

**QUALITY OF HEALTH AMONG
METHADONE MAINTENANCE
TREATMENT (MMT) PROGRAM CLIENTS
IN MYANMAR**

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METHADONE MAINTENANCE
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by

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LIST OF ABBREVIATIONS

ASI	Addiction Severity Index
ATS	Amphetamine-type stimulants
ART	Antiretroviral therapy
IBBS	Integrated Bio-Behavioural Survey
BC	Before Christ
BZD	Benzodiazepine
CDR	Centre for Drug Research
DDTRU	Drug Dependency Treatment and Research Unit
DIC	Drop-in-centre
DTC	Drug Treatment Centres
HIV	Human Immunodeficiency Virus
IDU	Injecting drug users
IEC	Information, Education and Communication
INGO	International Non-Governmental Organization
HTC	HIV testing and counselling
JIAS	Journal of International AIDS Society
MMA	Myanmar Medical Association
MMT	Methadone maintenance treatment
NGO	Non-Government Organization
NSEP	Needle and syringe exchange programmes
OST	Opioid substitution therapy
PWID	People who inject drugs
RCT	Randomized Controlled Trial

QOL	Quality of life
STI	Sexually Transmitted Infections
THC	Tetrahydrocannabinol
TLFB	Timeline Follow back
VSSS-MT	The Verona Service Satisfaction scale for methadone treatment programs
UNODC	United Nations Office on Drugs and Crime
UNAIDS	The Joint United Nations Programme on HIV/AIDS
USM	Universiti Sains Malaysia (University of Science, Malaysia)
WHO	World Health Organization

LIST OF GLOSSARY

Abstinence	Refraining from drug use, whether as a matter of principle or for other reasons
Addiction	“Addiction” was more commonly used in the past and has, to a large extent, been replaced by “dependence” as it is considered stigmatizing. It refers to the repeated and compulsive use of a psychoactive substance or substances despite knowledge of the negative consequences.
Analgesic	A substance that reduces pain and may or may not have psychoactive properties
ASI-lite	Addiction Severity Index - Lite Version (ASI-Lite); The Addiction Severity Index, Lite version (ASI-Lite) is a shortened version of the Addiction Severity Index (ASI). The ASI is a semi-structured instrument used in face-to-face interviews conducted by clinicians, researchers or trained technicians. The ASI covers the following areas: medical, employment/support, drug and alcohol use, legal, family/social, and psychiatric area. The ASI obtains lifetime information about problem behaviours, as well as problems within the previous 30 days. The ASI-Lite contains 22 fewer questions than the ASI, and omits items relating to severity ratings, and a family history grid.
Buprenorphine	A partial opioid agonist used for the treatment of opioid dependence

Dependence	A syndrome characterized by compulsive use of a substance despite knowledge of the negative consequences of such use
Detoxification	The process by which an individual is withdrawn from the effects of a psychoactive substance. Detoxification may or may not involve the administration of medication.
Drug half-life	The time the body takes to remove 50% of an administered medication
HIV	Human immunodeficiency virus (HIV); The virus that causes HIV/AIDS is transmitted through blood, semen, vaginal fluid and breast milk. There are treatments available to prevent the progression of HIV to AIDS.
Illicit drug use	Illicit drug use was determined from examination of urine with urine test kit. A positive result indicated illicit drug use by the respondents.
Linked anonymous testing	Informed consent and no personal identifiers or names obtained. Coded specimen was applied and code given to client so that only answer of the client can be linked to urine specimen results.
Maintenance treatment	Long-term provision of medication that has the same or similar action as the patient's drug of dependence. The goal is to reduce illicit drug use and the harm resulting from it.
Methadone	A synthetic opioid drug used in maintenance therapy for those dependent on opioids. It has a long half-life and can be given orally, once daily, under supervision.
Motivational	A style of interviewing that aims to increase a patient's

interviewing	motivation to change their behaviour
Opiate	One of a group of naturally occurring alkaloids derived from the opium poppy (<i>Papaver somniferum</i>). It activates opiate receptors in the brain and has the ability to induce analgesia, euphoria and, in higher doses, stupor, coma and respiratory depression. The term opiate includes heroin and morphine and excludes synthetic opioids.
Opioid	The generic term applied to alkaloids from the opium poppy (<i>Papaver somniferum</i>), their synthetic analogues, and compounds synthesized in the body, which interact with the same specific receptors in the brain, have the capacity to relieve pain and produce a sense of well-being (euphoria). The opium alkaloids and their synthetic analogues also cause stupor, coma and respiratory depression in high doses. Examples include codeine, methadone, buprenorphine and (dextro) propoxyphene.
Peer educator	The member of a given group who involves in peer education typically for effect change among other members of the same group. The changes aimed at include modifying their knowledge, attitudes, beliefs or behaviours. A peer educator helps group members define their concerns and seek solutions through the mutual sharing of information and experiences.
Polysubstance use	The concomitant use of multiple psycho active substances. It is also called multiple substance (or drug) use.

Problematic substance use	The use of psychoactive substances resulting in negative consequences for the individual
Psychoactive substance	A substance which, when ingested/inhaled/injected, affects mental processes, e.g. cognition or affect
Relapse	A return to drug use by a formerly dependent person after a period of abstinence, often accompanied by reinstatement of dependence symptoms. Some distinguish between relapse and lapse (“slip”), with the latter denoting an isolated occasion of drug use. Relapse is very common and most drug users relapse several times before they achieve long-term abstinence.
Substitution	Substitution means replacing the harmful opioid on which the individual is dependent (commonly heroin or buprenorphine in the South-East Asia Region) with a less harmful opioid.
Tolerance	A decrease in response to a drug dose that occurs with continued use. Increasing doses of drugs are required to achieve the effects originally produced by lower doses.
VSSS-MT	The Verona Service Satisfaction scale for methadone treatment programs
Withdrawal	A group of symptoms of variable clustering and degree of severity that occur on cessation or reduction of use of a psychoactive substance which has been taken repeatedly, usually for a prolonged period and/or in high doses. The

syndrome may be accompanied by signs and symptoms of physiological disturbance. A withdrawal syndrome is one of the indicators of a dependence syndrome.

WHO QOL-BREF The WHOQOL-BREF (WHO Quality of Life-BREF) instrument comprises 26 items, which measure the following broad domains: physical health, psychological health, social relationships and environment. The WHOQOL-BREF is a shorter version of the original instrument that may be more convenient for use in large research studies or clinical trials.

