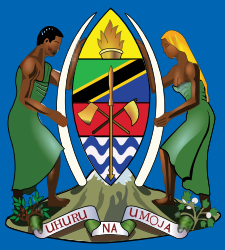


THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY AND CHILDREN

NATIONAL GUIDELINES FOR COMPREHENSIVE MANAGEMENT OF OPIOID USE DISORDER

July 2019

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY AND CHILDREN

NATIONAL GUIDELINES FOR COMPREHENSIVE MANAGEMENT OF OPIOID USE DISORDER

JULY 2019

Table of Contents

LIST OF ABBREVIATIONS AND ACRONYMS

UNODC	United Nation Office Drug Crime
HIV	Human Immunodeficiency Virus
PWUD	People Who Used Drug
PWID	People Who Injecting Drug
HCV	Hepatitis C Virus
HBV	Hepatitis B Virus
USD	United State Dollars
USA	United States of America
AIDS	Acquired Immunodeficiency Syndrome
PORALG	President's Office Regional Administrative and Local Government
NGOs	Non-Governmental Organization
CBOs	Community Based Organization
DCEA	Drug Control and Enforcement Authority
CSO	Civil Society Organization
WHO	World Health Organization
PMTCT	Prevention of Mother to Child Transmission
GBV	Gender Based Violence
STD	Sexual Transmitted Diseases
TAPP	Tanzania AIDS Prevention Program
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
MNMHH	Mirembe National Mental Health Hospital
MoHCDGEC	Ministry of Health, Community Development, Gender, Elderly and Children
TRRH	Temeke Regional Referral Hospital
MRRH	Mwananyamala Regional Referral Hospital
MDH	Management and Development for Health

FOREWORD

Substance use problems particularly Opioid Use Disorders such as Heroin, are known to cause the most harmful health, social and economic effects to individuals, families and communities at large. The United Republic of Tanzania is one among other countries in Africa with a significant number of people using and abusing illicit drugs. This may be due to availability of locally cultivated illicit drugs but also her geographical location which place it to be an important route for international drug trafficking where some drugs tend to remain behind for local consumption.

Upon realization of the extent of drug use problem and its burden in the health system; the Government of Tanzania through Ministry of Health, Community Development, Gender, Elderly and Children in collaboration with several key stakeholders made several responses to address drug use problem in the country.

This guideline has incorporated new research findings, lessons and experiences gathered throughout the implementation of methadone program in the country since its inception in 2011.

It is envisaged that, the guideline will be used as a reference by different stakeholders in the provision of service for Opioid Use Disorder particular those working in health facilities.

Dr. Zainab A. S. Chaula
PERMANENT SECRETARY (HEALTH)

ACKNOWLEDGEMENT

This Guideline was produced by the experience and technical inputs from Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC), Directorate of Curative Services in collaboration with Drug Control and Enforcement Agency (DCEA), Management and Development for Health (MDH), Muhimbili National Hospital (MNH), Muhimbili University of Health and Allied Sciences (MUHAS), Tanzania Aids Prevention Program (TAPP), Mirembe Mental Health Hospital (MMHH), Temeke Regional Referral Hospital (TRRH) and Mwananyamala Regional Referral Hospital (MRRH).

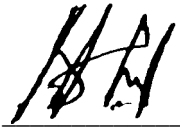
I would like to extend our gratitude to the Center for Disease Control and Prevention (CDC), which provided the financial assistance that facilitated development of this document.

Specifically, special gratitude is extended to the team of technical people whom without their tireless efforts this document would not have been realized; Dr. Sarah J. Maongezi, Dr. Omary Ubuguyu, Mr. Ambwene Mwakalobo, Mr. Florence T. Evaristi, Dr. Omary A. Nassoro, Dr Cassian Nyandindi, Prof Ayoub Magimba, Mr. Shadrack Buswelu, Dr. Eric Aris, Ms. Irene Macha, Dr. Jessie Mbwambo, Dr. Frank Masao, Ms. Zainab Mndeme, Mr. John Joseph Mwijage, Mr. Paul Mayengo, Dr. Dorothy Mushi, Mr. Philemon Kyara, Dr. Innocent Mwombeki, Dr. Norman Sabuni, Dr. Isack Rugemalira, Dr. Syangu Mkony and Ms. Elizabeth Fupe.

Further, special thanks are extended to the Department of Curative Services and entire management of the MOHCDGEC for valuable inputs,

Ms. Faith Makame and the administration team of MDH for the facilitation of all logistical arrangements throughout the process of producing this document.

I would also like to thank all those who have contributed in the revision of this guideline.



Prof. Muhammad Bakari Kambi
CHIEF MEDICAL OFFICER

DEFINITIONS OF TERMS

Opioid Use Disorders

Is defined by **ICD 10** as disorders related or resulting from abuse or misuse of Opioid.

DSM-V

Define Opioid Use Disorder as a condition related to two or more of the following within a 12-month period: (1) Using larger amounts of Opioids or over a longer period than was intended, (2)Persistent desire to cut down or unsuccessful efforts to control use, (3) Great deal of time spent obtaining, using, or recovering from use, (4) Craving, or a strong desire or urge to use substance, (5) Failure to fulfil major role obligations at work, school, or home due to recurrent Opioid use, (6) Continued use despite recurrent or persistent social or interpersonal problems caused or exacerbated by Opioid use, (7) Giving up or reducing social, occupational, or recreational activities due to Opioid use, (8) Recurrent Opioid use in physically hazardous situations, (9) Continued Opioid use despite physical or psychological problems caused or exacerbated by its use, (10) Tolerance (marked increase in amount; marked decrease in effect), (11) Withdrawal syndrome as manifested by cessation of Opioids or use of Opioids (or a closely related substance) to relieve or avoid withdrawal symptoms.

Opiate

Any of a group of alkaloids derived from opium poppy (*Papaver somniferous*) such as Morphine and Codeine including their other derivatives such as Heroin.

Opioid

A generic term applied to opiates and their synthetic analogues, with actions similar to those or Morphine, in particular the capacity to relieve pain

EXECUTIVE SUMMARY

National Guideline for Comprehensive Management of Opioid Use Disorder provides a framework and guidance for effective and comprehensive medical and psychosocial management of people with Opioid Use Disorders in Tanzania. This guideline shall be used by all health care providers working at MAT clinics and other stakeholders involved in provision of service for people with Opioid Use Disorder.

It is organized in chapters with sub-sections, figures and annexed materials to aid reader's understanding. The first chapter provides an overview, magnitude and consequences of Opioid Use Disorder and the national response towards addressing the problem of Opioid use. Further it describes the neurobiology of Opioid Use Disorders and the criteria used in formulating the diagnosis.

Scope and rationale of this guiding document is described in chapter two, where the goals are clearly explained.

MAT service in Tanzania is treated as a specialized service and has a specified model of delivering care to people with Opioid Use Disorders. Chapter three describes the various components that form the model of care for delivering methadone and other Opioid assisted treatments. Further, more emphasis is strengthened on the use of differentiated approach of care for people with Opioid Use Disorders in order to increase service uptake and provide quality of care.

Chapter four forms the backbone of the guideline and describes the management of Opioid disorders using different medications, their use and dosage, side effects, contraindications, interactions and management in various situations and special population.

People with Opioid Use Disorders tend to experience multitude of other co-occurring illnesses because of the nature of their illness. In some instances, Opioid use or use of any psychoactive drug may occur as a result of other physical illnesses. Chapter five describes co-occurring conditions and their management that program planners and providers should be aware of when providing MAT services.

Legal and ethical standards for provision of MAT services are described in chapter six while issues of monitoring and evaluations and safety measures are described in chapter seven and eight respectively.

CHAPTER ONE

1.1. Global, Regional and National overview of Opioid Use Disorders

Opioid is the third most abused psychoactive drugs in the world after cannabis and Amphetamines/Amphetamine Type Stimulants (ATS). According to 2018 world drug report, about 275 million people (approximately 5.6% of world population) aged 15 – 64 years used drugs at least once in 2016. Almost 31 million people who use drugs (PWUD) suffer from drug Use Disorders that warrant medical attention. The global concern now is on growing trend of increased abuse and trafficking of tramadol, Fentanyl and its analogues that reache 87 tons in 2016, which is similar to amount of Heroin seized in the same year[1].

In Tanzania, there is no recent data available for country estimates on people who use Opioid, however the latest country estimate done in 2014 showed that there are approximately **300,000** (range; 200,000 to 350,000) PWUD in Tanzania. The best size estimate for people who inject drug (PWID) was **30,000**, with a range of 20,000 to 42,500[2]. This growing problem of Opioid use particularly in urban towns and coastal areas has largely been fueled by drug trafficking activities as well as local manufacturing of illicit drugs.

1.2. Health and Socio-economic impact of drug use problem

1.2.1. Health impact

Problem drug use is associated with substantial health consequences. Opioids including Heroin, remain one of the most

harmful drug type as far as health is concerned. Opioids account for almost 76 percent of all death related to drug use. Nearly a half of 10.6 million people who inject drugs live with hepatitis and one in eight live with HIV[1].

In Africa, prevalence of HIV among Opioid injectors is 12.1 according to world drug report[3]. In Tanzania, the national estimates of HIV prevalence among PWUD and PWID is estimated to be 18-25% and 35% (22 – 43%) respectively, which is significantly higher compared to 5.1% of the general population[2]. Isolated findings from program data particularly methadone program data have shown prevalence of hepatitis C among Opioid injectors to be around 52.1% while tuberculosis infection in the same population is reported in the programs to be 14%[4].

1.2.2. Social and Economic Impact

Problems related to drug use have created significant social and economic instabilities among individuals, families and communities at large. Increased criminal activities, violence, morals and family disintegration, loss of jobs or education, homelessness and disruption of social support and relationships have been observed to cut across communities of people who use drugs. Governments or community authorities tend to incur substantial monetary costs in order to control drug problem such as; support affected families, conduct trials and/or incarcerate drug offence criminals depending on countries' prevailing laws as well as seize trafficked illicit drugs. In the United State of America over 200 billion USD is spent every year on drug related issues[2]. Treatment of people with Opioid Use Disorder is reported to be cost effective as compared to supply reduction

measures. According to National Institute of Drug Abuse USA, treating one person with methadone-assisted therapy annually is cost approximately $ 4,700, whereas imprisonment would cost approximately $24,000 per person per year[5].

