-9, 11-16]. In a specific example, a study by Moss et al. (1994) reported that the rate of concurrent drug use decreased from 33% to 15% and injecting drug from 19% to 6% after 5 years of follow up [17].

Lastly, this study also found an increase in condom use among study participants. The figures obtained from this study on the percentage of IDUs regularly using condoms with regular sex partners are higher than those reported in other studies (IBBS 2009 range: 20-30 %). There is thus clearly a need to enhance communication and counseling about safe sex behaviors and to reinforce these messages at treatment sites even the MMT program thus influenced the prevalence of practice of HIV risk behaviors among participants.

Research on MMT suggests that methadone medication accounts for most of the clinical benefits arising from treatment, with supporting psychosocial services contributing relatively fewer benefits. In addition, it is well acknowledged that methadone greatly supports treatment retention, a factor repeatedly proven to be closely associated with improved patient outcomes over time. A 180-day methadone-based detoxification study comparing standard MMT care with MMT offered alongside strengthened psychosocial care found that strengthened psychosocial support services did not help to retain participants in care once methadone doses reached critically low levels—at which point participants in both groups showed high dropout rates [35]. In addition, the group on standard MMT care showed higher retention rates and better adherence to treatment, along with lower rates of drug use [35]. The study thus concludes that even a slow, and psychosocial supported detoxification process leads to dropout and relapse once methadone dose levels are insufficient. In addition, a study by Connor et al. reported that methadone based treatment had better efficacy than one using Buprenorphine (BMT) [38].

The impact of MMT on HIV transmission has been demonstrated in several studies. Metzger et al. found that after 18 months of treatment, HIV incidence in the methadone treatment group was 3.5% compared to the 22% in the non-treatment group ($p < 0.01$ CI 1.99- 29.27) and that the risk of HIV infection in the non-treatment group was 6 times higher [6]. Another study found no new cases of HIV infection among drug users after 6 months of MMT [34]. Treatment time and treatment adherence are two factors that have been found to influence the risk of HIV infection. In two separate studies by Moss et al. (1994) and William et al. (1994), HIV incidence in a group with less than 12 months of treatment was higher than incidence in a group with more than 12 months of treatment (7.6% vs. 2.2%, $p = 0.002$). Two studies have also found lower incidence in groups with higher adherence to treatment compared to those with lower adherence (0.7% vs. 4.3%)[17, 39].

After 24 months of MMT, one new case of HIV infection, 27 new cases of HBV and 141 new cases of HCV were recorded. These new infections were possibly the result of persisting needle and syringe sharing among certain drug users. Hepatitis C is endemic among needle users worldwide; and, the time to HCV infection is much more rapid than that for HIV. High prevalence of HCV infection has been recorded among IDUs even when HIV prevalence is relative low (for example HCV prevalence is 85% in Hong Kong and 76% in Australia, while HIV prevalence is 0.3% in Hong Kong and less than 1% in Australia) [11, 18].

Researchers in Hong Kong also found an association between the frequency of injecting and needle sharing and HCV infection rates [18]. This suggests the need for further study on HCV among IDUs in Vietnam.

In this MMT pilot program, the starting methadone dose was decided based on criteria outlined by the MoH: patient's duration of opioid drug use, the most recent regular MMT dose, tolerance level of opioids and risk of overdose. The most commonly used starting dose worldwide is 20 mg/day, with methadone dosage adjusted starting from the first 3 to 10 days of treatment and increases of no more than 20 mg/week [11, 40-42](New South Wales Health Department 1999; Dolan, Shearer et al. 2003; Brown, Balousek et al. 2005; Guohong Chen 2009)(New South Wales Health Department 1999; Dolan, Shearer et al. 2003; Brown, Balousek et al. 2005; Guohong Chen 2009)(New South Wales Health Department 1999; Dolan, Shearer et al. 2003; Brown, Balousek et al. 2005; Guohong Chen 2009)(New South Wales Health Department 1999; Dolan, Shearer et al. 2003; Brown, Balousek et al. 2005; Guohong Chen 2009). In some countries, methadone dosage ranges from 50 to 80 mg, the average dose being 60 mg [11, 23, 34, 43-46]. While 80mg is considered to be a high dose, it is still in line with methadone dosage recommended by WHO at between 80 to 120 mg/day. There are also studies that have reported higher doses in the range of 100 - 150 mg. In our study, the average daily dose of methadone after 24 months was 105 mg, though dosage was higher among ART participants (175 mg versus 78 mg among participants not on treatment). ARVs (NNRTIs, EFV, NVP and potentially LPV/r) are known to increase the rate by which methadone is metabolized, and thus the use of these drugs likely account for the higher methadone dose needs among ARV participants. This indicates the need to revise the treatment guidelines issued by Ministry of Health of Vietnam (see Figure 8).

Here, we observed a reduction in methadone side effects over time, from 75.2 % in the first three months to about 6.34% by the end of 24 months. We found no evidence of sexual dysfunction as a side effect of the treatment even though the percentage of participants reporting sexual activity increased during the study. This finding contrasts results from a number of studies that have found an association between sexual dysfunction and high doses of methadone [20, 40, 47-49].

A study in the United States of America found that an IDU spent on average, 72% of his earnings on drugs [7]. Here, we found that IDUs spent all their income on drugs. The main source of IDUs' income in our study was support from relatives and family, which explains why nearly half of all participants in the study had committed crime and a relatively high number of participants, had conflicts with their family prior to treatment. The percentage of participants that committing crimes during the study declined by 2% after 24 months. There was also a substantial decline in family and social conflicts, suggesting that MMT encourages successful re-integration within communities.

We found that the quality of life of participants receiving methadone treatment significantly improved over time, especially after 3 months of treatment. The percentage of clients reporting a good and very good QoL increased from about 15% at baseline to about 50% at 3 months, a figure which was subsequently maintained throughout the duration of the study. Our results are similar to those reported by Xiao and Willenbring [23, 25]. The physical and mental health status of participants in this study also improved. Only 4% participants reported being depressed after two years of treatment, compared with almost 79% at baseline. The percentage of participants referred to and using support services remained low after 24 months though, especially for social support services. MMT clinics in this pilot program tended to focus more on referrals to medical and HIV-related services such as VCT and ART compared to other social services. Only half of the participants had vocational or professional training and it is clear that vocational training and jobs creation need to be integrated more deeply into the program to facilitate complete and sustainable reintegration of MMT participants into society. This might be due to a lack of available social services in community and limited coordination between the health and social sectors.

VI. Limitations of the study

1. Evaluation of an MMT program requires a longer follow-up period than that of this study as participants experience changes in physical, mental, and social wellbeing over the long-term. For example, treatment adherence can drop when treatment is prolonged. This phenomenon is common for all drug treatment programs, not only methadone.
2. The Hai Phong and HCMC clinics participating in this study had never before taken part in a similar project and study participants were selected according to criteria set by the Ministry of Health and local authorities. The study sample was thus not representative of all IDUs in the two cities or of all the IDUs on MMT.
3. Most information was collected through patient interviews and this invariably introduces self-reporting bias, especially when it comes to sensitive information on drug use or sexual behaviors. Participants tend to give favorable answers rather than the answers which reflect reality. Interviewees may also shy away from probing participants and this ultimately skews the data. However, the guarantee of privacy and confidentiality in this study is likely to have minimized the impact of such bias.

4. Patient records and counseling documents were incomplete and this may impact on the ability to report accurate findings. Currently there is no system for stringent data management in Vietnam and figures collected in Ngo Quyen (Hai Phong) and District 6 (HCMC) were particularly very limited. Such missing information can affect the final outcomes of the study (see below)
5. This was a cohort study, and participants dropping out are likely to have skewed measurements, particularly those based on percentages. For example, the study began with 965 participants prior to treatment but by month 24, 214 had dropped out. These participants are presumed as being lost to follow-up. The lack of information on participants who dropped out may also affect the study's results.

VII. Conclusions and recommendations

Conclusions

1. Retention rates in the MMT pilot program were high over the two-year study period, much higher than retention rates recorded in MMT programs of other countries. Of the 965 participants enrolled in the program, 171 dropped out during the study, leading to an average dropout rate of 8.3 cases per 1000 person-months.
2. Most participants showed good adherence to treatment, and the number of participants who missed 5 continuous daily doses (at which point they would need to re-start the whole treatment process) was minimal and also reduced over time.
3. Report of methadone side effects reduced over time, from 75.2% of participants in the first three months to about 6.34% after 24 months of treatment.
4. The daily average methadone dose in the program was higher (105.7mg/day) than average methadone doses used in studies conducted in other countries. In this study, the average methadone dosage for participants on ARVs, at 175.4 mg/day, was significantly higher than that for participants who were not on ARVs (78.3 mg/day).

5. Methadone maintenance treatment significantly reduced illicit heroin use in participants and, among those who did continue using heroin, greatly decreased frequency of injection.
6. MMT resulted in a reduction of HIV risk behaviors among participants. In addition to a decrease in frequency of injection, incidence of needle sharing also dropped. After 24 months into the study, only three cases of needle sharing were recorded. While sexual activity increased, condom use also increased and only one new case of HIV was detected over the two-year period.
7. Physical and mental health status of participants improved significantly over the course of treatment. At 24 months, the proportion of participants suffering from side effects of methadone, and potentially from other treatments (such as ARVs and TB) was 46.3%. Only 4.4% participants reported being depressed after two years of treatment, compared with almost 79% at baseline.
8. The quality of life of participants improved remarkably, especially during the first 3 months after treatment initiation.
9. The employment rate among study participants increased slightly and gradually over time. However, the percentage of participants who were not in full-time employment remained above 40% after two years of treatment. Most MMT participants who were employed worked in family businesses.
10. The percentage of participants reporting involvement in criminal activities reduced from 40% at baseline to 1.3% at 24 months. Report of family and social conflicts also saw a downward trend, suggesting strongly that MMT is an effective tool for community re-integration.
11. The rate of participants referred to and using support services remained low during the follow-up period, especially for social support services (such as legal or vocational support). MMT clinics seemed to pay more attention to referrals of participants to medical services such as VCT and ART.

Recommendations

1. Given the positive outcomes reported from the MMT program, it is recommended that the program be expanded quickly to increase treatment coverage in Hai Phong and HCMC. The program should also be scaled up to other cities/provinces nationwide in order to ensure that more drug users can benefit from the demonstrated positive life changes and that a greater number of communities can capitalize on the beneficial impacts of the MMT program.
2. The referral system should be further developed in order to facilitate and coordinate access to other health and social services needed by MMT participants.
3. National methadone treatment guidelines should be revised in a way that will provide appropriate dosage-increase schedules for various types of participants (such as ARV and TB participants). Specific criteria should be outlined to determine when a patient is stable on methadone, and assist clinicians in monitoring participants on ARVs and other drugs that interact with methadone.
4. Local authorities should offer more support to MMT clients, especially social support programs that focus on:
 - Vocational training and job creation, and
 - Communication to reduce stigma and discrimination.
5. Other studies should be conducted to identify the optimal model for delivery of MMT and related services in Vietnam, and to address issues such as the underlying reasons for dropouts and concurrent drug use, and the facilitators and barriers to participation in MMT programs.

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