KUALITI KESIHATAN DI KALANGAN KLIEN PROGRAM TERAPI GANTIAN METADON (MMT) DI MYANMAR

ABSTRAK

Kadar prevalen HIV di kalangan PWIDs (orang yang menyuntik dadah) di Myanmar adalah tinggi pada 28.5% berdasarkan pada keputusan IBBS 2014. Lebih daripada 13,441 (16% daripada anggaran 83,000 PWIDs) telah berdaftar untuk rawatan metadon pada 2017. Penilaian program metadon adalah penting untuk penyampaian perkhidmatan yang efisien. Kajian ini bertujuan untuk memahami konteks dan faktor-faktor penting rawatan berhubung program terapi gantian metadon (MMT) di kalangan klien di Myanmar. Sebanyak 210 responden direkrut melalui persampelan rawak berstrata dari lima bandar di Myanmar di mana program MMT telah wujud. Beberapa instrumen kajian seperti soal selidik WHO-QOL-BREF, soal selidik Skala Kepuasan Perkhidmatan Verona untuk Rawatan Metadon (VSSS-MT), dan Indeks Keterukan Ketagihan (ASI) digunakan. Ujian urin dadah juga telah dilakukan untuk mengesahkan status penggunaan dadah responden. Hasil kajian menunjukkan bahawa 45% (n=93) tidak pernah menyuntik heroin dalam 30 hari yang lepas, sementara 55.5% (n=116) menyuntik heroin. Purata dos metadon harian responden dalam kajian ini adalah 83mg. Tiga puluh tujuh peratus (n=74/200) mempunyai HIV, dan 16.27% (n=34/209) melaporkan jangkitan ko-infeksi (HIV/HCV). Lebih daripada satu pertiga (36.5%, n=76) menerima dos metadon yang tinggi (melebihi 80mg), sementara 63.46% (n=132) menerima dos rendah. Dos metadon yang lebih tinggi dikaitkan dengan penurunan penggunaan heroin (p=0,034). Dalam mengkaji Kualiti Hidup (QOL) responden, jumlah purata skor (QOL) responden adalah 60.8%; khususnya, 60.1% dalam domain fizikal, 63.1% dalam domain psikologi, 59.9% dalam domain hubungan sosial, dan 60.4% dalam

domain persekitaran. Skor QOL yang rendah dikaitkan dengan kepuasan perkhidmatan metadon yang rendah. Tambahan pula, pada menganalisis indeks keterukan penagihan (ASI), purata skor ASI responden adalah; Pekerjaan (47.4%), Penggunaan dadah (16.3%), Alkohol (13.5%), Leluarga-sosial (10.7%), dan Undang-undang (10.5%). Skor ASI yang lebih tinggi menggambarkan situasi yang teruk. Mereka yang tidak menyuntik dalam 30 hari lepas mempunyai skor ASI yang lebih rendah berbanding dengan mereka yang menyuntik ($p=0.026$). Majoriti (85%, $n=178$) sangat berpuas hati dengan perkhidmatan metadon. Lebih daripada dua pertiga (89.47%, $n=187$) sangat berpuas hati dengan kategori kakitangan (dokter, jururawat, dan lain-lain), 91.87%, $n = 192$) pada item intervensi asas, dan 74.64% ($n = 156$) pada item intervensi spesifik program MMT. Dos metadon yang lebih tinggi boleh mengurangkan tingkah laku suntikan, dan turut mencegah transmisi HIV di kalangan PWIDs. Dalam anggaran kepuasan rawatan MMT, kepuasan responden berbeza dengan status jangkitan yang berbeza selepas mengambil kira penyesuaian dos metadon. Oleh sebab penggunaan poly-drug adalah prevalen, langkah-langkah pengurangan kemudatan yang lain dilihat penting untuk mencegah risiko ketagihan dan penyakit berjangkit. Penilaian rawatan berterusan adalah sangat penting untuk mengenal pasti domain yang mencabar dalam kategori perkhidmatan program MMT (contoh pemulihan individu, psikoterapi dan terapi kumpulan), dan sokongan untuk jangkitan ko-infeksi HIV/HCV diperlukan untuk memastikan penyampaian perkhidmatan yang berkesan.

QUALITY OF HEALTH AMONG METHADONE MAINTENANCE TREATMENT (MMT) PROGRAM CLIENTS IN MYANMAR

ABSTRACT

HIV prevalence rate among PWIDs (People who inject drugs) in Myanmar is high at 28.5% based on 2014 IBBS results. More than 13,441 (16% of the estimated 83,000 PWIDs) have been on methadone treatment in 2017. Evaluation of the methadone program is vital for efficient service delivery. This study aimed to understand the context and important treatment factors of methadone maintenance treatment (MMT) program among clients in Myanmar. A total of 210 respondents were recruited through stratified random sampling from five cities in Myanmar where MMT program existed. Several study instruments such as WHO-QOL-BREF questionnaire, Verona Service Satisfaction Scale questionnaire for Methadone Treatment (VSSS-MT) and Addiction Severity Index (ASI) were used. The urine drug test was also conducted to confirm respondents' drug use status. Study results showed that 45% (n=93) never injected heroin in the last 30 days, while 55.5% (n=116) injected heroin. The average daily methadone dose in this study was 83mg. Thirty-seven percent (n=74/200) had HIV, 16.27% (n=34/209) reported co-infection (HIV/HCV). More than one-third (36.5%, n=76) received high methadone dose (above 80mg), while 63.46% (n=132) received low dose. Higher methadone dose was associated with decreased in heroin use (p=0.034). In reviewing the quality of life (QOL) of the respondents, the total average score of respondents (QOL) was 60.8%; specifically, 60.1% in the physical domain, 63.1% in the psychological domain, 59.9% in the social relation domain, and 60.4% in the environmental

domain. Low QOL scores were associated with low methadone service satisfaction. Furthermore, on analysing addiction severity index (ASI), the average ASI scores of the respondents are; Employment (47.4%), Drug use (16.3%), Alcohol (13.5%), Social-family (10.7%), and Legal (10.5%). Higher ASI score reflects the worse situation. Those who did not inject in the last 30 days had lower ASI scores compared to those who injected ($p=0.026$). The majority (85%, $n=178$) were highly satisfied with methadone services. More than two-thirds (89.47%, $n=187$) were highly satisfied with the staff category (doctor, nurse, etc), 91.87%, $n=192$) on basic intervention items, and 74.64% ($n=156$) on specific intervention items of the methadone program. Higher methadone dose can reduce the illicit drug injection and subsequently prevent HIV transmissions among individuals who inject drugs. In the estimation of treatment satisfaction of methadone program, the satisfaction of respondent varies with different infection status after taking into consideration of adjustment of methadone dose. Since poly-drug use was prevalent, other harm reduction measures are seen important to prevent the risk of addiction and infectious diseases. Continuous treatment assessments are vital for identifying challenging areas like special service categories of MMT program (e.g individual rehabilitation, psychotherapy and group therapy) and support for HIV/HCV co-infections are needed to ensure effective service delivery.

CHAPTER 1

INTRODUCTION

1.0 Introduction

This is the first chapter of the thesis. The world drug abuse problem and drug abuse problems in Myanmar, as well as the study problem statement, study significance and scope of study have been clearly described in this chapter of the thesis.

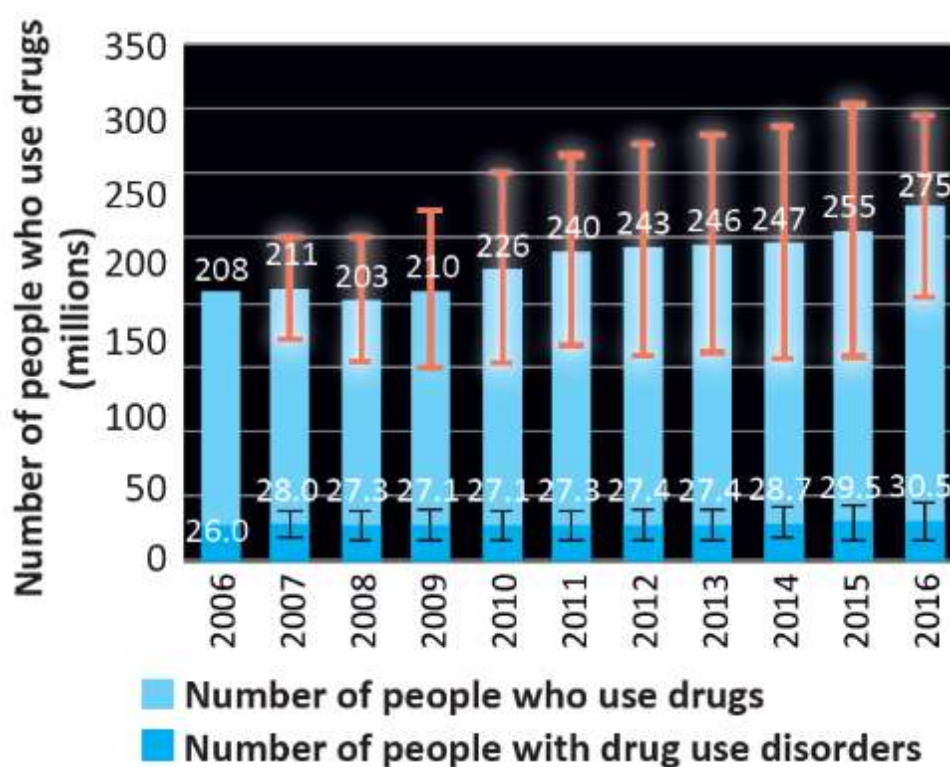
1.1 World Drug Abuse Problem

This part of the chapter will discuss the world drug use problem mainly to understand the current situation of the drug use problem in the world. Additionally, it will inform the extent of the severity of the global drug use problem and health issues related to the abuse of illicit substances. Latest figures from United Nations Office on Drugs and Crime (UNODC) estimated that there are more than 275 million people (5.6% among 15-64-year-old) who used drugs at least once in 2016 (UNODC, World Drug Report 2018, 2018). Out of that figure, 192 million are Cannabis users, 34 million are opioid users, 34 million are amphetamines and prescription stimulant users, 21 million are ecstasy users, 19 million are opioid users and 18 million are cocaine users. Of them, opioid is the leading cause of harm, while 76% of the reported deaths are linked to opioid overdose. More than half of injecting users are living with hepatitis C infection and has been infected with Human Immunodeficiency Virus (HIV) among one eighth of injectors.

Non-medical use of drugs is also a major problem and has contributed significantly to the incessant increased in mortality incidents in North America.

Based on the 2018 World Drug Report, there was also an increasing trend of non-medical use of drugs in different parts of the world; fentanyl mixed with heroin in North America, non-medical use of methadone, buprenorphine and fentanyl in Europe, non-medical use of tramadol (a pharmaceutical opioid) in West and North Africa, the Near and Middle East, as well as in Asia countries.

Graph 1.1 Global trends in estimated number of people who uses drugs, 2006-2016 (UNODC, World Drug Report 2018, 2018)



Source: UNODC, responses to the annual report questionnaire.

Note: Estimates are for adults (aged 15–64 years) who used drugs in the past year.

1.2 Definition of Health and Improving care for drug use disorders

World Health Organization defines “Health” as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Furthermore, with interventions and strategy differences by country to country,

health outcomes need to set out in the preamble of the WHO constitution for “Unequal development in different countries in the promotion of health and control of diseases, especially communicable disease, is a common danger” (WHO, Constitution).

The non-medical use of psychoactive drugs and psychotropic substances associated significant health risks and drug use disorders; “harmful pattern of drug use” and “drug dependence”. Drug use disorder affects the individual and community with morbidity and mortality of drug user, lost productivity, increased healthcare expenditure, cost to criminal justice system, social welfares and social consequences. As drug use disorder is not a “single acquired bad habit”, it is complex health conditions which need to work together with comprehensive multi-disciplinary public health-oriented responses (WHO, Improving care for drug use disorders). WHO recommends opioid withdrawal management with pharmacological managements;

1. gradual cessation of an opioid agonist (methadone)
2. short-term use of a partial agonist (buprenorphine)
3. sudden opioid cessation and use of alpha-2 adrenergic agonists to relieve withdrawal symptoms.

For the successful intervention example, WHO published an example that rapid expansion of methadone maintenance treatment programmes not only improve in the quality of life (QOL) of drug users and their families, but also reduce HIV spread among that population (Wu & Clark, 2012). This treatment service not only reduce or stop opioid use, but also improve social functioning.

Additionally, it is important to support the psychological health with structured professional interventions (e.g. cognitive behaviour therapy or insight-oriented

psychotherapy) or non-professional interventions (e.g. self-help groups). Improvement in social environment of the opioid user will help them to improve both the quality and duration of life (WHO, Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence, 2009).

1.3 Drug Abuse Problem in Myanmar

Myanmar is also notoriously known for its opium production in history. According to the Association of South East Asian Nations (ASEAN) Drug Monitoring Report (2017), a whopping amount of 570.62 kilograms of heroin (769.26 kilograms in 2016) and over 72.82 million of stimulant tablets were seized in 2017 (over 98.35 million in 2016), reflecting challenges in drug abuse activity in Myanmar (asean.org, 2018).

There is also a considerable heroin problem in Myanmar according to the Drug Dependency Treatment and Research Unit (DDTRU, Annual Report 2017, 2018). Among the new patients registered for treatment, 78.77% were abusing heroin, followed by amphetamines (13.04%), as shown in Table 1.1 (DDTRU, Annual Report 2017, 2018).

Table 1.1 Table showing new admissions to drug treatment services by types of drugs used in 2017 (DDTRU, Annual Report 2017, 2018).

Types of drug use	Total (=n)	Percent (%)
Heroin	5936	78.77
Opium	319	4.23
Marijuana	23	0.31
Tranquilizer	3	0.04
Amphetamine	983	13.04
Others	272	3.61
Total	7536	100.00

In order to address the widespread drug use problem in Myanmar, various interventions such as supply reduction, demand reduction and harm reduction interventions has been implemented.

Supply Reduction: In the 2017 report, total opium poppy cultivation in Myanmar was 41,000 hectares (1 hectare= 10,000 m²), though a 25% decreased was recorded, opium production stood at 550 tons in 2017. Other precursors and narcotic drugs were also seized by the relevant enforcement agencies as shown in Table 1.2 (asean.org, 2018).

Table 1.2 Seizures of narcotic drugs in Myanmar (asean.org, 2018)

Type of drugs	2012	2013	2014	2015	2016	2017
Opium (Kg)	1,470.35	2,356.93	1,828.40	888.84	945.7096	1,256.169
Heroin (Kg)	335.79	238.93	435.46	186.04	769.2589	570.622
ATS Tablet (Million)	18.16	10.18	12.65	49.95	98,353.462.5	72.816
ICE (Kg)	426.66	173.00	47.11	2,261.69	2,464.0834	1,107.491
Mitragyna speciosa (Kg)	330.15	218.95	605.31	687.35	1,409.4324	651.127
Cannabis (Kg)	80.27	40.94	205.54	87.70	188.7805	198.826
Case	4,006	4,928	6,696	6,414	8,800	9,544
Suspect	5,740	7,137	9,425	9,188	13,591	14,000

On the other hand, as a member of the United Nations, Myanmar is a signatory to the following conventions and has been implementing these International Conventions.

- Single Convention on Narcotic Drugs (1961)

- The Convention on Psychotropic Substances (1971)
- The Protocol Amending the Single Convention on Narcotic Drugs (1972) and,
- The Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988).

To comply with the conventions, Myanmar has enacted Narcotic Drugs and Psychotropic Substances Law in 1993, Rules Relating to Narcotic Drugs and Psychotropic Substances in 1995, and Rules Relating to Supervision of Controlled Precursor Chemicals in 2004. Central Committee for Drug Abuse Control (CCDAC) was formed in 1976 and was chaired by the Union Minister for Home Affairs with 16 members and has been taking various measures to control the abuse of narcotic drugs in Myanmar (DDTRU, Annual Report 2017, 2018).

Demand Reduction: With the cooperation of Ministry of Health and Sports, Social Welfare and CCDAC had operated drug treatment and rehabilitation centres, while Ministry of Education implemented awareness programs at school and integrated life skills curriculum alongside with the implementation of public talks and debates, exhibitions and competitions (asean.org, 2018).

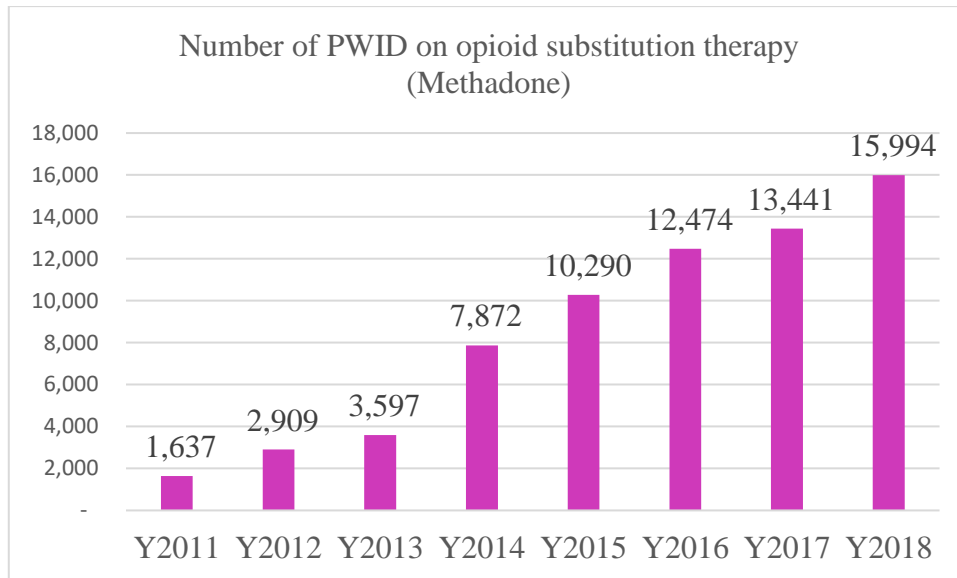
Harm Reduction: Harm Reduction interventions are primarily implemented for prevention of blood-borne infections such as HIV and hepatitis C infections (asean.org, 2018) from the injection of unsafe needle sharing practices, as well as for addressing the nine components of harm reduction interventions. Myanmar has implemented all the nine harm reduction interventions and they include needle and syringe programmes (NSPs), Methadone Maintenance Therapy (MMT), HIV testing and counselling (HTC), Anti-retroviral Therapy (ART), targeted information, education and communication, condom distribution program for People who inject

drugs (PWIDs) and their sexual partners, testing, vaccination for hepatitis B and testing for hepatitis C, prevention, diagnosis and treatment of tuberculosis, and diagnosis and management of sexually transmitted infections (Myanmar T. G., 2018).

1.4 Brief Introduction of Methadone

In addressing opioid/ opiate use harms among people who inject drugs (PWIDs), Myanmar has introduced methadone as an opioid substitution therapy (OST) since 2006. Methadone is a substitution therapy or medicine-assisted treatment that is commonly used as a substitute for opioids. Methadone is shown to suppress withdrawal symptoms and eliminate an addict's compulsion to take heroin (Substance Misuse: Heroin, 2016). With its long half-life of between 24-36 hours in tolerant individuals, methadone will eliminate withdrawal symptoms of opioid by 'narcotic blockade' in a single oral dose that is serving on a daily basis (Granerud & Toft, 2015). Methadone is commonly used for reducing dependence on opioid (WHO, The methadone fix, 2008). Various studies have shown that methadone use was associated with reduction in illicit opioid use and transmissions of blood-borne diseases such as HIV and hepatitis C among PWIDs.

Graph 1.2 Graph showing number of PWID clients on opioid substitution therapy (Methadone) in Myanmar (2011-2018) (Myanmar G. , 2018)



1.5 Problem Statement and Justification

HIV prevalence among PWIDs has increased to 34.9% in 2017 based on the Integrated Bio-Behavioural Survey findings (IBBS) (National AIDS Program, IBBS 2017 Myanmar, 2019), compared to the 2014 IBBS report where HIV prevalence among PWIDs stood at 28.5%. The HIV prevalence in the general community in Myanmar was at 0.57% (National AIDS Program, 2016). HIV transmission among PWIDs is still considered a major health problem in Myanmar since 28% of the newly reported HIV infections stemmed from sharing of non-sterile/contaminated injecting equipment's (National AIDS Program, 2016). Many reforms have been implemented for addressing the drug abuse issues in Myanmar according to the National Strategic Plan (2016-2020). Additionally, area-focused sub-national operation planning initiatives are also expanded in combating drug use threat in Myanmar. Notably, unsafe injection practices have contributed significantly to disease burden like communicable diseases; HIV, hepatitis B and C, syphilis (Editorial, 2017), and malaria (Alavi, Alavi, & Jaafari, 2010). Therefore, supporting of needle and syringe exchange program (NSEP) and opioid substitution therapy

with methadone seem to be the only promising harm reduction interventions currently being implemented in Myanmar. Since there is an increased risk of HIV transmission among people who inject drugs (PWIDs) and subsequent infections from injection, National Drug Abuse Prevention and Control Programme (also known as DDTRU) has decided to increase the opioid substitution therapy with the expansion of methadone resources and sites. Since methadone treatment have been extensively scaleup a decade ago, thus it was necessary that a study being conducted to evaluate the effectiveness of the implemented harm reduction interventions in Myanmar.

Findings from this prospective study have many advantages. First, policy makers can identify methadone users' demographic and behavioural characteristics. Second, treatment providers can also identify current treatment challenges and needs among clients enrolled in methadone treatment program in Myanmar. Third, findings from this study can also provide important information on clients' social functioning, methadone dose and treatment satisfaction among clients in methadone treatment program in Myanmar. Last but not least, policy makers and treatment providers can also use the study findings to make informed decisions on expanding the methadone treatment program in Myanmar.

1.6 Research Questions of the Study

Methadone program was initially introduced in Myanmar in 2006 under the purview of Ministry of Health and Sports. Meanwhile, regarding the methadone services, National Strategic Plan III (2016-2020) had declared to increase the number of PWIDs into methadone treatment to 32,000 by 2020 (National AIDS Program, 2016). Despite the treatment expansion plan for opioid substitution in

Myanmar, so far, no major studies have been conducted to determine methadone treatment effectiveness or factors that could undermine client's treatment compliance in methadone treatment program in Myanmar. Due to this research gap, this study aims to explore the followings;

1. What are the demographic characteristics of methadone patients in Myanmar?
2. To what extent methadone dose could affect the social functioning of methadone patients?
3. Are patients in methadone program receiving adequate dose and/or what are the other contributing factors that are associated with illicit drug use among clients in methadone program in Myanmar?

It could be hypothesized that if patients are prescribed with optimum methadone dose, there could be significant improvement in social functioning of methadone patients.

1.7 Study Objectives

1.7.1 General Objectives

The followings are the general study objectives;

1. To identify the demographic characteristics of methadone patients in Myanmar
2. To determine the relationship between methadone dose and social functioning of methadone patients in Myanmar
3. To determine methadone treatment compliance with the current illicit drug use status of methadone patients in Myanmar

1.7.2 Specific Objectives of the study

The followings are the specific study objectives;

- a. To determine the relationship between methadone dose and frequency of illicit drug use among methadone users in Myanmar
- b. To determine the relationship between methadone dose and treatment satisfaction among methadone patients in Myanmar
- c. To determine the relationship between methadone dose and social functioning of methadone patients in Myanmar
- d. To determine the relationship between methadone dose and quality of life (QOL) of methadone patients in Myanmar
- e. To assess the risky injecting and sexual behaviour among methadone patients in Myanmar
- f. To determine the type of preventive and treatment services provided by Drop-in-Centre and Out-Reach Workers in Myanmar

Ways for Addressing the Objectives of the Studies

To address the objectives of the research, the following tools and questionnaires were utilised in the survey.

For objective (a) relation between methadone dose and frequency of illicit drug use; questionnaires on illicit drug use with Timeline Follow Back (TLFB survey) (NIDA-CTN, 2014) was included to answer the objective.

For objective (b) relation between methadone dose treatment satisfaction; questionnaires on (VSSS-MT) the Verona Service Satisfaction Scale for methadone-treated Opioid-dependent patients (Cobos, et al., 2002) was integrated in the survey.

For objective (c) relation between methadone dose and social functioning of methadone patients; questionnaires on Addiction Severity Index- Lite (ASI) was used (McLellan, Cacciola, Carise, & Coyne, 1999) in the survey.

For objective (d) relation between methadone dose and quality of life, questionnaires from WHO QOL BREF (WHO, The World Health Organization Quality of Life (WHOQOL)-BREF, 2004) and Addiction Severity Index- Lite (ASI) (McLellan, Cacciola, Carise, & Coyne, 1999) were included in the survey.

For objective (e) to assess the risky injecting and sexual behaviour among methadone patients, questionnaires to prove the injection practice, needle sharing behaviour, condom uses with different type of partners were included.

For objective (f) to determine the preventive and treatment services provided by drop-in-centre and out-reach workers; questionnaires to prove the utilization practice of drop-in-centre and out-reach workers, and the availability of needle and syringe exchange programme (NSEP), condom and health education programme, referral and availability of testing and treatment of HIV services were included.

1.8 Scope of Study

The key scope of study was to determine some of the challenges faced by clients who are enrolled in methadone treatment programs in Myanmar. The relationship between methadone dose and other vital variables (e.g. current illicit drug use status, social functioning, quality of life, etc.) was explored through a cross-sectional design study.

1.9 Significance of Study

Findings from this preliminary cross-sectional study have much significance. First, treatment providers can determine the overall effectiveness of the methadone

maintenance treatment (MMT) program in Myanmar. Second, findings from this study can highlight some of the challenges faced by clients in MMT program in Myanmar. This in turn, can help treatment providers to improve treatment compliance among MMT clients. Third, the relationship between methadone dose and its association with current illicit drug use status and other dimensions of social functioning can be clearly determined, so that proper interventions can be introduced to address MMT limitations. Fourth, policy-makers can use the study findings to make informed-decisions about finding ways to enhance client's treatment compliance. Fifth, findings from this study can also be used to develop future studies on MMT program in Myanmar. Last but not least, findings from this study have huge policy implications in scaling-up MMT program in Myanmar.

1.10 Conclusion

In conclusion, the world drug abuse problem, drug use problems in Myanmar, information on MMT program in Myanmar, study problem statement, research questions and study objectives, scope of study, study significance and limitations has been clearly delineated in this chapter. The next chapter is the literature chapter. Below is a brief summary of all the chapters in the thesis.

Chapter 1 addresses the background of the drug use information and interventions that were taken places in local context and global context.

Chapter 2 talks the information review on drugs, drug substitution therapy, methadone treatment as opioid substitution and other illicit drug issues in Myanmar.

Chapter 3 reports the research methodology in detail with the justification for conducting this research. It also includes how outcomes arise from recruiting the methadone patients, strategies to address the associated risks and survey responses,

study designs and implementation of research data collection. The chapter also ensures in discussion of how survey questionnaires were prepared and tested as well as for ethical consideration of the research participants.

Chapter 4 discusses the results from the survey findings with the different objectives on

- Determining the relation between methadone dose and frequency of illicit drug uses
- Methadone dose and treatment satisfaction
- Methadone dose and social functioning of methadone patients
- Methadone dose and QOL of methadone patients
- Association of methadone dose and injection and risky behaviour
- And determining the preventive and treatment services provided for methadone patients

In **Chapter 5**, different findings were discussed from the survey analysis with

- Reported heroin injection within 30 days among patients of different methadone dose
- Findings on different methadone dose requirements with the different HIV status and patients on Anti-retroviral therapy
- Different methadone dose requirement among co-infected methadone patients
- Impact of methadone dose on the treatment satisfaction
- methadone dose effects on the social functioning and criminal profile

CHAPTER 2

LITERATURE REVIEW

2.0 Introduction

This is the literature chapter. All the relevant literatures related to the scope of study is clearly analysed, compared and delineated in this chapter. This chapter begins with detail information on the drug prevention work and opioid substitution program in Myanmar, harm reduction intervention components, the importance of methadone treatment, consequences of risky drug injecting and sexual behaviours linked to opioid use and blood-borne diseases or health problems that are associated with opioid misuse.

2.1 Drug and Illicit Substance Use History

Drug use was deeply rooted among mankind for several thousand years since prehistoric times. Different forms of preparation were used; alcohol made from fermented honey was first used in 8,000BC, beer and wine came up in 6,000BC, ancient Sumerians used opium in 5,000BC, China used cannabis in 3,000BC and Coca leaves (source of cocaine) had been chewed for thousands of years (Social Problems: Continuity and Change, 2015).

2.1.1 Illicit Substance Uses and Consequences

Illicit drug use can be defined as non-medicinal use of drugs which has officially prohibited by international laws. Drugs include plant-based drugs; cannabis, heroin, cocaine, to synthetic produced drugs; amphetamine (methylenedioxymethamphetamine; MDMA; ecstasy) (World-Health-Organization, 2004). However, those drugs using for treatment of opioid substitution

therapy, buprenorphine and methadone were also included under illicit drug without the proper prescription (Degenhardt & Hall, Extent of illicit drug use and dependence, and their contribution to the global burden of disease, 2012)

These illicit drugs associate with physical dependence and mental disorders including psychoses. Major cause of mortality can be seen in the illicit opioid use from fatal overdose and dependence. Other illicit drug injection results in HIV, hepatitis B and C from unsafe needle sharing practices (Degenhardt & Hall, Extent of illicit drug use and dependence, and their contribution to the global burden of disease, 2012).

2.2 Drug Problem in Myanmar

2.2.1 Drug Use in Myanmar History

In historic record, it was found that opium was used in country and Myanmar kings acted on prohibiting of the usage. There was opium consumption in lower Burma during Kong Baung Dynasty (1752-1886) and prohibited drugs and alcohol in Burmese emperor with strict legal command issued by King Bodawpaya (1784-1819) (James, 2006). Widespread addiction of opium became after the first Anglo Burmese war in 1824-26, where the colonial administration in lower Burma encouraged it. The use of opium was encouraged with gave away of free-dipped of betel leaves in the opium to establish a taste for it. British traded large quantities of opium from India to Burma and down to Penang, Singapore and Australia (James, 2006).

2.2.2 Drug Production History

Since British administration era, there had been opium cultivation in Myanmar. Later in 1980, Myanmar had become the largest illicit opium producer.

Then in 1996, annual production level of opium in Myanmar was 1,600 tons. Government and local authorities developed 15-year plan to eliminate illicit crop production by 2014 (UNODC, Myanmar Opium Survey 2017, 2017). In 1991, Afghanistan became world largest producer of opium. After Afghanistan, Myanmar is the largest producer of opium poppy in the world. In terms of opium poppy cultivations, estimations of 41,000ha has been cultivated in Shan and Kachin states and it was decreased by 25% compared to 2015 estimates according to the 2017 Myanmar Opium Survey (UNODC, Myanmar Opium Survey 2017, 2017) . However, total opium poppy eradication reported by the Government of Myanmar has 3,533ha which was decreased by 74% compared to 2015 estimates (UNODC, Myanmar Opium Survey 2017, 2017) . According to the World Drug Report 2018, Myanmar was still accounting for 5% of the world's total opium production in 2017. Myanmar takes part in Mekong Memorandum of Understanding mechanism a six-country regional initiative with Cambodia, China, the Lao People's Democratic Republic, Thailand and Viet Nam to strengthen regional cooperation on drug control matters.

2.2.3 Drug Use Interventions in Myanmar

Myanmar has a long history of medicinal drug use of opium and its abuse can be traceable back to 17th century. British administration first acted to address the opium act (1875) and extended to upper Burma in 1886 after conquering the remaining Kingdom, exception to Trans-Salween states where the best poppies were grown. In 1917, the Burma Excise Act (1917) was enforced (burmalibrary.org, 2018). After independence in 1948, Opium Enquiry Committee was formed in 1953 for addressing ways and means to solve the problem of opium cultivation and addiction problem in Myanmar. Opium and cannabis were abused until the early

1970s and later heroin addiction spread rapidly and reached epidemic proportions which prompted the authorities to adopt new legislations in 1974 as “the Narcotic and Dangerous Drugs Law” which provided for compulsory treatment to drug users and severe penalties for drug-related violations. Authorities not only addressed the legislation and law enforcement issues, but also introduced prevention and community measures for interrelated strategies to combat drug abuse among young people and introduced community programmes like the "Red Cross" and voluntary fire brigades (UKhant, 1985).

Progressive law and policy reform on drug use and harm reduction work is currently being executed by the Government. The first National Drug Control Policy developed by the Central Committee for Drug Abuse Control (CCDAC) with support from the United Nations Office on Drugs and Crime (UNODC) was adopted on 23 November 2017. Myanmar revised the Burma Excise Act (1917) to decriminalise the unlawful handling of syringes among PWIDs and amendments to the Narcotic Drugs and Psychotropic Substances Law (1993) to remove the punishments for clients identified as drug users. The 1993 Narcotic Drugs and Psychotropic Substances Law which was enacted by the Union Parliament (Pyidaungsu Hluttaw) (Pyidaungsu Hluttaw Law No.66/2015, 2015) in 2018, also introduced social and rehabilitation support system despite the former punishments (Hluttaw P. , 2018).

HIV transmission among the PWIDs is still a major health problem in Myanmar, since 28% of the newly reported HIV infection stemmed from sharing of non-sterile/contaminated injecting equipment's (National AIDS Program, 2016). There are many reforms for addressing drug use issues in Myanmar according to the National Strategic Plan (2016-2020). Myanmar has substance abuse policy, law,

treatment services for substance use disorders with the government funded facility and supportive treatment services by the private sectors. Public treatment centres and public mental health hospitals are the main service providers for provision of methadone maintenance therapy across the country. The private sector also facilitates in supporting methadone treatment services in a few sites under the guidance of the MMT Programme. Myanmar government also commits the annual budget for the prevention and treatment of the drug use issues.

2.2.4 Drug User in Prisons

According to the Myanmar drug control policy report, 48% of Myanmar's 60,000-80,000 prisoners were detained for drug related offences across the country. Meanwhile, drug related offences were accounted for 70-80% in some prisons in Myitkyina and Lashio (Central Committee for Drug Abuse Control, 2018).

2.2.5 Description of Drug Treatment Programme in Myanmar

Between 1976 and 2002, 30 Drug Treatment Centres (DTCs) have been established throughout the country. Methadone program was implemented in 2006, where about 260 patients were registered into methadone program in Myanmar. In 2015, 26 major DTCs, 47 minor DTCs and 2 youth Rehabilitation and Correction Centres were developed in Myanmar. Based on the DDTRU Report (DDTRU, DDTRU Report (2015), 2015), approximately 9,080 patients have enrolled into methadone treatment at the end of June 2015. The registration number was expected to increase with the opening of newer MMT sites in areas plagued with drug use problems. Out of the 83,000 estimated people who inject drugs, 14,325 PWIDs had enrolled into methadone programme in June 2018 (Myanmar T. G., 2018). As drug dependence was mentioned as multi-factorial health disorder with relapsing and remitting in nature, comprehensive intervention packages were also implemented in

Myanmar. Meanwhile, harm reduction initiatives are being advocated to the administrative and legislative communities for desensitization of drug use criminalization. Currently, administrator and legislators are working on revising the narcotic drugs and psychotropic substances law and excise law. Excise law was successfully amended in 2018 from Myanmar parliament (Hluttaw P. , 2018). With the public and private sector support for harm reduction with substitution therapy, evaluation of the intervention is important for improvement in harm reduction.

2.3 Opioid

In refreshing of the opioid and other related drug pharmacokinetics and consequences, some highlights of the compounds will be discussed in this chapter. In opioid history, *Papaver somniferum* seed pots were used 4200BC and different parts of the plant were used in food, anaesthesia, and ritual purposes. The liquid from the plant contains 16% of morphine, isolated since 1806 as a major active ingredient in opium. Later, codeine was isolated. In 1898, heroin was claimed as safer, efficacious, highly potent analgesic properties with rapid metabolism due to higher blood-brain barrier penetration and better lipid solubility.

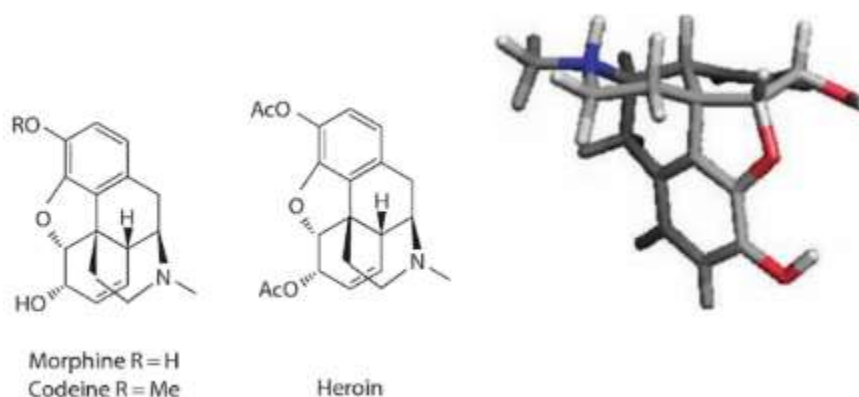


Figure 2.1 Chemical structure of morphine, codeine, and heroin. 3D structure of morphine (Stromgaard, Krogsgaard-Larsen, & Madsen, 2009).

However, the use of opioid is significantly affecting its users in negative impact, which account for 76% of deaths from drug use disorder in 2015. Estimated 34.3 million opioid users in 2016 were equivalent to 0.7% of aged 15–64 year of global population; of which 4.2% were prevalence in North America and 2.2% in Oceania.

Out of opioids users, 19.4 million were heroin and opium users in 2016; equivalent to 0.4% of aged 15–64 year of global population; of which Central Asia and Transcaucasia prevalence was 0.9%, Eastern and South Eastern Europe prevalence was 0.7% and 0.8% in North America (UNODC, World Drug Report 2018, 2018).

Opioid is the most utilized drug in Myanmar according to the presented data of the DDTRU of Myanmar. Heroin contributed to the majority of drug use (78.77%) which was followed by Amphetamine-type stimulants (ATS) 13.04% in 2017 (DDTRU, Annual Report 2017, 2018).

Table 2.1 Type of illicit drug use data from national report of DDTRU

Type of illicit drug	Percentage from National data
Morphine in urine / (Heroin)	78.77%
Cannabis (THC) in urine	0.31%
Methamphetamine in urine	13.04%

2.4 Other Illicit Substances

2.4.1 Amphetamine-type stimulants (ATS)

Amphetamine-type-stimulants (ATS) (e.g. meth/amphetamines) are a group of synthetic stimulants including methamphetamine, amphetamine, methcathinone, and ecstasy-group substances and 3,4-methylenedioxymetamphetamine (MDMA or

ecstasy). Amphetamine not only increases the synaptic concentration of dopamine (dopamine transporter protein; DAT) competing with dopamine for uptake via DAT), but also by promoting reversal of transport resulting in effect of dopamine via the transporter, dramatically increases the levels of extracellular dopamine which is important for psychostimulatory properties of Amphetamines.

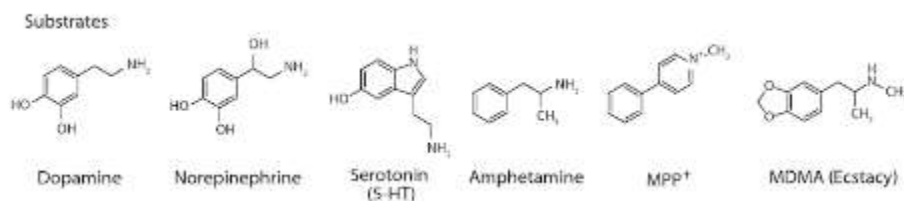


Figure 2.2 Structure of Amphetamine and other drugs and enzyme (Stromgaard, Krogsgaard-Larsen, & Madsen, 2009)

The use of Amphetamine-type-stimulants (ATS); Methamphetamine use continued increasing in most countries in East and Southeast Asia as the primary or secondary drug of use. Lao PDR and Myanmar reported the use of crystalline Methamphetamine too. Meanwhile, the precursor chemicals to Methamphetamine manufacturers are based in India and Pseudoephedrine tablets, Ephedrine and Ketamine were smuggled. (UNODC, Patterns and Trends of Amphetamine-Type Stimulants and Other Drugs: Challenges for Asia and the Pacific, 2013). In the meantime, 1,600 tons of precursors were seized in 2016 according to the drug situation report of China. Caffeine, adulterant used in Methamphetamine had been seized in Myanmar in 2015 and 2016. With the increased production and uses arise, 287 million methamphetamine tablets were seized in 2015, where most of these from six countries of the Greater Mekong subregion.

Methamphetamine pills are called;

- Yama in Cambodia, Lao PDR, and yama, seik kwyay say, and myin say in Myanmar

- Yaba in Cambodia, Lao PDR, and Thailand, bingdu pian in China

2.4.2 Cannabis (*trans-Δ⁹-tetrahydrocannabinol*; THC)

Cannabis became the most commonly used drug in 2016 with 192 million users. *Cannabis sativa* (marihuana) contains principal psychoactive constituent as *trans-Δ⁹-tetrahydrocannabinol* (THC) and it has been used for recreational and medicinal uses from old Chinese, Assyrian and Roman literature.

THC is one of the constituents of the Cannabis, THC effects on cerebral cortex, basal ganglia, hippocampus, and cerebellum in which all have specific Δ⁹-THC receptors. Potential two endogenous compounds from THC; anandamide (N-arachidonoyl ethanolamine or arachidonoyl ethanolamide) and 2-arachidonoylglycerol (2-AG), lipoproteins “on demand” and activates two receptors; cannabinoid receptor-1 (CB1- receptor) and cannabinoid receptor-2 (CB2-receptor) and produces hypomotility, analgesia, catalepsy and hypothermia (Stromgaard, Krogsgaard-Larsen, & Madsen, 2009). THC in Marijuana causes euphoria, and pleasantly altered perceptions in recreational doses, but it slows thinking and impairs judgment. Its effects usually last 1 to 3 hours and heavy use can last symptoms for 1 to 2 days. Marijuana reduces REM sleep (Rapid Eye Movement sleep) too (Clinical Neurology for Psychiatrists, 2007).

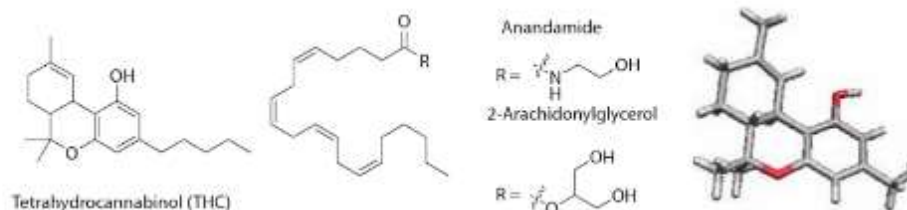


Figure 2.3 Plant Cannabinoid (THC) and two endocannabinoids structure (Stromgaard, Krogsgaard-Larsen, & Madsen, 2009)

Cannabis is still a widely used illicit drug in Asia Pacific Region and Myanmar had a stable trend of cannabis use in 2012. However, Cannabis herb seizures increased in 2016 with 188kg according to the 2017 INCB report of the International Narcotics Control Board (INCB). Cathinone and synthetic cannabinoids were mostly among 170 new psychoactive substances in the region between 2008 and 2016.

2.4.3 Benzodiazepines (BZD)

Benzodiazepines is a class of psychoactive drugs and enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the receptor (γ -Aminobutyric acid type A; GABAA), result in sedation, sleep-induced hypnotic effect, anxiolytic effect, anti-convulsant and muscle relaxant effect (Page C, 2002). The rate of action is associated with the ability to cross the blood brain barrier and peak blood concentration occurs within 1-3 hours. BZD effects can be potentiated with ethanol (alcohol) (Medscape, 2018).

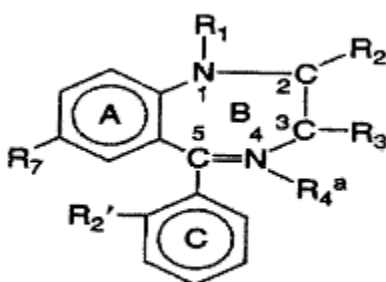


Figure 2.4 Structure of benzodiazepines (Stromgaard, Krogsgaard-Larsen, & Madsen, 2009) Chemical structure of Benzodiazepines: A) benzodiazepines (general formula)

The term benzodiazepine refers to the portion of the structure composed of a benzene ring (A) fused to a seven-membered diazepine ring (B). Benzodiazepines

contain a 5-aryl substituent (ring C) and a 1,4-diazepine ring, the term has come to mean the 5-aryl-1,4-benzodiazepines (Petrovic, Mariman, Warie, Afschrift, & Pevernagie, 2003).

Non-medical use of benzodiazepine is a problem in some countries in the region including Myanmar. It is also a noticeable drug abuse as non-medical use of benzodiazepine as one of the main drug use problems in 60 countries. Benzodiazepine causes increased risk of overdose when in combination with heroin (UNODC, World Drug Report 2018, 2018). Moreover, benzodiazepine is also involved in fatal overdose with use of opioid such as methadone. Methadone patients taking benzodiazepine experienced euphoria, drug liking, strength of drug effects, as well as reduced psychomotor performance, risks in driving or operating machinery, due to the delayed impairment in reaction time which of that effects peaked at 1–2 hours after dosing (Ghodse & Galea, 2009). So, this study included benzodiazepine in urine drug examination and history taking of drug use to understand more on illicit drug use issues among methadone patients.

2.5 Interventions for Drug Treatment

Opioid substitution therapy (OST) is an evidence-based intervention for opiate dependents which substitutes illicit opioid with medically prescribed, orally administered opioids such as buprenorphine and methadone. OST is a part of a comprehensive package of nine core interventions for Injecting drug users (IDU) programs endorsed by UNAIDS, UNODC and WHO that collectively maximize impact for HIV prevention and treatment (WHO U. U., 2012 Revision).

Recommended core interventions include:

1. Needle and syringe programmes (NSPs)