1.3. National Response of Drug use problem

National response of drug use problem started to be implemented in early 2000s following growing problem of drug use in the country. Global concerns, local studies and anecdotal finding that were present at that time pressured the government and various stakeholders to convene efforts that aimed to reduce demand for drug use and related health and socio-economic problems. The first official action to be implemented was development of Drug Control Act 5 of 1995 which led to the establishment of Drug Control Commission (DCC). The DCC mandate was to oversee drug problem in the country through multi-sectorial coordination and sensitization of stakeholders within and across the country to respond to the same[6]. There were several legal amendments of the Act and other legal documents to support implementation, but the latest change of the Act to The Drug Control and Enforcement Act No. 5 of 2015 aimed to improve existing drug control measures and led to the establishment of Drug Control and Enforcement Authority[7].

The actual response towards Opioid use problem started in the early 2000s and was precipitated by series of research done by professionals within the country and across. Study findings of the interface of HIV and Drug use through risky injecting practices were alarming to both the government and stakeholders locally and internationally. Higher incidences of HIV and other blood

born infections were reported in different studies done at different time and places[8]. In 2004, study indicated HIV was 31.3% among people who inject drugs while in 2006, another study indicated it escalated to 42% while that of general population was 5.8%[9, 10].

As a result of this alarming spread of HIV and recognizing the inter-link between PWID and the general population, it was necessary for the government and allied stakeholders to launch a quick intervention program that targeted PWID and their networks. Medically Assisted Treatment with methadone medication was therefore launched as the first pilot project that aimed to prevent HIV infection among PWID. Ministry of health, DCC and Muhimbili National Hospital through department of psychiatry pioneered the process and still work in collaboration to expand services to reach more drug users across the country as a result of successful outcomes of the pilot project[11, 12, 13]. Currently there are 6 methadone clinics (3 in DSM and the rest are in Mbeya, Mwanza and Dodoma). Services in these clinics are supported by several community-led civil organizations.

The initiation of MAT services led to the development of several documents and research projects that evolved the program significantly and warranted expansion of MAT services to other regions of the country with higher estimates of drug use problem. Some of the documents are; Minimum Standard for Health facility providing medically assisted treatment of Drug Dependence, Guideline for Medically Assisted Treatment for Opioid dependence in Tanzania[14, 15].

Most recent clinic data gives a total of 5871 people with Opioid Use Disorders utilizing MAT services[4].

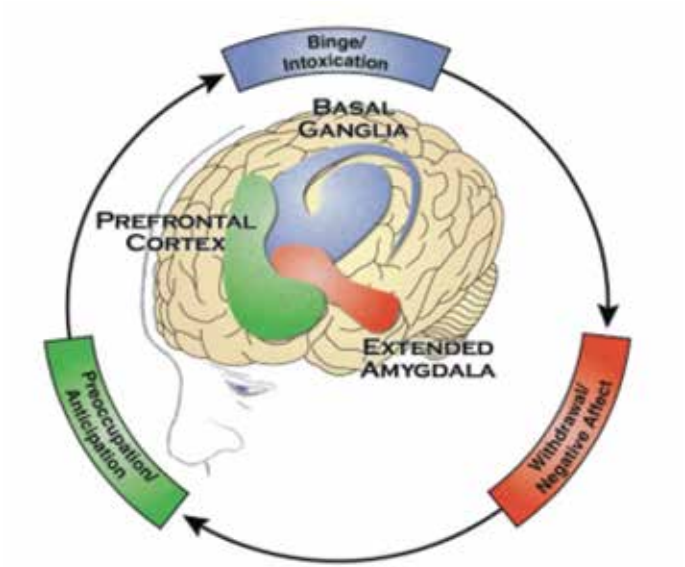
1.4. Basic facts About Opioid Use Disorder

According to the *"Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM 5)* Opioid Use Disorder is described as a problematic pattern of Opioid use leading to clinically significant impaired control, social impairment, risky use and pharmacological changes. It ranges from mild to severe form in which the mild form may include misuse and dependence or addiction being the severe form. In most cases Opioid Use Disorder is a chronic, relapsing brain disease that is characterized by compulsive Opioid seeking and use, despite harmful consequences. It is a complex disorder with mechanisms affecting the brain and its capacity to control use of substance. There is no known cause for substance Use Disorders; however there are many factors attributing to this condition[16].

1.4.1. Neurobiology of Opioid Use Disorders

Opioid acts on brain cells and affect the central nervous system. This lead to altered perception of reality as a result changes person's behaviors such as mood, thoughts or sensory perceptions.Once Opioid are taken most of it enter the brain within seconds and attaches to Opioid receptors in the brain cells, where they release signals that muffle perception of pain and boost feelings of pleasure. This powerful rush of pleasure that lasts for few minutes or an hour drives users to repeat drug taking in an attempt to recollect the transitory pleasure state. Opioid mimics natural neurotransmitters hence interfere with the way neurons send, receive and process signals and normal communication between neurons. Repeated use of Opioids continue to interfere with normal brain functions hence causing restructuring of brain circuit in various areas of the brain leading to abnormal signaling.

Fig. 1a : The three stages of addiction cycle



Alteration in functions of important brain areas such as prefrontal cortex, amygdala and basal ganglia can drive the compulsive drug use that marks addiction. Severely affected functions include motivation and rewards circuit functions of the basal ganglia, emotional experiences leading to irritability, anxiety or sadness which are controlled by amygdala and the ability to plan, think and make decisions which are controlled by the prefrontal cortex[17, 18].

Effect of drugs on these brain areas attributes to the concept of three stages of addiction cycle which clarifies the whole concept of mechanisms of addiction and key areas for treatment and prevention strategies. The experiences occurring in all three phases explain signs and symptoms of Opioid Use Disorder at different level of severity[18].

These three stages are:-

1. **Binge / Intoxication:** at this stage individual consumes substance and experiences its rewarding or pleasurable effects. The rewarding effects of addictive substance makes individuals to use such a substance (eg. Opioid) more often and/or at higher dose than intended. Continuous use of addictive substances trigger changes on the way a person respond to stimuli connected with the use of those substances. Therefore whenever an individual is subjected to similar place, people or paraphernalia will trigger strong urge to use drugs, the phenomeno known as **incentive salience** which persist for longtime. This experience is the one of key issue in recovery as it can cause relapses. In another mechanisms, the effects of addictive drugs also extended to area of the brain which control habit formation hence continuous use may result in compulsive drug seeking behaviours.

2. **Withdrawal/Negative Affect;** The stage at which an individual experiences a negative emotional state in the absence of the substance. This stage is triggered by diminished effects of reward system and activation of stress system in the amygdala. Irritability, anxiety and physical symptoms such as pain, abdominal cramps, diarrhoea, palpitations and body malaise can be some of the presenting symptoms during withdrawal state.

3. **Preoccupation/Anticipation;** the stage at which one seeks substances again after a period of abstinence. In this stage, prefrontal cortex is highly driven by environmental cues and drug habit forming and hence individual craving for substance grow big and big resulting in impulsive drug use.

1.4.2. Uses of Opioid

Opioids can be obtained naturally from the poppy plant (e.g. Morphine), semi synthesized (e.g. Heroin) or synthesized in a laboratory (e.g. Fentanyl, Methadone). They can be used as strong pain relieving agents, anesthetics and cough suppressants in hospital settings. Due to its strong pleasurable effects (euphoria), Opioid is one of the most abused drugs in the hospital and outside hospital settings. The most commonly abused, widely produced and smuggled Opioid globally is Heroin. It is normally taken through smoking, snorting or injecting. Risky practices such as unsafe injection may expose drug users to fatal overdose, infection of HIV, hepatitis C as well as other blood borne infections[19].

1.4.3. Risk for developing Opioid Use Disorder

The likelihood of developing Opioid Use Disorder varies from person to person. There is no single factor that determines whether a person will become addicted to Opioid. The more risk factors a person has, the greater the chance that taking drugs will lead to drug use problem and/or addiction. These factors can be widely determined by biological, genetical, psychological, social, cultural and environmental factors. Biological risk factors may include genetics, stage of development especially teenagers, as well as presence of mental disorders. Environmental factors such as childhood experience for example living with parents or family member who abuse drugs or alcohol, living in a chaotic family or experience abuse may predispose to risks of substance use. Having friends and other peers who use drugs or having difficulties at school including poor social skills may also become risk factors to substance use.

1.4.4. Factors protecting use of Opioid

Protective factors, on the other hand, reduce a person's risk. Some of protective factors may include having stable family, good social skill, presence of laws and regulations that prohibit or control availability and promotion of Opioids.

1.4.5. Diagnosing Opioid Use Disorder

Diagnosis is made using a set of symptoms in standardized diagnostic tools mainly ICD-10 and DSM V. According to DSM V criteria, for an individual to meet diagnostic criteria for Opioid Use Disorder, at least two of the following 11 criteria have to be met within 12-month period[16].

S/No.	DSM V - Diagnostic Criteria
Impaired Control	
1.	Opioids are often taken in larger amounts/ over longer period than intended
2.	Persistent desire or unsuccessful efforts to cut down or control Opioid use
3.	A great deal of time is spent in activities necessary to obtain the Opioid, or recover from its effects
	Craving, or a strong desire or urge to use Opioids
Social difficulties	
5.	Opioid use result in a failure to fulfill major role (at work, school, or home)
6.	Continued Opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of Opioids.
7.	Important social, occupational, or recreational activities are given up or reduced because of Opioid use

Risky Opioid use	
8.	Recurrent Opioid use in situations in which it is physically hazardous
9.	Continued Opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
Pharmacological Criteria	
10. Tolerance as evidenced by	
i.	A need for markedly increased amounts of Opioids to achieve intoxication or desired effect
ii.	A markedly diminished effect with continued use of the same amount of an Opioid.
11. Withdrawal as manifested by either of the following	
i.	Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms

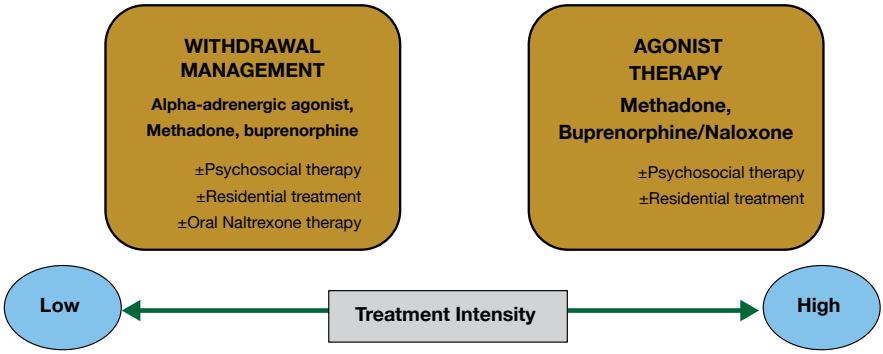
Severity depends on number of symptoms scores;
Less than 2 = no disorder, 2-3 = mild disorder; 4-5 moderate;
6 or more = severe

Other investigations necessary to confirm Opioid use and monitor treatment progress include urine drug screening for Opioid (UDS).

1.4.6. Management of Opioid Use Disorder

Management of Opioid User disorder is long term and may require a combination of medical and psychosocial treatment for better outcome. Treatment can be grouped in the spectrum of low to high intensity depending on the duration of treatment and combination of interventions (figure 1b below).

Figure 1b: spectrum of Opioid Treatment Services (ref.British Columbia - 18)



1.4.6.1. Withdrawal management Strategies (Detoxification)

This refers to treatment modality focusing on management of acute withdrawal symptoms resulting from abruptly cessation of Opioid use. When used as a stand- alone treatment modality, withdrawal management/detoxification is not effective treatment modality. It has shown to have poor outcomes in terms of retention to treatment, high risk of fatal overdose and increased risk to HIV[17]. In most cases it is recommended to be used with other treatment modalities especially psychotherapeutic counseling, contingency management or with adjunct oral naltrexone. Most of patients in residential treatment also use this mode of treatment. Alpha 2- adrenergic agonist such as clonidine, methadone or buprenorphine can be used depending on availability, client responses to treatment as well as conveniences of service provider[18]. Details on how this treatment modality works is further elaborated in section four.

1.4.6.2. Agonist Treatment

This mode is superior to withdrawal management in terms of retention to treatment, sustained abstinence from Opioid use and reduced risk of morbidity and mortality related to Opioid use. Methadone and Buprenorphine/naloxone are the most common agonist treatments used. In some settings slow release oral Morphine can also be used[20].

Regardless of type of treatment administered Opioid agonist treatment should incorporate: -

- Provider led counseling
- Long term substance use monitory (assessment, Urine Drug screening)
- Provision of comprehensive prevention and primary care
- Psychosocial treatment
- Access to specialized care for mental and physical health problems
- Access to legal, economic and social services

1.4.6.3. Opioid Antagonist Therapy

Naltrexone is the only Opioid receptor antagonist used to treat Opioid dependence. It acts by blocking the euphoric effects of Opioids and hence reduces craving and compulsive use of Opioid. It is available as oral medication, injection or patches with sustained release of naltrexone. Naltrexone injection and patches were reported to have good outcome in terms of relapse prevention, however there is increased risks of fatal overdose due to loss of tolerance[21].

1.4.6.4. Psychosocial treatment and support

Psychosocial support improves overall outcome of medical treatment for Opioid withdrawal. When used in combination to any of the medical management above it improves retention to treatment, reduce Opioid use during treatment and relapse preventions. There are numbers of psychotherapeutic interventions such as addiction counseling, contingency management, family therapy, group therapy and cognitive behavioral therapy (CBT). Community rehabilitation and restoration of social and occupational skills as well as reintegration of clients into his natural environment have significant treatment outcome[22].

1.4.6.5. Harm Reduction

Harm reduction is an intervention aimed to reduce adverse health, economic and social consequences of substance use. In most cases it provides additional interventions that focus to inform clients about risks and appropriate ways to reduce harm related to use of Opioid and/or other substances. Currently in Tanzania, there is only one organization that offers harm reduction services. These services include needles, syringes and other injection supplies, training of safe injecting practises and over- dose management and referral for overdose management[23].

1.4.7. Medically Assisted Therapy (MAT)

In Tanzania, MAT services currently use methadone for management of Opioid Use Disorders; however there are plans to include other available options in future. MAT services combines harm reduction, agonist therapy and comprehensive HIV, TB and Hepatitis services as co-located interventions within a tertiary

facility. All clients are linked with community organizations for continuous psychosocial services available at their communities. These includes reintegration with their families, income generating activities, peer led psychosocial interventions as well as legal and other social support services.

CHAPTER TWO

2.1 Scope and Purpose of this Guideline

This guideline is developed to provide guidance on effective management of Opioid Use Disorders in Tanzania. It builds on the existing policies, laws and standards necessary for establishment and maintenance of treatment services for Opioid Use Disorders.

2.1.1 Target Users of this Guideline

This guideline is intended to be used by providers working in MAT program and other interested stakeholders both government and non-government e.g. Ministries, departments and institutions, development partners, NGOs and CSOs, clients and community at large.

2.2 Objectives

The broad objective of this guideline is to provide comprehensive medical and psychosocial interventions for people with Opioid Use Disorders in Tanzania.

2.3 Specific Objectives

1. To strengthen effective management of Opioid Use Disorders
2. To provide management of co-occurring diseases.
3. To provide guidance on coordination of services in MAT program
4. To strengthen linkage and referrals of people with Opioid Use Disorders
5. To guide on reporting and quality care for comprehensive Opioid dependence treatment services

CHAPTER THREE

3. Delivery of MAT services

MAT services in Tanzania are delivered in public health facilities as an integrated service that includes both medical and psychosocial services. Currently Methadone is the only available medication for treatment of Opioid Use Disorders. Other medications such as buprenorphine and naltrexone are yet to be used in the country. However scientific evidences support use of these medications and hence should be made available for use in the country in future.

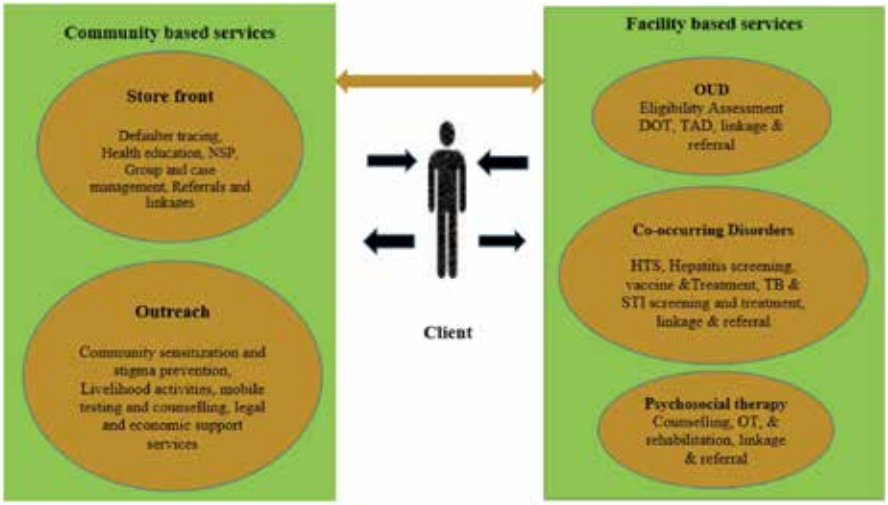
3.1 Model of delivering MAT services[4]

MAT services for people with Opioid Use Disorders requires continuum of care. Currently in Tanzania a range of client centered services are delivered both at the level of community and facility; and form a treatment delivering model for MAT services. Methadone forms a corner stone of MAT program and is delivered as directly observed treatment (DOT). Clients who are on DOT must attend clinic daily for medication usually between 5am and 12 noons. Due to long working hours, congestion of clients and other inconveniences, Take Away Dose (TAD) was introduced especially for stabilized clients, those with co-occurring medical and mental conditions needing hospitalization or those with higher methadone doses which requires split into twice daily. Special TAD can also be given for people needing to travel within the country for one reason or the other away from MAT facility.

Provision of MAT services encourages use of differentiated model of care approach which is client-centered i.e. allowing flexibility on service provision to improve accessibility and ensure quality of services provided. In this model stable clients are given less time to attend consultation and counseling sessions and more time is focused to less stable clients. The model focus on client's needs and allow multiple services to run in parallel to ensure quality of care. Example of differentiated model at MAT clinic may include having three dispensing models that is DOT, TAD and having satellite dispensing sites where clients may need to identify nearby facilities to obtain their methadone. Other example may include client being able to choose type of psychotherapeutic sessions he/she wants to attend between twelve steps facilitation, addiction counseling, or intensive psychotherapy like CBT.

The diagram below shows range of services that should be offered in MAT program. It indicates client flow plan from the community to the facility and back to the community. Program planners and providers are recommended to follow this model when considering provision of MAT services.

Fig. 2: Model of delivering MAT services for PWUD in Tanzania



a. Community based services

These are services targeting people with Opioid Use Disorders and the affected population. They should be operated as store front and outreach services. These services normally are; Health Education on drug use and co-occurring disorders, self-help groups which includes either PWUD themselves or affected members like families or both, case management or referral and linkages, defaulter tracing and Needle and Syringe program in authorized demonstration sites.

b. Facility based services

These are services targeting people with Opioid Use Disorders who are willing and eligible for provision of medically assisted treatment. They include management of Opioid Use Disorder

using pharmacotherapy, psychotherapy interventions and management of co-occurring disorders. Management of OUD at MAT facility typically includes the following services; assessment for eligibility, severity of substance use problems and other social and psychological problems using assessment tools and drug toxicology, medication dispensing, follow up visits, medical management for co-occurring disorders (HIV, TB, Hepatitis, STI and MI), linkage and referral for medical conditions and other social services including occupational therapy.

3.2 Integration of services in MAT program

Existence of co-occurring medical and mental health disorder among people with Opioid Use Disorder warrants MAT services to be integrated.

Services which are integrated follow a comprehensive package recommended by WHO/UNODC/UNAIDS for prevention, treatment and support among people who use drugs (PWUD) and National KVP guideline[24, 25].

Based on these guidelines and the Tanzania context experience, the following services should be integrated or linked to MAT program for successful program outcomes; Needle and Syringe program which is currently offered as a demonstration project; HIV testing services which include testing and counseling and linkage to care and treatment services for provision of Anti-retroviral drugs for those diagnosed to have HIV infection but also as pre-exposure prophylaxis (PrEP) and post exposure prophylaxis (PEP) for prevention; screening and treatment of tuberculosis, hepatitis B & C and sexually transmitted diseases; provision of targeted

information, education and communication materials; condom distribution for prevention of HIV infection; psychosocial support; treatment for mental health disorder; linkage and referral for other medical conditions; Overdose prevention and management; and support for special groups such as pregnant women, nursing mothers and their infants through integration of PMTCT, family planning and prevention of gender based violence[24,25].

Occupational therapy, creation of enabling environment and use of peers as a strategy to support interventions should also be integrated to support recovery of people with Opioid Use Disorder.

3.3 Optimization of MAT services

Services within MAT program needs to be optimized to enhance easy accessibility, uptake and adherence to program services. Strategies that need to be considered when thinking of optimizing MAT services include;

a. Low Threshold High Volume

Low threshold refers to removal of barriers that limit or delay access to MAT services. It requires services to allow referrals from any source including self- referral, however for self–referral provider is required to ascertain that client is withdrawing from an Opioid use through clinical examination and urine toxicology. Low threshold programs tend to make minimal demands on the patients while offering services without attempting to control their intakes of drugs.

High volume focuses on strategies designed to retain patient in services such as no mandated group or individual counseling, urine tests are scheduled and not random and results are not used punitively rather they are used to integrate the client in behavior change modification interventions. All MAT services in Tanzania should follow "Low threshold high volume" concept for better treatment outcomes.

b. Extended working hours

Opening hours for MAT services should be extended to allow flexibility in accessing services. Issues of employment or engagement in livelihood activities, family and social responsibilities such as nursing of young ones and special situations like pregnancy or breastfeeding should be considered when setting time for opening and closing of services especially the dispensing window for DOT services.

c. High Staff morale with non-judgmental attitude

MAT program should ensure staff have high morale and are non-judgmental towards clients in order to ensure high quality of care for people with Opioid Use Disorders. Staffs should observe and adhere to professional ethics for provision of MAT services. Activities that foster high staff morale are such as adequate staff number, low staff turnover and trainings; these have been shown to be associated with better treatment outcome such as client's retention to services. Non-judgmental attitude among staff is critical in provision of MAT services and should be used as a strategy of minimizing service dropouts.

d. Linkage and Access to other medical services

In order for MAT program to deliver continuum of care for people with Opioid Use Disorder, linkage and access to other services is mandatory. This document guides that allied medical services should be within a facility offering MAT services (i.e. co-located) or nearby preferably a walking distance to facilitate escorted referral.

e. Psychological and social welfare services

Recovery of people with Opioid Use Disorder requires psychosocial interventions along with medical services. These services should include counselling services, occupational therapy, legal and economic support.

f. Involvement of peers and the affected community

MAT program should ensure meaningful involvement of people with Opioid Use Disorder and the affected community at all level of care from designing, planning to implementation in order to optimize service uptake and retention to services.

3.4 Administration, management and Supervision

Effectiveness of MAT program requires good administration, management and supervision of services and resources at all levels of continuum of care. These include administration, management and supervision of equipment and supplies, data collection tools, services, human and material resources. All MAT services at all levels are required to report to relevant authorities as guided in the M & E section. Publication and report dissemination to stakeholder should be among activities implemented within MAT programs.

CHAPTER FOUR

4. Management of Opioid Use Disorders

Combined interventions are the most effective approaches in comprehensive management of Opioid Use Disorders. They help to reduce or stop Opioid use; improve well being and psycho-social functioning as well as preventing relapses, overdoses and subsequent deaths. MAT program should therefore provide both pharmacological and non-pharmacological interventions[26].

4.1. Pharmacological Management of Opioid Use Disorder

Recommended pharmacological management of OUD should include use of the following treatment options:

i. Opioid Agonist for maintenance Therapy

a. Full Opioid agonists for maintenance therapy (i.e. methadone)

b. Partial Opioid agonists as maintenance therapy (i.e. buprenorphine)

ii. Management of Withdrawal symptoms

a. Opioid Agonist for Management of Opioid withdrawal (Methadone and Buprenorphine)

b. Alpha-2 adrenergic agonists for management of Opioid withdrawal (i.e. clonidine)

iii. Opioid antagonists for Opioid relapse prevention (i.e. naltrexone)

iv. Opioid antagonists for managing Opioid overdose (i.e. naloxone)

4.1.1. Treatment of OUD using Methadone

Methadone is the most widely available medication for treatment of OUD and has been shown to be effective and safe for more than 40 years[26]. It is the treatment of choice for OUD by many countries. Methadone has been successfully used in Tanzania to treat people with OUD since February 2011 and has remained the only available pharmacological medication since that time.

a. Pharmacology of Methadone

Methadone is a synthetic pure Opioid agonist with good oral bioavailability, and when taken by mouth, more than 86% of it reaches the blood system. It works by blocking the euphoric effects of other Opioids without producing euphoria itself. It is administered once daily due to long half life in the blood circulation of about 24 to 36 hours. Due to its long half-life, a steady-state of methadone blood level is achieved between three to five days after starting a new dose. After reaching a steady state, a single daily dose is able to maintain constant blood levels and suppressing the withdrawal symptoms from Opioids for more than 24 hours.

Methadone is predominantly metabolized by the liver enzymes cytochrome P450 and converted to inactive metabolite which is excreted in the urine. Since it is a lipid soluble medication, it can also be secreted in breast milk and umbilical cord plasma[27].

b. Drug/food interactions with Methadone

Methadone may interact with other drugs or food substances due to their synergistic or antagonistic effects. Presence of one drug/food may affect its absorption, distribution, metabolism or elimination of methadone. Concurrent use of methadone and

other drugs/food substances may induce or inhibit cytochrome P450 enzymes; hence potentials for drug/food interactions should be evaluated at all time when using methadone. A list of common drug/food interactions that should be evaluated during provision of MAT services is attached in *Annex 2.*

c. Methadone Unwanted effects

Use of methadone, like other Opioid such as Heroin, may lead to experiences of different types of unwanted effects such as constipation, drowsiness, lack of concentration, reduced libido or sexual dysfunction, suppression of cough reflex, urine retention, itching, flushed skin, dry mouth, hypothermia etc. Therefore, interventions of unwanted effects should be done properly as they can reduce the client's adherence to MAT program. Management of these unwanted effects should be achieved without compromising the maintenance treatment dose of methadone.

Methadone alone or in combination with other medications that prolong QT interval in the ECG assessment should be used with caution, as they may further increase the risk of QT prolongation leading to cardiac arrhythmias and death. However, compared to methadone, buprenorphine does not appear to produce clinically significant prolongation of the QT interval. Annex 2 also provides a list of some medications/conditions that are known to prolong QT interval[28, 29].

d. Treatment Precautions with Methadone

Methadone should be dispensed with precautions in patients with severe hepatic, renal or respiratory insufficiency, cardiac dysfunction as well as known hypersensitivity to Methadone.

e. Methadone Treatment Phases

The provision of methadone for individuals with Opioid Use Disorders should be divided into four phases that are initiation, stabilization, maintenance and termination phases.

i. Initiation Phase

Clients shall be initiated methadone treatment once they have completed baseline clinical assessments and are concluded eligible for receiving MAT services. The initial dose of methadone should range between 5 and 30mg on the first day of treatment based on the clinician assessment. No more than 30mg can be administered to a client on the first day. Clients deemed physically unwell, those with co-occurring disorders and those who are clinically weak, should start methadone at the lowest possible dose compared to those who are physically stable.

ii. Stabilization Phase

The aim of stabilization phase is to increase the dose of methadone until when Opioid withdrawal features are successfully controlled. The phase shall be attained between two to eight weeks from treatment initiation, although some clients may take longer period of time. Dose adjustments should range from 5-30mg per each visit which normally takes 3 to 5 days from the last visit. The key principle for dose prescription is “start low - go slow”. However, this principle may not always be the case as rapid increase of methadone dose is warranted to some clients (i.e. when clients use medications that lower serum levels of methadone e.g. clients on ARTs or anti-T.B treatment, pregnant women in severe withdrawal etc.). The rapid increase should not be less than 24 hours of dose adjustment and should be done thoroughly in order to minimize risks related to Opioid overdose and other complications.

Criteria for dose adjustment should include both objective and subjective findings, which are Opioid withdrawal features as determined by COWs tool (*see Annex 3*), reports of continued use of Opioids and/or testing positive for Opioids on UDS, persistent cravings for Opioids (e.g. drug dreams, intrusive thoughts, etc.), excessive drowsiness and other features of Opioid overdose. Continuous assessments of mental health functioning of the clients are imperative and should be conducted prior to dose adjustment as some symptoms of anxiety and depression mimic the Opioid withdrawal features[30].

iii. Maintenance Phase

Maintenance phase should be achieved when a client has reached an optimal dose of methadone and is clinically stable. Usually, it takes two to eight weeks from methadone initiation until this phase is attained. Clinical stability can be shown when the client reports that subjective and objective withdrawal features related to Opioid use are eliminated and problematic substances or alcohol uses are well managed.

Once stability is reached, the client should be planned to remain on treatment for a minimum of two years. It is generally known that the longer the clients stay on MAT program the better the outcome; hence clients must be encouraged to stay on treatment for as long time.

In Tanzanian setting, the majority of clients should be maintained at a methadone dose ranging from 80-120mg once daily although a few have been maintained at very low (10mg per day) or very high doses (500mg per day). The health care providers should remain aware of the facts that higher doses of methadone (>80

mg) result in better retention to treatment than lower doses (<60 mg). Methadone at higher levels of 300mg and above should be split into twice daily in order to minimize the unwanted fatal effects.

Routine monitoring of clients during maintenance phase should be a mandatory practice as a clinical aid for safe prescribing, dosing and successful treatment outcomes. It should be done through client's self-report, information from relatives/peers, urine drug screening, alcohol breathalyzer test and clinical observation. Thorough clinical reassessment to establish the reasons for continued substances use while on treatment should be conducted in order to guide proper and relevant interventions. It should be conducted at 6th, 12th and 24th months of treatment same clinical assessment tools.

iv. Termination from Methadone Treatment

Termination from MAT program should either be voluntary or involuntary depending on circumstances or needs of the client. During termination from treatment, tapering of methadone dose should be given a priority to minimize possible unwanted effects of Opioid withdrawal features.

a) Voluntary termination

from methadone treatment is warranted to clients who have been on medication for not less than two years and have demonstrated significant physical, mental, social and behavioral improvements. The decision to withdraw voluntarily from treatment should be shared between client and health provider in order to minimize risks of relapse from Opioid use.

b) Involuntary discharge

from methadone is given to clients who have shown evidences of causing harm or threats to other clients, staffs and properties. Usually it is a mandatory procedure done by a team of service providers after they have gathered sufficient information about client's misconduct and reached a satisfactory decision that the client should be removed from the program. At all time service providers should seek other options to help the client remain in the program rather than removing the client from the program e.g. transfer to another clinic or suspend for a short time to attend behavioral modification programs.

v. Principles of termination of methadone treatment

Long term use of methadone may cause physical dependence. Hence to avoid withdraw symptoms, termination should not be done abruptly as this may lead the client to relapse from Opioid use and avert the benefits of treatment outcomes. Gradual tapering is advised when cessation from methadone is considered, however in some situation it may not be the case. The following are principle of termination of methadone in MAT program:-

a) Gradual tapering

of methadone dose is warranted to minimize unwanted withdrawal effects hence slow tapers must be encouraged whenever possible. A minimum of 12 months is highly recommended to complete slow tapering process for clients who are discharged on voluntary basis. Under voluntary discharge plan, no client should be discharged if they are not willing to exit even if their methadone dose is 1mg /day.

b) Rapid tapering

from treatment should be donein a situation where clients are unable to gradually reduce their methadone dose (i.e. impending incarceration, long time travel where methadone services are not available etc.). Rapid dose reduction should be done in a period of not less than 21 days. When a client is rapidly removed from medication, principles of withdraw management should be adhered.

i. Abrupt cessation

is a type of rapid tapering where methadone cessation is very sudden. Usually it is done when the client is unable to continue with methadone program (e.g. serious threats to others, urgent travels where MAT services are unavailable etc.). In this situation, supportive treatment is mandatory in order to reduce cases of severe withdrawal symptoms. Medical detoxification or withdraw management should be offered for symptomatic treatment of Opioid withdrawal features.

i. *When consensus to withdraw client (voluntarily or involuntarily) from the treatment program is reached, the best methadone cessation approach must be planned to minimize unwanted withdrawal effects and reduce the risks of relapse into Opioid use. Methadone treatment cessation should therefore be conducted through gradual, rapid or abrupt cessation methods depending on the aim of termination from MAT treatment.*

ii. *Tapering of methadone dose above 120mg/day should be reduced at a rate between 30mg to 20mg per every 4 weeks. If the dose is between 120mg and 80mg/day, tapering rate should be between 20mg to 10mg/day per every 4 weeks. When the dose is between 80mg and 30mg/day, tapering rate has to be between 10mg to 5mg per week while the dose below 30mg/day, should be tapered at a rate of 5mg per every 4 weeks. Clients who have reached a dose level of 5mg/day should now be discharged from the methadone treatment if they are comfortable. Should they complain of Opioid withdrawal features once discharged at a 5mg/day, further tapering should be done at a rate of 1-2mg per every two weeks until when they are free of withdrawal features.*

vi. Readmission into MAT Treatment

When relapse occurs after voluntary termination from treatment, and clients are seeking readmission into treatment program after relapse, they should be admitted without intimidation. So long as the client is clinically suitable and eligible for treatment, there should be no barriers for readmission after leaving the program.

vii. Follow-up and Aftercare

Follow up of clients who successfully completed methadone treatment, should be conducted at MAT clinic for at least 12 months. During this time, clinical evaluation, drug toxicology tests and psychosocial services should be offered to the client at least quarterly. After care is an ongoing process and should be offered at the facility and community to complement the continuum of care approach for management of people with Opioid Use Disorders. Records and contacts of the clients and their supportive networks should be maintained both at the facility and community program data base at all time.

d. Consideration for Special Groups

MAT program in Tanzania consider clients who are female, pregnant women, nursing mothers, adolescents and neonates to be special due to their vulnerability, hence should be given special attention when methadone provision is considered.

i. Women

Female drug users often tend to be sexually and physically assaulted by various population groups in the community, hence it is recommended that MAT programs should have gender based violence policies in place in order to protect female clients. Additionally, methadone may increase the potential for fertility among female Heroin users of reproductive age, hence should be informed about the possibility of getting pregnant and counselled about use of contraception in case they are not ready.

ii. Pregnant clients

For pregnant clients, the dose of methadone should be titrated according to their needs. Providers should be mindful that methadone is a lipid soluble medication; hence its presence in the blood once taken orally can cross the placenta barrier. Therefore, pregnant women who are taking methadone should be educated about the potential risks of methadone to their newborn during ANC or MAT clinic visits.

iii. Neonates

All neonates born by a client on methadone treatment should be assessed for presence of withdraw symptoms "neonatal abstinence syndrome (NAS)" using Modified Finnegan Scale *(See annex 4)* within 2 hours of delivery. Assessment should be done by a team of providers from MAT and neonatology/paediatric unit in order to ensure early diagnosis and treatment of withdrawals[31, 32].

Management of Neonatal Abstinence Syndrome

For neonates with average scores of more than 8 for three consecutive modified Finnegan scale, dose of Morphine syrup should be given as follow; 0.04mg/kg every four hours but not exceeding 0.1mg/kg. Once the neonate is stabilized for three to five days, the dose should be gradually tapered by 10%every other day and discontinued when the total single dose is less than 0.08mg. During Morphine therapy, the neonate should be treated as inpatient in postnatal ward with her mother or in neonate ward in case there is other related complication.

iv. Nursing Mothers

All clients who are breastfeeding should be given first priority during MAT clinic visits. For those clients whose babies are admitted due to NAS or any other reasons, methadone dose should be dispensed in their wards as timely as possible.

4.1.2. Treatment of Opioid Use Disorders using Buprenorphine

Buprenorphine is an Opioid partial agonist. This means that, like other Opioid, it produces effects such as euphoria or respiratory depression though the effects are weaker than those obtained from full Opioid agonists such as Heroin.

Buprenorphine as a sublingual tablet contains buprenorphine hydrochloride available in 2 mg and 8 mg strengths. Fixed dose combination of buprenorphine and naloxone is also available at the ratio of 4:1. The tablets are administered sublingually because of poor oral bioavailability (they are inactivated by gastric acid and have a high first pass metabolism). It can be affected when taken with acidic drinks such as citric acid as well as coffee. Because buprenorphine is a long-acting agent, many clients may not necessarily have to take it every day. The Opioid effects of Buprenorphine increase with each dose increment until when the dose stabilizes and becomes steady even with further dose increment. This "ceiling effect" lowers the risk of misuse, dependency, and unwanted effects[33, 34, 35].

The buprenorphine/naloxone tablet is designed to decrease the likelihood that people will dissolve and inject buprenorphine. When client with Opioid Use Disorder takes a buprenorphine/naloxone tablet sublingually, will predominantly get the buprenorphine

effect while when dissolves and injects the tablet, client will predominantly get the naloxone effect that precipitates Opioid withdrawal. Clinical and laboratory monitoring of the clients on buprenorphine should be done similarly to clients on methadone.

Buprenorphine should be used for Opioid Use Disorder in situations where use of methadone has failed or where contraindications exist such as clients with prolonged QT interval secondary to methadone treatment or any other cause, clients with respiratory depression, acute bronchial asthma, also clients who are unable to tolerate or are hypersensitive to methadone. Treatment of Opioid Use Disorder with buprenorphine is most effective when provided in combination with counseling services, which can include different forms of behavioral therapy and self-help programs.

Treatment with Buprenorphine should be provided in three phases namely initiation, stabilization and maintenance phase as described in fig 4.

i. Initiation phase

This is the medically monitored startup of buprenorphine treatment that should be performed in MAT clinic using approved buprenorphine products. The medication is administered when a person with an OUD has abstained from using Opioid for 12 to 24 hours and is in the early stages of Opioid withdrawal. It is important to note that buprenorphine can bring an acute withdrawal for clients who are not in the early stages of withdrawal and who have other Opioids in their bloodstream.

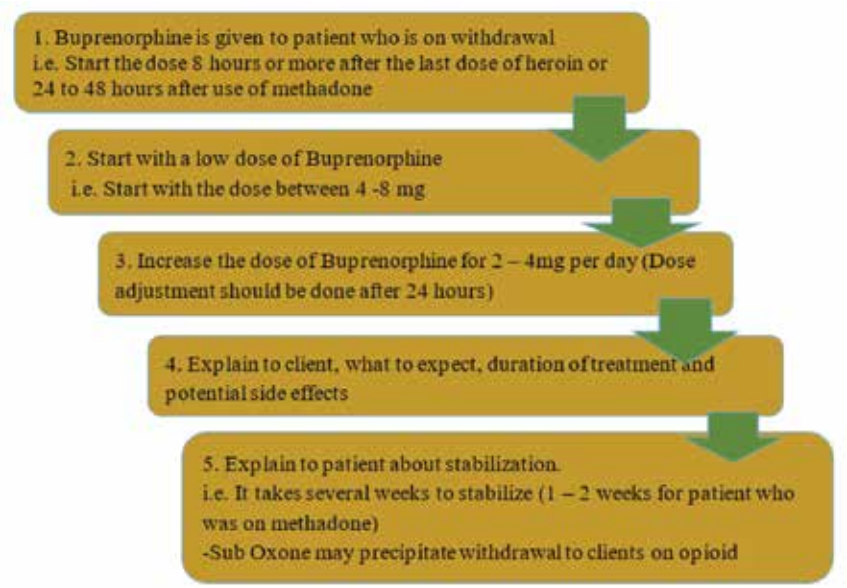
ii. ***Stabilization phase***

The second phase of buprenorphine therapy should begin after a client has discontinued or greatly reduced their use of Opioid, no longer has cravings, and experiences few, if any, unwanted effects. The buprenorphine dose should be adjusted during this phase by increasing the dose slowly to attain maximum effects of controlling Opioid withdrawal and craving features. Because of the long-acting effects of buprenorphine, once clients have been stabilized, they can sometimes switch to alternate-day dosing instead of dosing every day.

iii. Maintenancephase

This is the third phase which should occur when a client is doing well on an established steady dose of buprenorphine. The length of time of the maintenance phase is tailored to each client and could be indefinite. Once an individual is stabilized, an alternative approach would be to go into a medically supervised withdrawal, which makes the transition from a physically dependent state smoother. Clients then can engage in further rehabilitation, with or without MAT, to prevent a possible relapse.

Figure 3: Treatment of OUD using Buprenorphine



4.1.3. Management of Opioid withdraw using Clonidine

Clonidine is marketed for the treatment of hypertension and attention deficit hyperactivity disorder (ADHD). Because of its α-adrenergic agonistic effects, clonidine is also an effective agent for management of withdrawal from Opioids.

Indication

Clonidine is used to decrease signs and symptoms of excessive autonomic activity such as anxiety, tachycardia, chills, pilo-erection and hypertension; hence it can be used to manage acute Opioid withdrawal features, although it is not curative for Opioid disorders.

Dosage

Clonidine in a tablet form is started on 0.1 to 0.2 mg every 4 hours while clients are being monitored for bradycardia and/or hypotension. Over the next several days, the doses should be adjusted depending on the withdrawal symptoms a client is experiencing. By the end of the week, any signs of withdrawal from Opioid use should start to subside. Once this happens, clients should be tapered off from clonidine doses until it is no longer needed[36].

Side Effects

Detoxification with clonidine roughly takes seven days, during this time close monitoring of blood pressure and pulse rate is mandatory. Hence it is most effective when used in an inpatient setting to avoid unwanted side effects. Some of the common unwanted effects that clients should be informed and assessed include vomiting, body weakness, headache, and constipation. Other, but rare unwanted effects of clonidine include pimples, rashes, swelling, irregular heartbeats, mood changes, and difficulty in breathing. Some individuals have also become dependent on clonidine

Interactions

Some drugs may cause adverse effects when used with clonidine while clonidine can also negatively impact some of the drugs prescribed to clients. Therefore, before clonidine is administered, MAT providers should talk to clients to elicit any medication that are currently used so as to minimize the risks related to clonidine interaction. Some of the drugs known to interact with clonidine include different types of antihypertensive and medications for managing cardiac disorders, antidepressants, sleeping pills, medications for managing anxiety and antiepileptic medications.

4.1.4. Opioid Relapse Prevention using Naltrexone

Naltrexone is an Opioid antagonist which works by blocking the Opioid receptors; Hence when taken together with an Opioid the usual euphoric effect 'High' is not felt. Furthermore, naltrexone decreases the general urge to use Opioid and therefore helps to maintain abstinence from Opioid use in highly motivated clients. It is most effect when used with cognitive behavioral therapy.

Dosage

Naltrexone is available in 50-mg tablets and is taken once daily. Its effect last within 24 to 36 hours and it should only be given to clients who are free of Opioid withdrawal features. Therefore Opioid detoxification should precede naltrexone initiation. Extended-release injectables of 380mg used once monthly are also available and are particularly useful for clients in an outpatient rehabilitation program. Duration of treatment with naltrexone varies, however most clients would require at least six months.

Side Effects

Unwanted effects of naltrexone include gastrointestinal upset, fatigue, and insomnia, as well as elevated levels of liver enzymes when taken at higher doses. It is important to note that naltrexone decreases tolerance to Opioid, hence poses greater risk for Opioid overdose during relapse. Providers should inform clients of this risk in advance.

4.1.5. Management of Opioid Overdose using Naloxone

Drug overdose refers to ingestion or use of a drug or other substances in quantities greater than what can be can be tolerate by an individual leading to complications that may precipitate death. Common overdose signs include; shallow breathing, reduced heart rate (bradycardia) drowsiness, loss of consciousness and tiny or constricted pupils. The risk of overdose increases in the following situations; concurrent use of other depressants such as alcohol or substances which potentiate effect of Opioid or other depressants; reduced tolerance due to long term abstinence; chronically ill people especially those with liver problems; older or very young aged clients. Naloxone is an antidote that rapidly reverses the respiratory depression, bradycardia and hypotension associated with overdose.

Management of overdose with naloxone starts with resuscitation of airway, breathing and circulation (ABCs) which may also include providing mechanical support ventilation for clients who present with signs of hypoxia. This is then followed by a thorough clinical evaluation to ascertain cause of overdose and establish management plan. During this time provider should continue to monitor vital signs i.e. temperature, pulse rate, respiratory rate, blood pressure, urine output and oxygen saturation.

Naloxone is administered as a bolus intra-muscularly or intravenously. Initial dose is 0.4-2 mg and can exceed up to 10mg per day. If client still does not respond re-assess and establish possibilities of other causes. Discontinuation of naloxone is dependent on whether the client has responded or maximum daily dosage has been reached with no success. Duration of action of naloxone is 30 to 60 minutes depending on route of

administration. Treatment of the methadone-overdosed client should require serial dosing of naloxone every 20 to 60 minutes because the toxic effects of this long-acting opiate recur. The client must be carefully observed following the termination of naloxone therapy to detect any reappearance of Opioid overdose. An intravenous infusion of naloxone should be appropriate if high doses are needed or if the patient has recurrent respiratory depression. Naloxone can also be available as a nasal spray commonly designed to be used as an antidote in community settings.

Naloxone crosses placenta barrier, hence if given to pregnant women who are overdosed with methadone can precipitate severe Opioid withdrawal symptoms to fetus and the pregnant woman. Therefore it should not be given as an antidote for Opioid overdose. In cases of overdose, stabilize the client and her fetus first before transfer to Intensive Care Unit (ICU) while keeping close monitoring of the fetus to avert fetal distress and premature delivery[37, 38, 39, 40].

4.2. Psychosocial Management of Opioid Use Disorder

This is an umbrella term that covers an array of non-pharmacological interventions for effective management of Opioid use. Psychosocial interventions help address motivational, psychological and environmental factors that contribute to use of Opioid. They enhance pharmacological treatment efficacy by increasing adherence, retention in treatment, and acquisition of skills that reinforce the effects of medication. This helps promote abstinence and relapse prevention.

Type and intensity of psychosocial interventions to be administered depends on individual needs and findings from assessment of the patient, stage of recovery as well as competencies of providers on the type of therapy. Some of the most recommended psychotherapies on management of Opioid Use Disorders include individual counseling, contingency management, cognitive behavioral therapy, twelve step facilitations and various forms of group therapies. Psychoeducation, brief interventions, motivation interviewing, occupational therapy and other forms of social interventions are also very important for successful recovery program.

a. Brief Interventions

It is a technique used to initiate change for unhealthy or risky behavior such as Opioid use. The aim is to identify current or potential problems with Opioid use and motivate those at risk to change their substance use behavior. In primary care they can range from 5 minutes of brief advice to 15-30 minutes of brief counseling.

b. Motivational Interviewing (MI)

This is a directive, patient-centered counseling style that enhances motivation for change by helping clients to clarify and resolve ambivalence about behavior change. To increase the person's intrinsic motivation based on the person's own personal goals and values. Motivational interviewing is the process of helping an individual move through the stages of change, which includes: Pre-contemplation, contemplation, preparation, action and maintenance.

c. Cognitive Behavioral Therapy (CBT)

This is the most researched psychotherapy in the management of substance Use Disorder. CBT is intensive individual sessions covering up to 12 sessions conducted on weekly basis or more. In management of Opioid Use Disorder CBT is used to explore consequences of substance use resulted from dysfunctional pattern of thinking to maladaptive behaviors hence help individual gain initial skills to maintain abstinence or in reducing their drug use, develop coping skills such as self-monitoring and craving recognizing coping skills. It has proven to have good outcome even in an individual with co-occurring mental disorders.

d. Behavioral therapies

It's a psychotherapy that seeks to extinguish or inhibit abnormal or maladaptive behavior by reinforcing desired behavior and extinguishing undesired behavior. This approach includes behavioral contracting where clients have opportunities to earn rewards for a specific desirable behavior.

i. Individual and Group Counseling

Individual counseling is very useful intervention in addiction treatment. It helps client ***to be aware of substance use problem and develop strategies to learn new behavior,*** cope with craving and better understanding of individual attributes predisposes to OUD. Individual counseling has shown to be very effective as compared to group counseling in terms of abstinence from Opioid use, retention to treatment and sustained recovery. Group therapy is always offered to individual who attend other form of individual therapies, when provided alone, group therapy shown no significant outcome on retention and sustained recovery.

ii. Contingency Management

This is a type of psychotherapy that uses incentives to enhance learning of new behaviors. In this intervention a tangible reward is given to individual has shown positive behavior changes such as participating in all treatment sessions as planned, sustained drug free UDS tests or punctuality at the clinic sessions including dispensing sessions. CM is not commonly practiced in our settings, however in some few clinics individuals who are doing better on their treatment are assigned duty to supervise other clients and given some token which act as tangible rewards. Most of these clients continue to do better to maintain their status as well as to ensure they continue to get incentives. Contingency management is very important in maintaining desired behavior and hence sustained recovery. This intervention work best when combined with other psychological intervention.

iii. Twelve-Step Facilitation Therapy

This is the most popular form of self-help group, which is performed in most of addiction rehabilitation centers and other treatment settings in the world. This intervention consists of a brief, structured and manual-driven approach to facilitating early recovery from alcohol abuse/alcoholism and other drug abuse/addiction. It is implemented on an individual basis in 12 -15 sessions and is based in behavioral, spiritual and cognitive principles that form the core of 12-step fellowships. TSF seek to facilitate two general goals in an individual with alcohol or other drug use problem; acceptance of the need for abstinence and surrender or the willingness to participate actively in 12-step fellowships as a means of sustaining sobriety. MAT clinics and community organization should provide access to TSF or link clients the facilities which provide such kind of services.

e. Social interventions

Addressing social issues is very important for successful recovery. Some of these issues may be addressed during psychotherapeutic and counseling sessions. However, addressing social re-integration and stigma reduction may need deliberate effort on community engagement, advocacy and awareness creation. With this regard, all MAT clinics should work with NGOs/other agencies or departments that works directly into the community where clients are coming from to ensure that there is satisfactory level of clients' engagement in community. Whenever possible outreach and community sensitization meetings, dialogues and organized events should be planned for better outcome.

Clients should also be engaged or encouraged to participate on income generation activities through restoration of lost skills, training new skills and given opportunities to participate in skilled and non-skilled jobs. Other social services such as legal, employment, school opportunities may be available through linkages to other service providers therefore all MAT facilities should link clients with appropriate service providers.

CHAPTER FIVE

5. Management of co-occurring disorders

HIV, hepatitis, tuberculosis and co-occurring mental disorders are highly prevalent among people with Opioid Use Disorders[4, 41]. These clients can safely be given methadone for Opioid management, however for clients with HIV; dose adjustment or change of treatment regime is mandatory because of the pharmacological interactions of some antiretroviral therapies with methadone and other psychotropic. Clients with hepatitis normally do not require methadone dose adjustment except in situations where impairment of the liver function is observed. Due to that, clients who are being started on methadone will require lower doses than those individuals with normal liver function, and the principle of starting low and going slowly is highly applicable. Special considerations are also needed in clients with co morbid pain. Other co-occurring conditions include chronic wounds, dental caries and malnutrition.

5.1 Management of HIV at MAT

MAT program is designed in a manner that HIV services are offered in an integrated or co-located model at the facility premise or a nearby preferably walking distant CTC clinic respectively. This is due to high risk of HIV transmission in this sub-group of population and the need to offer comprehensive quality care. Ideally, all MAT clinics should have adequate HIV services in place. HIV services typically starts at the store fronts where community base HTS are offered. These includes; HIV Screening (Mobile or Outreach services at Hotspots, Standalone client initiated testing service, PITC in outreach services) and linkage of HIV positive

to Care and treatment Clinic (CTC) of their choice. Some clients choose to enroll in the MAT integrated or co-located Care and Treatment services while others choose to enroll to a different CTC somewhere else.

5.1.1. HIV Testing Services (HTS)

The five core HTS guiding principles as indicated in National Guidelines on Management of HIV/AIDS and National Guideline for comprehensive package of HIV intervention for Key and Vulnerable Populations should be followed[42]. Great emphasis should be on index testing targeting sex partners, needle sharing partners of HIV positive client or biological children of HIV positive mother. MAT clients fall under the high-risk group HIV thus testing should be offered every six months for those who test negative. HTS modalities employed should include but not limited to Provider initiated Testing and Counseling (PITC) at the health facilities and Home Based HTS at Hotspots. However, it is important to note that, these services should be integrated in MAT clinic because of high prevalence of HIV, increased retention and adherence to the CTC among PWUD.

Drug use and addiction do not preclude successful ARV treatment. HAART is as effective for HIV positive PWUD as it is for other people with HIV/AIDS. Given appropriate support, former and active PWUD can adhere just as well as others and should have equal access to ART.

5.1.2. ART for people with OUD

Special attention should be paid to the particular needs for the PWUD when administering ART, including those related to

substance dependence, co-morbidities and co-infections. For the ART naïve patient ART should be initiated after all the initial clinical assessments investigations depending on the client's needs have been done.

The currently used NNRTIs, Nevirapine (NVP) and Efavirenz (EFV) and to a less extent Lopinavir and Ritonavir induce metabolism of methadone through cytochrome CYP 450 3A with a net effect of reducing serum concentration of Methadone. EFV for example decreases methadone plasma concentration up to 50% overtime. Use of combined (Tenofovir) TDF back bone with preferably (Dalutegravir) DTG or alternatively use of ritonavir boosted Atazanavir (ATV/r) is recommended. These are not associated with significant decreases of methadone plasma concentration. Thus the preferred regimen for client with Opioid Use Disorder (OUD) is TDF/ (FTC or 3TC) +DTG.All treatment experienced patients on other regimens who are identified to be client with OUD during the course of treatment should be switched to TDF/ (FTC or 3TC) +DTG regimen because of the methadone and ART drug interactions. Tenofovir Lamivudine Efavirenz (TLE) the recommended first line is safe but decreases serum level of methadone and therefore will require methadone dose adjustment.

5.2 Hepatitis

This is a viral infection of the liver that causes hepatocellular necrosis and inflammation. The infection is antecedent to cirrhosis and hepatocellular carcinoma.

5.2.1. Hepatitis B screening and treatment

All clients on MAT services should be screened for hepatitis as it has been found to be highly prevalent (19.9%) among PWUD. Hepatitis Screening involves testing for Hepatitis B surface antigen (HBsAg) in serum, routine assessment of HBsAg positive person is needed to guide Management. Additional serological markers of Hepatitis B infection include: Hepatitis B core antibody serology, which indicates previous infection or vaccination and Hepatitis B envelope Antigen (HBeAg), which indicates active infection.

Assessment of the severity of the liver disease should also include testing of liver enzymes (ALT) level. HBsAg positive patients should be referred for possible treatment and their contacts followed up and screened for hepatitis. All patients with positive HBsAg should be tested for HBV DNA using a quantitative assay if possible /available. In situations where quantitative assay is unavailable, elevated ALAT (more than 10-fold increase) in aHBsAg positive possibly indicates active infection. The choice of ARV for Hepatitis B should consist of two active agents, which are active against hepatitis B (e.g. Tenofovir and Emtricitabine as Truvada), Lamivudine is also available but has high resistance. Interruption of anti-HBV agents may reactivate HBV and cause serious hepatocellular damage. Care should be taken on the drug interaction of the Methadone and ARV.

5.2.2. Hepatitis C (HCV) Screening

HCV- RNA can be detected in blood within 1- 3 weeks after exposure while average time from exposure to sero-conversion is 8-9 weeks. Clinical characteristics are similar for all types

of acute viral hepatitis. Specific type (Hepatitis C/B) must be distinguished by serologic testing. Acute versus chronic infection approximately 15%–25% of persons clear the virus from their bodies without treatment and do not develop chronic infection; the reasons for this are not well known. HCV infection becomes chronic in approximately 75%–85% of cases.

5.2.3. Counseling patients with Hepatitis

Patients should be counseled to reduce the risk of transmission to others. They should be informed about the low but present risk for transmission with sex partners, avoiding sharing personal items that might have blood on them and ensuring cuts and sores on the skin are covered to keep from spreading infectious blood or secretions. Patients should also be informed that donating blood, organs, tissue, or semen can spread HCV to others. Furthermore, it should be known that HCV is not spread by sneezing, hugging, holding hands, coughing, sharing eating utensils or drinking glasses, or through food or water. Information on factors that worsen the course of hepatitis including alcohol, smoking and hepatotoxic medications should be provided. Education on condom use and safe sex practices, disclosures of sero-status to partners, referral to STI screening and treatment is also important. Key contacts should be encouraged to get hepatitis B vaccination.

5.3 Tuberculosis

TB is common among PWUDs than in the general population (12.5% vs 0.2% respectively) likewise for the cases of multidrug resistance[4]. Observations from three pilot MAT clinics indicate that TB is a leading cause of mortality among clients with OUD living with HIV. If a client is an active Opioid user with TB, the first

priority of the treatment service should be to treat the active PTB infection to prevent further spread. MAT facilities should ensure that the clinic environment is set in such a way to avoid risk of transmission of TB to all people at the clinic.

5.3.1. Screening diagnosis and treatment of TB

A set of standard screening questions is available as per the National tuberculosis screening tool. If client report yes to one or more questions indicates suspicious for TB

1. Cough of any duration
2. Fever of any duration
3. Noticeable weight loss for new TB patients or a 3kg weight loss in a month (In a subsequent visits)
4. Excessive sweating at night of any duration

Clients who have OUD can pose great challenges in screening and treatment for the TB. Challenges associated with screening for the active symptoms has to do with hypothermia and cough suppression due to Opioid use, and those due to chronic Opioid use such as weight loss due to poor dietary intake, malnutrition and neglected self-care. Treatment challenges include late diagnosis associated with delays in initiation of treatment, non-adherence to treatment with increased risk to multidrug-resistant TB.

TB treatment should observe National TB and Leprosy guideline which is the same to all patients. Anti TB drug such as rifampicin tend to induce the metabolism of methadone therefore titration of the methadone dose to alleviate symptoms of Opioid withdrawal effects and attainment of the optimal dose is of paramount importance.

All HIV positive clients who test negative for TB should be offered Isoniazid Preventive Therapy (IPT). To Intensifying community TB prevention peers should be used to trace contacts as well as defaulters.

5.4 Pain treatment in patients with OUD

Pain in patients with OUD is often exacerbated by the lowering of the pain threshold that tolerance to Opioids can induce. Clients with OUD are more resistant to pain management with Opioid, due to either their tolerance to the use of Opioids or to blocking effects of used treatment medication.

Patients with OUD should receive adequate pain relief however some patients will try to manipulate the health system to obtain Opioids. Measures to minimize misuse of prescription Opioids should include managing pain through a single health service, adequately defining the nature of the painful condition and resolving acute pain rapidly and then moving quickly to longer acting Opioids that have less potential for abuse. Opioids should be titrated to pain response, with close assessment of the clinical features of withdrawal and intoxication, to determine appropriate dose levels.

5.4.1. Acute pain treatment for patients not on methadone

Acute pain is defined as pain of less than or equal to 6 months. For patients using illicit Opioids without Opioid agonist maintenance treatment, starting Opioid agonist maintenance treatment with methadone allows for combined management of OUD and pain. Inadequate analgesia often contributes to patients self-administering illicit Opioids.

5.4.2. Acute pain treatment for client on methadone[42]

For mild or acute pain non-Opioid analgesics (e.g. paracetamol, diclofenac) should be given, which can be given orally or parenterally. For elective surgery, adequate pain management should be done in a hospital. It is should be noted that patients on methadone who are experiencing acute pain in hospital often receive inadequate doses of Opioid for their pain. For patients in MAT, the same analgesic techniques should be used in the same way as for other patients; such techniques include the use of injectable analgesia. Because of their tolerance of Opioids, patients taking methadone will require larger doses of Opioid analgesia for adequate pain relief. Partial agonists, such as buprenorphine, should be avoided because they may precipitate withdrawal symptoms. There is evidence of cross-tolerance between methadone and anesthetic agents; thus, patients on methadone may require higher doses of anesthetic agents in the event of dental or surgical procedures.

5.4.3. Chronic pain treatment for client on methadone

Chronic pain is pain that occurs for greater than 6 months. Treatment of chronic pain should focus on longer acting Opioids that may provide better long-term analgesia and avoid the utilization of short acting Opioid. Dose increases of methadone or the introduction of additional Opioids may be required to achieve adequate analgesia in these clients.

5.5 Mental disorders

Psychiatric co-morbidities are common among Opioid use clients. Some of the common co-morbid conditions include but not limited to major depressive disorder, anxiety, post-traumatic

stress disorder and personality disorders. The presence of these co-morbidities can have a negative impact on the treatment outcome of OUD. Clients who are identified and started on appropriate treatment can have dramatic improvements both in their psychological wellbeing as well as their sobriety from drug of abuse. All MAT facilities should offer services for psychiatric disorders. Screening for the mental disorders should be done during intake and whenever deemed necessary for good outcome of OUD treatment.

There is an increased likelihood in uptake of treatment if provided by the same medical practitioner or at the same facility in an integrated service.

Pharmacological treatment should be initiated by a qualified mental health practitioner. There are some side effects and drug interactions that should be noted when prescribing psychotropic in patient who is using methadone.

5.6 Poly-substance use and methadone treatment

The poly-substance user is a more complicated client than the individual with pure Opioid dependence and is classified into two categories: polysubstance use of drugs that increase overdose risk and those drugs that do not increase the risk of overdose.

5.6.1. Use of drugs that increase overdose with methadone

Alcohol and sedatives such as benzodiazepines when combined with Opioids such as methadone can increase the risk of overdose. Individuals with ongoing alcohol or sedative use should be maintained at lower doses of methadone. Use of

Opioid agonists like methadone is contraindicated in clients with acute alcohol intoxication. If there is evidence of a central nervous system depressants usage, precaution should be taken in terms of provision of methadone and it is recommended to do frequent follow up assessments in such a client.

5.6.2. Use of drugs that do not increase overdose with methadone

Stimulants and cannabis have different pharmacological action with Opioids such as methadone and do not increase the risk of respiratory depression. Due to that no need for dose reduction neither higher dose of methadone to treat stimulants and cannabis use, therefore specific interventions should be employed to treat other substances.

CHAPTER SIX

6. Legal and Ethical Considerations

6.1. Legal framework

The existing legal framework governing people with Opioid Use Disorder falls under the National Drug Control and Enforcement Act No. 5 of 2015 and it's Amendment No. 15 of 2017. The Act has given room for treatment of people with drug Use Disorders. It stipulated that people with addiction of any drug upon convicted for an offence and under the discretion of the court he or she may be offered treatment as an alternative to a penalty[7].

Section 31 of the act states that "*Where an addict is convicted of an offence under section 18 and the court by which he is convicted is of the opinion regarding to; (a)age, character, antecede or (b)physical or mental health of the offender that is expedient so to do, the court may instead of sentencing that person to imprisonment, upon his consent, direct that to be released for undergoing medical treatment for detoxification or de-addiction from a hospital or an institution maintained or recognized by the government*"

Opioid Use Disorder is categorized as a mental health disorders[44]. Hence management of Opioid use should adhere to mental health Act 21 of 2008.

Similarly, the TFDA Guideline for Dealing in Controlled Drugs of September 2015 has provided guidance for importation, stocking and disposal of controlled medication. Since medications used in MAT program are controlled, their handling should adhere to TFDA guideline.

Program planners and providers should familiarize themselves with the existing legal framework governing people with Opioid Use Disorder and maintain close collaboration with existing regulatory authorities throughout implementation of their services.

6.2. Ethical standards

Universal ethical standards call for respect for human rights and dignity. Treatment of people with drug Use Disorder should therefore base on standards that ensure autonomy and highest attainable standards of health[45]. These includes nondiscriminatory actions, autonomy of the patient, confidentiality, avoidance of punitive, humiliating and degrading interventions and recognizing people with Opioid Use Disorder as persons suffering with health problems and deserving treatment similar to those with other psychiatric or medical problems.

This document has adopted the UNODC-WHO international ethical standards outlined under principle 2 of the international standard for treatment of drug Use Disorder[46]. Therefore, providers of MAT services for people with Opioid Use Disorders in Tanzania should adhere to the following standards; -

1. MAT services should respect rights and dignity of people with Opioid Use Disorder and be non-humiliating or non-degrading.
2. Client should consent before initiating treatment and he/she should be free to withdraw from treatment at any time. This standard recognizes that, the right to consent to treatment implies also the right to refuse treatment. Therefore, if a patient is judged as having the capacity to give consent, then refusal of such consent must also be respected.

3. In an event a person is incapable to consent for one reason or the other such as concurrent mental illness, principal of beneficence outweigh the autonomy. In such situations programmers and providers should follow medical legal procedures that allows waiving of consent process.

4. Clients should be adequately informed of any procedure and processes required for treatment including the right to withdraw from treatment at any time.

5. MAT services must ensure strict confidentiality and protection of client information guided by legislative measures and supported by appropriate staff training and service rules and regulations.

6. Any research in treatment services involving human subjects should be subjected to review of ethical committees, and participation of clients in the research should be strictly voluntary with informed written consent ensured in all cases.

7. Staff of MAT services should undergo training on provision of Opioid Use Disorders and comply with ethical standards, human rights principles and norms i.e. be respectful, non-stigmatizing and non-discriminatory towards clients.

8. Health care providers should abide to their professional codes of conduct while other supporting staffs should abide to procedures guiding standard operation of MAT services in Tanzania.

CHAPTER SEVEN

7. Monitoring and Evaluation[47]

Monitoring is a routine follow-up of services through data collection, analysis and reporting. It helps to identify trends and patterns, adapt strategies and inform decision for management of MAT service. Evaluation on the other hand critically examines the design, assessment, implementation and result of an ongoing or completed project, programme or policy. Evaluation of MAT service aim to determine the relevance of objectives, efficiency, impact and sustainability. Monitoring and evaluation of MAT services should involve data collection and management, supportive supervision and quality assurance

7.1. Data collection and management[47, 48]

This category focuses on the mechanisms through which data are collected, verified, and transformed into useful information. Examples of M&E tools that are used to collect data at MAT services are supervision tools, assessment tools and pharmacy tools. The clinical information that is filled out during first interaction will serve as baseline for the target indicators that are defined in M&E framework. MAT service provider and data personnel should use standardized tools at facilities to be able to collect data.

Information collected include the following:

Demographic, Risk behaviors, Opioid Use Disorder, Physical and Mental disorders and psychosocial information

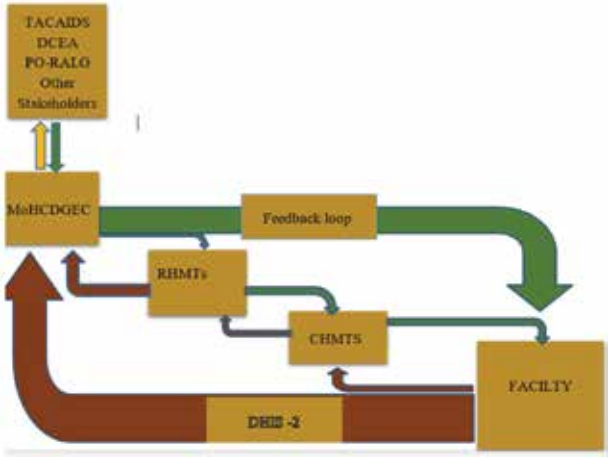
7.1.1. Data Verification[47, 48]

This approach should determine whether MAT service provider at facility levels have accurately recorded data related to the selected indicator(s) on source documents. It should then be traced to see whether they have been correctly aggregated or manipulated as they are moved from the facility to the national level.

7.1.2. Data Reporting[24, 47, 48]

Reporting for MAT services should be done monthly, quarterly, semiannual and annual depending on the level of reporting and needs. It should include information on client's characteristics, management Opioid use and co-occurring disorder, methadone dosage as indicated in draft M&E framework. All information should be channeled to the existing health management information system of the country. Other relevant authorities can receive information through existing health information system.

Figure 4: Data Flow from Health Facility to National Level



7.2. Supportive supervision[24, 48]

Supportive supervision is important in MAT facilities in order to ensure quality service outcomes. It helps to strengthen communication, identify and solving problems, facilitate team work as well as provide leadership and support to empower health staff to monitor and improve their own performance. A supervision team from the Ministry of health should visit MAT facilities at least twice a year and use supervision tools to assess data quality i.e. SIMS. They may form a team with other relevant stakeholders from other institutions as deemed necessary i.e. DCEA, TACAIDS, PO-RALG etc.

Among other things, the team should monitor all tasks that are properly performed including training and supplies, which are available to staff to carry out their duties. Supportive supervision should monitor and assess availability of methadone and medical supplies. A supervision team should ensure all facilities performed well in documentation and reporting. Generally, the team should ensure the set minimum standards of MAT services are met.

7.3. Quality Assurance[49]

MAT services should be evaluated against standard requirement to meet client's satisfaction and to ensure services are provided at a comprehensive manner and high quality. MAT service performance indicators should reflect needs of services through process reviews, documentation and monitoring of action plan regularly. It is important that the Work Improvement Teams (WIT) at MAT facilities are functional so as to enable timely assessment of performance indicators.

CHAPTER EIGHT

8. Infection Prevention Control and Safety measures[50]

According to WHO, Infection prevention and control (IPC) is define as a scientific approach and practical solution designed to prevent harm caused by infection to patients and health care workers. Safety measures are activities and precautions designed to improve safety that aimed to reduce risk related to human health.

8.1. Rationale for IPC in MAT services[51,52,53]

Various studies have shown that people with Opioid Use Disorders are disproportionately highly infected with HIV, hepatitis and TB, hence risk for cross infection among themselves and providers is very high. Due to these reasons, all MAT facilities should adhere to national standards for IPC in order to minimize risk of infection to clients and providers.

This guideline has adopted and recommended few key IPC standards for MAT services from national IPC standard for hospitals in Tanzania. However it does not limit providers and program planners to include other standards necessary to ensure infection prevention.

Recommended standards for IPC at MAT facilities are:-

- Physical structures should be conducive for prevention of health-care associated infections
- There should be a standard IPC procedure
- Providers should be trained in IPC practice and procedures

- IPC materials and supplies should be sufficient available and accessible
- Proper waste management plan should be available
- Post Exposure Prophylaxis (PEP) standard procedures should be available
- Hepatitis B vaccine should be available to all health care providers
- Clients should be educated and encouraged to adhere to IPC practice and measures

8.2. Rationale for Safety Precautions in MAT services

People with Opioid Use Disorders tend to be prone to various social problems such as violence, criminal activities and other behavioral difficulties. In order to provide quality MAT care, protection of both clients and providers is necessary. Hence, MAT facilities should ensure safety measures are adhered at all times.

Safety measures at MAT includes:-

- Inspection for presence of any dangerous items within MAT premises
- Restriction of non-service users and providers within MAT premises
- Decongestion of clients as much as possible at all times for easy evacuation in cases of emergencies
- Presence of security guard at all times within MAT premises in order to ensure security for clients, providers, controlled drugs and other supplies and equipment

Annex 1: Post Exposure Prophylaxis Standard Procedures

- PEP should be Initiated promptly to reduce the risk of HIV infection in exposed HCP/client in MAT services
- For effectiveness and efficiency of PEP management, the exposed individuals should report the event immediately and start PEP within 2 hours and not later than 72 hours' post-exposure
- HCPs working in MAT facilities should be trained on PEP guidelines.
- PEP Guideline should be available at MAT facilities
- Starter pack of PEP should be available and easily accessible to all HCPs at MAT facilities.

Annex 2: Medications and food that interact with methadone

Medicines which Lowers Methadone Levels/Effects	Medicines which increases Methadone level/effects
· Rifampin · Carbamazepine, phenytoin, barbiturates · Ethanol (chronic use) · Nevirapine, efavirenz · Ritonavir, nelfinavir, amprenavir, