

Describing the Programme on Methadone Maintenance Therapy in Selangor, Malaysia

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Abstract

Introduction: Drug addiction and drug abuse is a serious public health problem worldwide. Millions of people worldwide suffered from drug use disorders, directly and indirectly, attributable to drug use and included deaths related to HIV and hepatitis C acquired through unsafe injecting practices. Many parts of the world have a shortfall in prevention and treatment for drug use disorders, with only less than 10% of people with drug use disorders receiving treatment yearly. Medication-assisted treatment of opioid dependence like Methadone is used in maintenance therapy or detoxification helps people with drug use disorders.

Material and Methods: Secondary data from an existing electronic dataset in Ministry of Health (MOH) from 2015 until 2019, which includes registered patients who had undergone Methadone Maintenance Therapy (MMT)

either government or private facilities were included. The dataset divided into few domains namely socio-demographic, treatment modalities, clinic location and history of infection.

Results: A total of 37 various government and private facilities deliver MMT programme in the state of Selangor offered to a total of 5337 patients. The youngest patients were in the early twenties and oldest were in late seventies. The median age of patients was 45 years and the majority were males. Most of them were having secondary education (SPM holder) and below. Most of MMT programme takers were opioid drug users then followed by Amphetamine Type Stimulant (ATS) as the second most used. Among MMT programme takers, about 34.1% were reactive for Hepatitis C, 6.6% reactive for HIV, 4.2% reactive for Hepatitis B and 1.7% acquired tuberculosis infection. Almost 5% of MMT takers had passed away, which the three main causes of death were AIDS, alleged motor vehicle accident and septic shock. None of MMT takers was died due to methadone.

Conclusion: It is a great concern of the nation in combating drug-related problems due to the growing number of substance abusers. This review concluded that the MMT programme that widely available had shown a positive outcome by keeping lower mortality among MMT patients.

Keywords: drug addiction, methadone maintenance therapy (MMT), opioid abuse, substance abusers, anti-retroviral treatment

1. Introduction

1.1 Background

Drug addiction and drug abuse are serious concerns or known as non-medical use of prescription drugs becoming a major public health problem worldwide. Globally about 275 million people worldwide used drugs in the past year (United Nations Office on Drugs and Crime UNODC, 2018). Some 31 million people in the world who use drugs suffer from drug use disorders and they experienced harmful conditions where they may need treatment (United Nations Office on Drugs and Crime UNODC, 2018). Almost 500,000 drug users died as a result of drug use in 2015, according to the World Health Organization. Among those deaths, about 23% related to attributable in most cases due to opioid use disorders (World Health Organization, 2018). An estimation of almost 11 million people who inject drugs, of which 1.3 million are living with HIV (Human Immunodeficiency Virus), 5.5 million with hepatitis C, and 1 million with both HIV and hepatitis C (World Health Organization, 2018). Prevention and treatment continue to fall short in many parts of the world, with only less than 10% of drug users who need such treatment are receiving the effective and inexpensive treatment (World Health Organization, 2018; World Health Organization, 2004).

The usage of drugs in the '70s and '80s was rapidly escalating in Malaysia. Overwhelming supply for drugs with the establishment of "The Golden Triangle" in Indochina region and cultural revolution reflected as "hippie" movement had contributed to the rise in drug usage during this period (Gill JS, Sulaiman AH, & Habil H, 2007). Opioid addiction is the commonest type of addiction in Malaysia even though addiction with newer drugs is rising in numbers (Reid G, Kamarulzaman A, & Sran SK, 2007). Out of 300,000 people who use drugs (PWUD) based on the registry, 170,000 people were estimated as people who inject drugs (PWID) with heroin (Vicknasingam B, Dazali MN, Singh D, Schottenfeld RS, & Chawarski MC, 2015).

The first Human Immunodeficiency virus (HIV) infection in Malaysia was reported in 1986 (World Health Organization, 2011). At the initial state, the majority of HIV cases in Malaysia was contributed by people who inject drug (PWID) (Ministry of Health, 2018). Similarly, from the year 1988 till 2005, Selangor state had recorded more than two-third of HIV transmission through intravenous drug use (IVDU) compared to 8.7% contributed by a man having sex with a man (MSM). Transmission of HIV among PWID showed an increasing trend without having a concrete plan or policy in place. This resulted in the implementation of harm reduction programme in October 2005. This programme comprises of methadone maintenance therapy (MMT), needle syringe exchange programme (NSEP) and condom distribution. By the year 2018, the percentage of PWID who are living with HIV was reported as low as 13.5% with further expansion of harm reduction programme at nationwide to both public and private healthcare facilities (Ministry of Health, 2018).

1.2 Medication-Assisted Treatment of Opioid Dependence (MATOD)

Medication-assisted treatment of opioid dependence helps in elimination of withdrawal, control or eliminate cravings or block euphoric effect resulting from the use of morphine. These medications act on the opioid receptor as agonist, partial agonist or antagonist (Stotts, Dodrill, & Kosten, 2009).

Drugs such as methadone, morphine, heroin, oxycodone and hydromorphone are examples of full opioid agonists (Stotts, Dodrill, & Kosten, 2009). These drugs act as full agonists by binding to mu receptors available in the brain.

Being the full mu agonist, increasing the dose of a drug produces increasing effects. Methadone is used in maintenance therapy or detoxification (Stotts, Dodrill, & Kosten, 2009; Kampman & Jarvis, 2015). Newer drug such as levomethadyl acetate is also an opioid agonist which is found to be superior to methadone in maintenance therapy. However, this drug is not available in Malaysia.

Buprenorphine is an example of partial muopioid agonist (Stotts, Dodrill, & Kosten, 2009). The drug act at mu opioid receptors in the brain. Being partial mu agonist, the drug as ceiling effect which means the effects reaches a maximum level that is not increased further with increasing dose. By occupying mu receptors partially, buprenorphine prevents further occupation by full agonist. This drug was made available since 2002 for treating opioid addiction (Vicknasingam, Dazali, Singh, Schottenfeld, & Chawarski, 2015). Despite having superior treatment efficacy compared to methadone, the cost and the lack of post detoxification outcomes on long term benefit has hampered its use as a popular choice of opioid dependence treatment (Stotts, Dodrill, & Kosten, 2009).

Naltrexone and naloxone are opioid antagonists. These drugs bind to the mu opioid receptors in the brain too. However, these drugs do not activate the receptors. By occupying the receptors, these drugs prevent agonist drugs from binding to those particular receptors (Stotts, Dodrill, & Kosten, 2009).

1.3 Methadone Maintenance Therapy

MMT plays an important part in harm reduction programmes. The MMT component began in the year of 2005 and was carried out by medical practitioners involving both public and private health clinics (Reid, Kamarulzaman, & Sran, 2007). However, the NSEP component was conducted by non-governmental organisations in partnership with the Ministry of Health (MoH), Malaysia since 2006. Drop-in centre and outreach are two major approaches adopted to execute the NSEP. Besides exchanging used needle and syringes for sterile ones, the programmed also aimed at safe disposal of used injecting materials, educating on HIV/AIDS (Acquired Immune Deficiency Syndrome) and safe sex. Importantly, NSEP had created an outlet for the PWID to be referred for rehabilitation, health screening for both communicable and non-communicable diseases and to the welfare agencies for financial aid and accommodation. The NSEP regarded as an important point of entry into the MMT programme.

The MMT programme was first piloted in 17 sites involving both public and private health facilities nationwide (Ministry of Health, 2018). In Selangor, the programme was first piloted in AU2, Keramat public health clinic at the same time with the nationwide move to expend the harm reduction programme. Gradually, the MMT programmed was successfully implemented in more facilities. Hence, this paper aims to describe the treatment program of MMT and its outcome on the patient's adherence.

2. Material and Methods

A secondary data was retrieved from an existing electronic dataset that was kept in the HIV Unit in Selangor State Health Department from 2015 until 2019. A total of 5337 patients were identified from the dataset. All registered patients who had undergone MMT either in the government facilities or private facilities that have collaboration with MoH, Malaysia to conduct MMT programme were included from this study. The data contains information on patients such as socio-demography, treatment modalities, clinic location and history of infection.

2.1 Description of process on Methadone Maintenance Therapy

2.1.1 Methadone Maintenance Therapy in public health clinics

Methadone had been used for some time as a treatment among heroin or other opioid abusers admitted to the hospitals. Despite having good safety profiles, methadone was only registered after 2005 as a component in methadone maintenance therapy. Introduction of the MMT programme in specialised clinics within the hospitals indicated phase 1 out of the 3 phases of the MMT programme implementation. The MMT services were further extended to public health clinics in the form of expanded scope to fulfil the growing demand from the increasing number of PWID. This was regarded as phase II of the programme. The phase III of the programme involves community drug rehabilitation centres and prisons (Wickersham JA, Zahari MM, Azar MM, Kamarulzaman A, & Altice FL, 2013).

2.1.2 MoH Organisational Infrastructure

Public clinics that were chosen to conduct MMT programme underwent basic renovations to the existing infrastructure of the clinic to facilitate the process of consultation, physical examination, collection of biological samples and dispense of methadone syrup. A team comprises of the medical officer, pharmacist, medical assistant, assistant pharmacist and staff nurse identified from the existing manpower of the clinic were given training before initiation of the programme.

2.1.3 Program Approach

Patients for the MMT programme were recruited based on selection criteria as stipulated in programme guideline. The patient should be diagnosed with mainly opioid addiction based on Diagnostic and Statistical Manual of Mental Disorder edition 5 (DSM 5). Patient with decompensated liver disease, uncontrolled mental disorder, severe acute medical illness and having a history of hypersensitivity are not eligible to participate in this programme.

Every qualified patient has gone through physical examination and screening investigations such as rapid test for HIV, HIV confirmatory test for those with reactive HIV rapid test, serology test for hepatitis B and C, liver function test, urine test for drugs, echocardiography and chest X-ray.

Patients who fit for methadone maintenance therapy, induced with syrup methadone at 20 – 30mg dose. The dose of methadone titrated every 3 days with the addition of 5-10mg while limiting the increment to the maximum of 20mg per week.

Maintenance dose was individualised taking into consideration the differences in methadone metabolic rate among patients, concurrent use of anti-TB, anti-retroviral, psychotropic drugs, pregnancy and polysubstance use.

Assessment of patient's stability for taking away dose was performed at those requested but with valid reasons such as travel overseas, travel to accomplish religious rights, being deep-sea fisherman, ill to commute daily and specific requirement of one's job.

Patients who missed their methadone for 1 to 2 days, an actual dose of methadone was served provided no signs of intoxication were observed. If methadone was missed for 3 days, only half the actual dose was served for those consuming more than 60mg. A maximum of 30mg methadone was served for those on their maintenance in between 30-60mg. The actual dose of methadone was served to those consuming less than 30mg. Meanwhile, for patients who miss their methadone for 4 days, a dose of 40mg or half of the actual dose whichever lesser in dose were served. Re- induction was done for the patients who had missed the methadone for more than 5 days.

2.1.4 Consent Approach

Informed written consent was obtained from all adult patients who fulfil the selection criteria. However, parental or guardian's consent was needed for adolescents with opioid addiction who aged below 18 years.

2.1.5 Program Monitoring

During the induction phase, the patients who newly started with methadone were monitored more frequently for symptoms and signs of withdrawal, intoxication and adverse effects of methadone. In this phase, the pharmacist daily observed and monitored all patients coming for directly observed therapy (DOT) for methadone. The follow up with the doctor was twice a week for the first 2 weeks, weekly for another 2 weeks, followed by every fortnight for a month. Stable patients on methadone were reviewed 3 monthlies thereafter.

2.1.6 Reporting

The number of new patients being recruited into the MMT programme with details on mode of referral e.g. by NGO, NADA, NSEP, walk-in and the cumulative number of patients was sent as a monthly return to the district health office by the 5th day of the month. The cumulative number was detailed out as the number of patients who had dropped out, died, re-joined, transferred in or out, terminated and currently active in the programme. The retention rate was calculated based on the number of active patients at the current month over the cumulative number of patients for the current year. Infective status of blood-borne infections like HIV, Hepatitis B and C among newly registered patients was reported on monthly basis.

2.1.7 Ethical Issues

All patients voluntarily participate in this program. A consent form was distributed to all participants. They were also requested to sign an agreement form to abide by the rules and regulation while in the program. All patients were informed regarding the progress related to the programme anonymously.

2.1.8 Advocacy

Inter-agency meetings involving the Ministry of Health, National Anti-Drugs Agency and narcotic division of the Royal Malaysian Police were held before the layout of policies and guidelines on conducting MMT programme. Policies and guidelines were disseminated to agencies responsible for executing the programme at specialised clinics at the beginning then expended to general healthcare settings and prisons. Medical officers and paramedics and pharmacists were trained to conduct similar training at their centres. Launching of the first methadone service was done in Hospital Kuala Lumpur which had received huge media coverage locally and internationally. The

MMT programme further gained advocacy through articles published in renowned newspapers. Non-governmental organisations (NGO) coordinated by the Malaysian AIDS Council (MAC) played an important role in advocating MMT amidst promoting NSEP among PWID via outreach approach.

2.1.9 Safety

Methadone is used officially as medication-assisted treatment for opioid dependence since the year 2005. It has a good safety profile. However, death has been reported during the first 3 to 10 days of induction of methadone which related to abnormal metabolism and fatal overdose. Thus, staffs involved in the MMT programme were trained to identify symptoms and signs of withdrawal or overdosing arises from the use of methadone. Patients who have subjective symptoms like craving for drug, anxious feelings, dysphoria, insomnia, hot/cold flashes, anorexia, nausea and abdominal cramps are suspected to have opioid withdrawal. Signs like dilated pupils, tremors, piloerection, rhinorrhoea, yawning, fever, diarrhoea, vomiting and excessive perspiring are objective findings in withdrawal. Such patients are referred immediately to medical officers and then to the hospital for specialised management.

3. Results

Table 1. List of Methadone Maintenance Therapy (MMT) centres and the total number of patients in the programme

MMT Centres		Registered n (%)	Transferred-in n (%)	Total N (%)	Active N (%)	Non active N (%)
		3667 (68.7)	1670 (31.3)	5337 (100.0)	2343 (43.9)	2994 (56.1)
Hospitals		1075 (20.1)	346 (6.5)	1421 (26.6)	464 (8.7)	957 (17.9)
1	Hospital Tengku Ampuan Rahimah	292 (5.5)	133 (2.5)	425 (8.0)	189 (3.5)	236 (4.4)
2	Hospital Tanjung Karang	119 (2.2)	24 (0.5)	143 (2.7)	47 (0.9)	96 (1.8)
3	Hospital Banting	131 (2.5)	16 (0.3)	147 (2.8)	39 (0.7)	108 (2.0)
4	Hospital Tengku Ampuan Jemaah	231 (4.3)	77 (1.5)	308 (5.8)	99 (1.9)	209 (3.9)
5	Hospital Sungai Buloh	302 (5.7)	96 (1.8)	398 (7.5)	90 (1.7)	308 (5.8)
Primary Health Clinics		1834(34.3)	932(17.5)	2766(51.8)	1443(27.0)	1323(24.8)
1	Klinik Kesihatan AU2	207 (3.8)	93 (1.8)	300 (5.6)	120 (2.2)	180 (3.4)
2	Klinik Kesihatan Serendah	123 (2.3)	84 (1.6)	207 (3.9)	117 (2.2)	90 (1.7)
3	Klinik Kesihatan Batu 9	172 (3.2)	95 (1.8)	267 (5.0)	151 (2.8)	116 (2.2)
4	Klinik Kesihatan Seri Kembangan	97 (1.8)	75 (1.4)	172 (3.2)	47 (0.9)	125 (2.3)
5	Klinik Kesihatan Pandamaran	230 (4.3)	121 (2.3)	351 (6.6)	207 (3.9)	144 (2.7)
6	Klinik Kesihatan Salak	121 (2.3)	76 (1.4)	197 (3.7)	88 (1.6)	109 (2.0)
7	Klinik Kesihatan Taman Ehsan	107 (2.0)	57 (1.1)	164 (3.1)	67 (1.3)	97 (1.8)
8	Klinik Kesihatan Telok Panglima Garang	144 (2.7)	24 (0.4)	168 (3.1)	87 (1.6)	81 (1.5)
9	Klinik Kesihatan Jeram	94 (1.8)	25 (0.4)	119 (2.2)	72 (1.3)	47 (0.9)
10	Klinik Kesihatan Sungai Air Tawar	31 (0.6)	11 (0.2)	42 (0.8)	21 (0.4)	21 (0.4)
11	Klinik Kesihatan Taman Medan	69 (1.3)	64 (1.2)	133 (2.5)	49 (0.9)	84 (1.6)
12	Klinik Kesihatan Ampang	56 (1.0)	49 (0.9)	105 (1.9)	87 (1.6)	18 (0.3)
13	Klinik Kesihatan Sekinchan	44 (0.8)	16 (0.3)	60 (1.1)	41 (0.8)	19 (0.4)
14	Klinik Kesihatan Seksyen 19	12 (0.2)	30 (0.6)	42 (0.8)	22 (0.4)	20 (0.4)
15	Klinik Kesihatan Bestari Jaya	40 (0.8)	13 (0.2)	53 (1.0)	35 (0.7)	18 (0.3)
16	Klinik Kesihatan Sungai Selisik	28 (0.5)	9 (0.2)	37 (0.7)	13 (0.2)	24 (0.5)
17	Klinik Kesihatan Tanjung Sepat	22 (0.4)	3 (0.1)	25 (0.5)	18 (0.3)	7 (0.1)
18	Klinik Kesihatan Semenyih	111 (2.1)	16 (0.3)	127 (2.4)	82 (1.5)	45 (0.8)

19	Klinik Kesihatan Rawang	37 (0.7)	12 (0.2)	49 (0.9)	23 (0.4)	26 (0.5)
20	Klinik Kesihatan Bukit Kuda	22 (0.4)	7 (0.1)	29 (0.5)	16 (0.3)	13 (0.2)
21	Klinik Kesihatan Bandar Botanik	19 (0.4)	2 (0.0)	21 (0.4)	2 (0.0)	19 (0.4)
22	Klinik Kesihatan Sungai Buloh	48 (0.9)	50 (0.9)	98 (1.8)	78 (1.5)	20 (0.4)
Private Health Clinics		603 (11.3)	55 (1.0)	658 (12.3)	332 (6.2)	326 (6.1)
1	Poliklinik Khafidz	93 (1.7)	2 (0.0)	95 (1.7)	44 (0.8)	51 (0.9)
2	Pusat Rawatan Dr. Mahmud	119 (2.2)	22 (0.4)	141 (2.6)	80 (1.5)	61 (1.1)
3	Poliklinik Damai Surgeri	354 (6.6)	0 (0.0)	354 (6.6)	170 (3.2)	184 (3.4)
4	Klinik Ikhlas	23 (0.4)	30 (0.6)	53 (1.0)	31 (0.6)	22 (0.4)
5	Poliklinik dan Surgeri Hata Mewah	14 (0.3)	1 (0.0)	15 (0.3)	7 (0.1)	8 (0.2)
Cure & Care Service Centres (CCSC)		12 (0.2)	137 (2.6)	149 (2.8)	104 (2.0)	45 (0.8)
1	CCSC Gombak	12 (0.2)	45 (0.8)	57 (1.0)	44 (0.8)	13 (0.2)
2	CCSC Hulu Langat	0 (0.0)	73 (1.4)	73 (1.4)	45 (0.8)	28 (0.5)
3	CCSC Kuala Kubu Baru	0 (0.0)	19 (0.6)	19 (0.4)	15 (0.3)	4 (0.1)
Prisons		143 (2.7)	200 (3.7)	343 (6.4)	0 (0.0)	343 (6.4)
1	Penjara Wanita Kajang	6 (0.1)	9 (0.2)	15 (0.3)	0 (0.0)	15 (0.3)
2	Penjara Lelaki Kajang	137 (2.6)	191 (3.6)	328 (6.1)	0 (0.0)	328 (6.1)

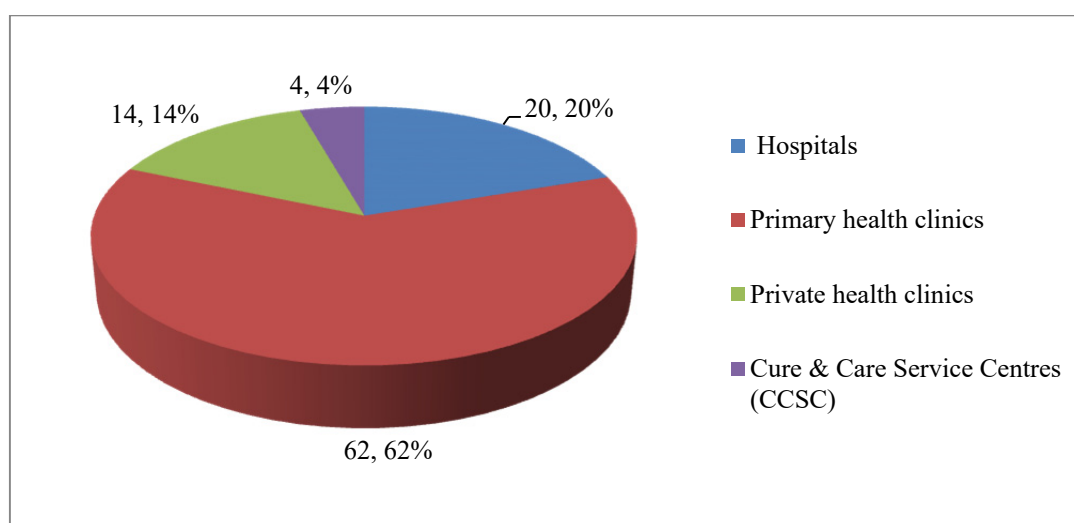


Figure 1. The percentage of active patients in the programme

3.1 Delivery of Methadone Maintenance Therapy in state of Selangor

There are 37 facilities which deliver the MMT programme in the state of Selangor. These facilities comprise of 5 public hospitals, 22 primary health clinics, 5 private general practitioner clinics (private health clinic), 3 Cure and Care Service Centres (CCSC) and 2 prisons as depicted in Table 1. The total number of patients in MMT programme is 5337. Majority of them (3667) is registered under the state of Selangor, meanwhile, 1670 patients were registered and transferred from other states. Out of 5337 patients, 2343 are still active in the programme. Majority of active MMT patients (62%) are seen in primary health clinics as shown in Figure 1. Among 5 public hospitals with MMT in Selangor, Hospital Tengku Ampuan Rahimah has the largest number of active patients (41%) as shown in Figure 2. Klinik Kesihatan Pandamaran (14%) has the highest number of active patients among 22 primary health clinics as shown in Table 1 and Figure 3. A total of 5 private general practitioner clinics were involved in MMT under MoH Malaysia programme and Poliklinik Damai Surgeri (50%) has the biggest number of active patients as shown in Figure 4. There are 3 cure and care service centres (CCSC) involved in the MMT programme under MoH serving 104 active patients as depicted in Figure 5. Meanwhile, there were no active MMT

patients in prison during the study period.

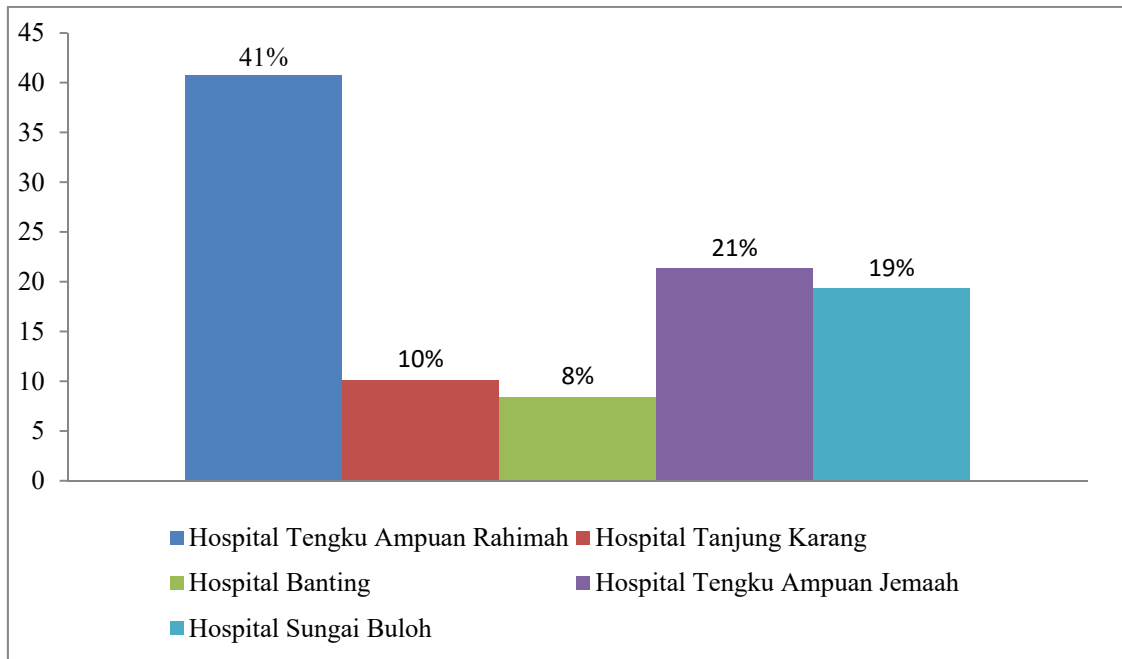


Figure 2. The percentage of active patients in hospital

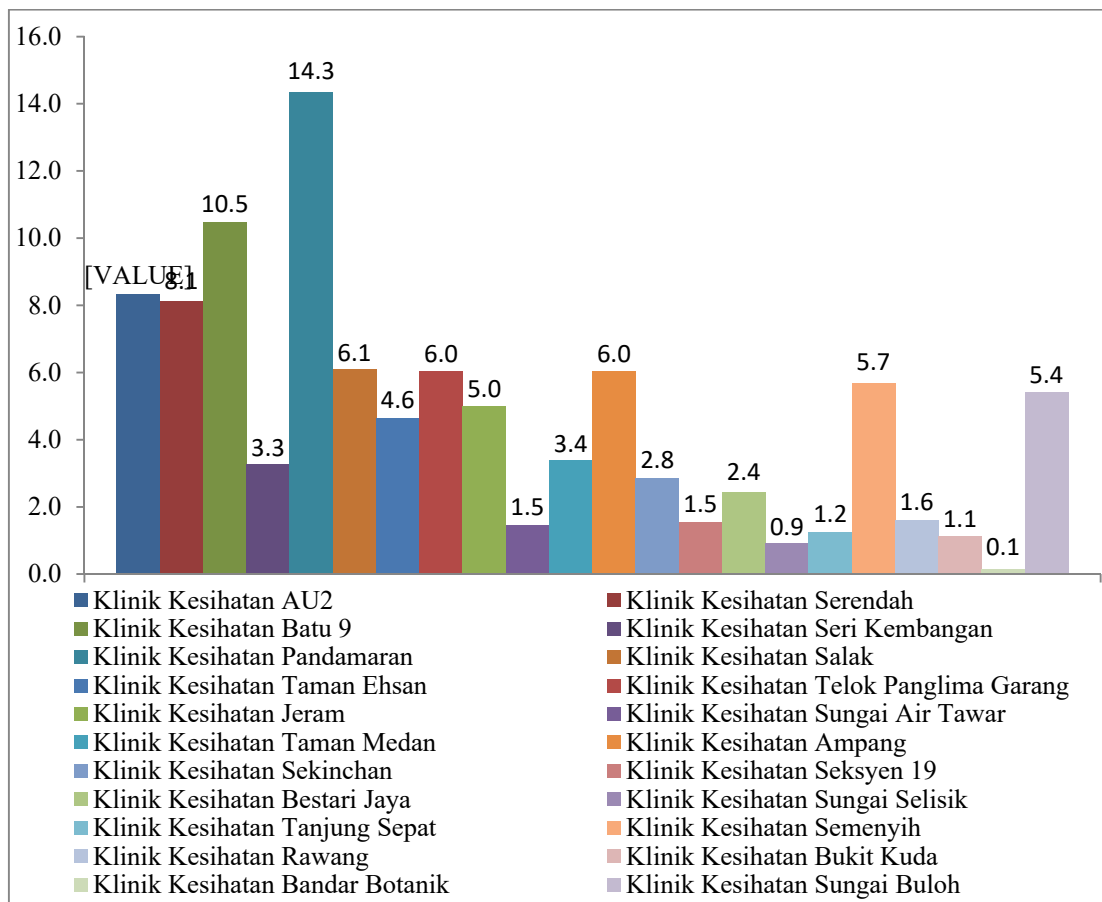


Figure 3. The percentage of active patients in primary health clinic

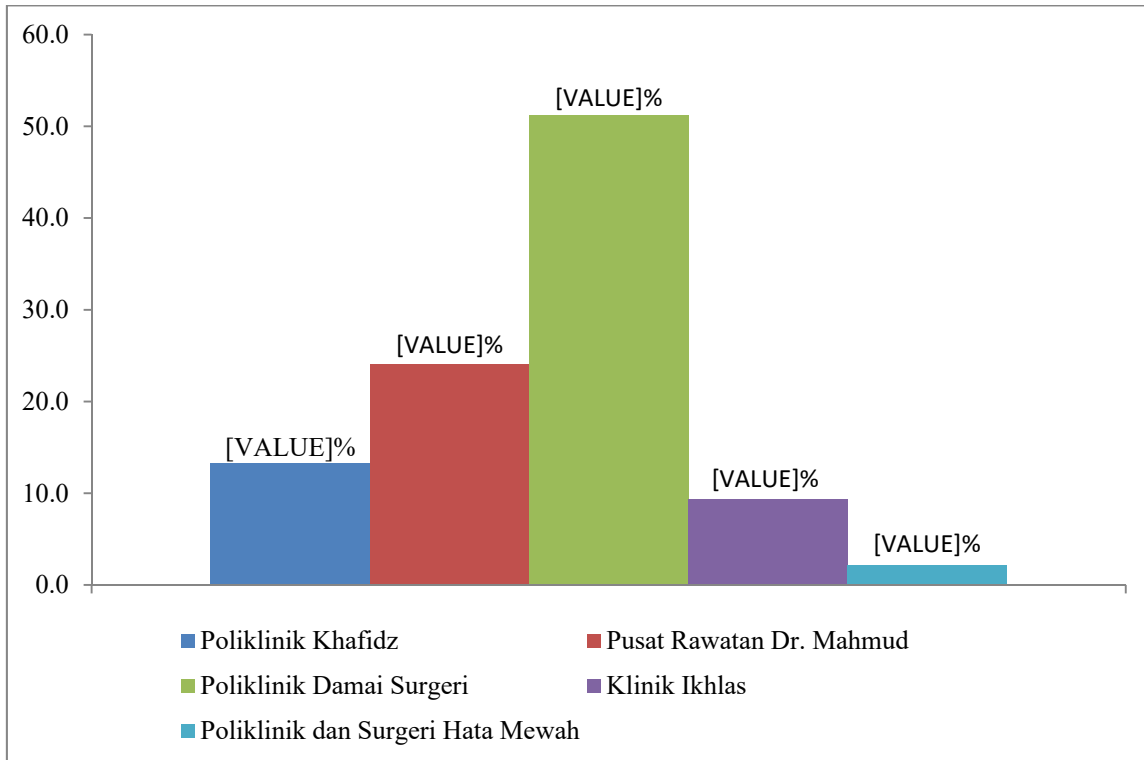


Figure 4. The percentage of active patients in private health clinic

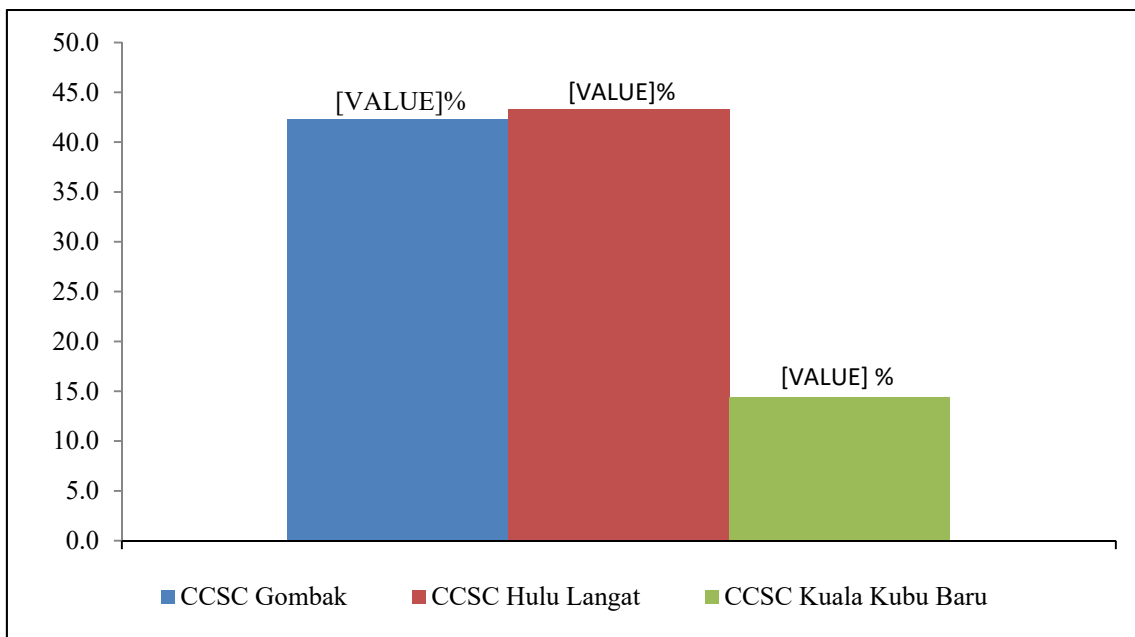


Figure 5. The percentage of active patients in Cure and Care Service Centers (CCSC)

Table 2. Sociodemographic characteristics of patients in Methadone Maintenance Therapy

Characteristics	Total N=5337 (n=5269)	Active n=2343
Age		
Median (IQR) (years)	45 (14)	45 (15)
Min	21	23
Max	77	75
Gender		
Male	5196 (97.4)	2288 (97.7)
Female	141 (2.6)	55 (2.3)
Ethnicity		
Malay	4426 (82.9)	1985 (84.7)
Chinese	513 (9.6)	226 (9.6)
Indian	383 (7.2)	127 (5.4)
Indigenous/ Sabahan/ Sarawakian	15 (0.2)	5 (0.2)
Education	(n=3235)	(n=1624)
No formal education	38 (1.2)	19 (1.2)
UPSR	566 (17.5)	272 (16.7)
PMR/SRP	975 (30.1)	482 (29.7)
SPM	1566 (48.4)	806 (49.6)
STPM	29 (0.9)	12 (0.7)
Diploma	59 (1.8)	32 (2.0)
Degree	2 (0.1)	1 (0.1)
Marital status	(n=3332)	(n=1680)
Married	1526 (45.8)	802 (47.7)
Unmarried	1550 (46.5)	736 (43.8)
Divorced	256 (7.7)	142 (8.5)
Employment	(n=3430)	(n=1730)
Permanently Employed	1326 (38.7)	736 (42.5)
Temporarily Employed	1695 (49.4)	751 (43.4)
Unemployed	409 (11.9)	243 (14.1)
Starting age	(n=1579)	(n=998)
Median (IQR) (years)	20 (5)	20 (5)
Min	10	10
Max	58	48

3.2 Sociodemographic Characteristics of Patients Following Methadone Maintenance Therapy

Males comprised the majority with a median age of 45 years in both groups as depicted in Table 2. The youngest patients were in their early twenties and the oldest were in their late seventies. In terms of ethnic group, Malays were majority followed by Chinese and Indian. The Majority had education qualification of SPM and below. Percentage of unmarried patients was higher than the married among the total MMT patients. However, this was opposite among the active MMT patients which showed 47.7% of the patients were married. Only a small percentage of MMT patients were unemployed in both groups. Median and minimum starting age for substance

use was 20 years and 10 years respectively and these were the same for both groups. However, the maximum starting age was much older at 58 years among total MMT patient compared to 48 years in the active group.

Table 3. Types of substance abuse among patients under Methadone Maintenance Therapy at registration

Types of Substances	Total (N=5337)	Active (n=2343)
Opioids		
Heroin	5337 (100.0)	2430 (100.0)
Morphine	90 (1.7)	39 (1.7)
Codeine	59 (1.1)	36 (1.5)
Opium	129 (2.4)	107 (4.6)
Amphetamine type stimulants (ATS)		
Amphetamine/methamphetamine	586 (11.0)	357 (15.2)
3,4-methylenedioxy-methamphetamine (MDMA)	187 (3.5)	121 (5.2)
Tetrahydrocannabinol (THC/Cannabis)		
Benzodiazepine	94 (1.8)	47 (2.0)
Ketamine	43 (0.8)	30 (1.3)
Lysergic acid diethylamide (LSD)	4 (0.1)	2 (0.1)

3.3 Types of Substance Abuse Among Patients Following Methadone Maintenance Therapy

The types of substance used by patients before joining the MMT programme is summarised in Table 3. All patients had opioid as main substance abuse in both total and active groups as per selection criteria to the MMT programme. Among the opioid group of substance, opium was the substance used the most by both groups. Amphetamine Type Stimulant (ATS) was found to be the second most used substance after opioids. This was followed by Tetrahydrocannabinol (THC/ cannabis), depressant (benzodiazepine), new psychoactive substance (ketamine) and Lysergic acid diethylamide (LSD).

Table 4. Status of bloodborne diseases, seroconversion and initiation of antiretroviral therapy among active patients in methadone maintenance therapy

Types of infection	Infected status (2015) at registration	Seroconversion status (2019)	ART initiated
	N (%) (n=2343)	N (%) (n=2343)	N (%) (n=174)
HIV infections			
Reactive	155 (6.6)	NA**	102 (58.6)
Non-reactive	1722 (73.5)	18 (0.8)	17 (9.8)
Not tested	41 (1.7)	0 (0.0)	0 (0.0)
Unknown	425 (18.1)	1 (0.04)	1 (0.6)
Hepatitis C infections			
Reactive	799 (34.1)	NA**	NA**
Non-reactive	987 (42.1)	87 (3.7)	NA**
Not tested	68 (2.9)	0 (0.0)	NA**
Unknown	489 (20.9)	0 (0.0)	NA**

Hepatitis B infections			
Reactive	99 (4.2)	NA**	NA**
Non-reactive	1674 (71.4)	1 (0.04)	NA**
Not tested	76 (3.2)	0 (0.0)	NA**
Unknown	494 (21.1)	0 (0.0)	NA**
Tuberculosis infection			
Positive	41 (1.7)	NA**	NA**
Negative	1466 (62.6)	NA**	NA**
Not tested	127 (5.4)	NA**	NA**
Unknown	709 (30.3)	NA**	NA**

*MMT: methadone maintenance therapy; **NA: not applicable.

3.4 Status of Bloodborne Diseases, Seroconversion and Initiation of Antiretroviral Therapy Among Active Methadone Maintenance Therapy Patients

The status of bloodborne diseases, seroconversion and initiation of antiretroviral therapy (ARV) among methadone maintenance therapy patients is shown in Table 4. Only 6.6% of the active MMT patients were reactive for HIV. About 34.1% of active MMT patients were reactive for Hepatitis C. Hepatitis B was reactive in 4.2% of active MMT patients. Only 1.7% of active MMT patients had ever acquired tuberculosis infection. Seroconversion for HIV infection was only noted in 19 active MMT patients. Antiretroviral therapy was initiated in 69% of active MMT patients with HIV. Seroconversion for Hepatitis C took place in 87 active MMT patients. Seroconversion for Hepatitis B infection was found to be the lowest and involving only 1 active MMT patient.

Table 5. Methadone dose used by active Methadone maintenance therapy patients from year 2015- 2019

Year	Active (n=2343)	Methadone dose		
		(Min) mg	(Max) mg	Median (IQR) mg
2015	529	10	150	55 (40)
2016	304	10	170	50 (45)
2017	360	5	230	50 (40)
2018	555	0	355	50 (35)
2019	672	0	280	55 (40)

3.5 Methadone Dose for the Last 5 Years (2015 - 2019)

The methadone doses used for the last 5 years from the year 2015 until 2019 by active patients in methadone maintenance therapy is shown in Table 5. The patients were titrated down their methadone doses till zero mg in the year 2018 and 2019. The maximum dose of 355mg methadone was recorded in the year 2018. The lowest median dose of 50mg and interquartile range of 35mg was recorded in the year 2018. The highest median dose of 55mg with interquartile range 40 was recorded in the year 2016 and 2019.

Table 6. The frequency of verbally reported cause of death among active patients in Methadone Maintenance Therapy programme

Cause of death	N (%) (n=264)
AIDS complications	26 (9.9)
Alleged MVA	20 (7.6)
Septic shock	18 (6.8)
Liver failure	13 (4.9)

Pneumonia	10 (3.8)
Heart attack	10 (3.8)
TB (PTB/ extra pulmonary)	8 (3.0)
Cancer	5 (1.9)
UGIB	5 (1.9)
Asthma	4 (1.5)
Renal failure	4 (1.5)
COAD	3 (1.1)
Stroke	3 (1.1)
Brain infection	2 (0.8)
Heart failure	2 (0.8)
Homicide	2 (0.8)
Suicide	2 (0.8)
Unknown	127 (48.0)

3.6 Verbally Reported Cause of Death Among Methadone Maintenance Therapy Patients

The verbally reported cause of death among active patients undergoing MMT programme by their peers and family members is summarised in Table 6. About 264 (4.9%) MMT patients had passed away till early 2019. The complication of AIDS, alleged motor vehicle accident and septic shock were three main causes of death which contributed about 27%, 21% and 17% of the total number of deaths respectively. No deaths related to methadone use had been reported. Cause of death was unknown in a large number of patients.

4. Discussion

The state of Selangor has been conducting Methadone Maintenance Therapy programme for the past 14 years. With concrete guidelines in place and commitment from relevant stakeholder, the service has been expanded successfully to 5 hospitals, 22 government health clinics, 5 private general practitioner clinics, 3 Cure and Care Service Centres and 2 prisons. About 43.9% of patients were still actively participating in MMT programme during the study period which is lower than finding from the MyTOS study (Ali et al., 2018). Nearly more than half of the active patients are only temporarily employed or unemployed and lower maintenance dose of methadone could be the contributing factors to poor adherence to the MMT programme. These factors have been already reported other studies (Gong et al., 2019; Ramli, Zafri, Junid, & Hatta, 2012). However, nature of work as a contributing risk factor for poor adherence to MMT programme was not covered in this study. Almost half of the active MMT patients acquired their service from the government-based clinic. The similar trend noted worldwide and the expansion of MMT programme to primary health clinics had shown positive impact in reducing the number of drug users and reduction in the crime rate among them (Yin et al., 2010; Parvaresh, Kheradmand, & Darijani, 2010). Majority of our participants were male in their median age of 45-year-old with a median starting age of 20 years old similar to findings from previous studies (Parvaresh, Kheradmand, & Darijani, 2010; Tran, Nguyen, Tran, & Latkin, 2018). Opioids, ATS and THC were 3 common drugs that abused among our MMT patients. Opioid remained as commonly used substance among adults even though methamphetamine and cannabis are gaining popularity among the younger population (Hadland et al., 2012). The percentage of unmarried patients was similar to studies conducted locally (Ali, Aziz et al, 2018; Sharifa, Noor, Rushidi, Raminder, & Ruhani, 2009). However, this percentage was much lower in other country but from the same region (Tran, Nguyen, Tran, & Latkin, 2018).

More than two-thirds of patients had their secondary level of education and were employed either permanently or temporarily. This finding is concordant with a local study done in primary health care centres in Selangor and Hospital Kuala Lumpur. The high volume of educational centres and job vacancies in Selangor state likely would have contributed to this (Sharifa, Noor, Rushidi, Raminder, & Ruhani, 2009).

Lower HIV infection was reported among active MMT patients during registration to the programme compared to other studies (Ali, Aziz et al, 2018; Grogan, Tiernan, Geoghegan, Smyth, & Keenan, 2005). Only 19 (0.84%) patients were seroconverted for HIV infection throughout the MMT programme which is similar to findings from

a local study (Ali, Aziz et al, 2018). Anti-retroviral therapy was started in 120 (69.0%) of active HIV patients. Anti-retroviral therapy takes up in our patients showed slightly higher percentage compared other studies that range from 50.2 – 65.8% (Uhlmann et al., 2010; Zhao et al., 2015). One third of active MMT patients were found to have hepatitis C. Current study had reported much lower percentage compared to other studies to range from 63.1 – 83.2% (Ali et al., 2018; Norsiah et al., 2010). The lower percentage in of hepatitis C infection in our patients likely due to the positive outcome of harm reduction program that leads to the significant drop in the number of PWID who shares injecting equipment (Ministry of Health, 2018). About 87 (3.6%) patients were seroconverted for hepatitis C infection while being in the MMT programme. Lower percentage of seroconversion was also reported in another study (Norsiah et al., 2010). Only 99 (4.2%) patients reactive for hepatitis B infection during registration and this finding is concordant to other studies (Ali, Aziz et al, 2018; Norsiah et al, 2010). Seroconversion for hepatitis B was noted only in 1 active patient which is similar to findings reported in MyTOS study (Ali, Aziz et al, 2018).

About 4 MMT patients had chosen to be abstinence from methadone and other substances while remaining in the programme. There are studies reported a minimum methadone dose ever consumed at 1mg per day (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003). The maximum dose of methadone ever consumed in our study was much higher than what was reported in MyTOS study. However, the median methadone dose ever consumed from our study replicated the findings reported in MyTOS study even though the recommended dose of maintenance should between 60mg to 100mg per day (Ali, Aziz et al, 2018; Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003).

Since the inception of the MMT programme in the state of Selangor, we have encountered 264 deaths among our patients. Complications from AIDS were found to be the main cause of death. However, it was just verbally reported statement by the peers that could be under or over-reporting. Our finding was similar to a meta-analysis that had reported complications of AIDS as one of the commonest cause of death among MMT patients (Mathers et al., 2013).

5. Conclusion

Opioid abuse remains as relevant health and psychosocial concern among the public. Despite the expansion of MMT services to public and private health sectors and detention centres, the growing number of substance abusers indicates challenges faced by service providers in combating drug-related problems. Widely available MMT programme which substantiated by comprehensive health care and anti-retroviral treatment had shown a positive outcome by keeping a lower seroconversion rate for blood-borne diseases hence the lower mortality among the MMT patients.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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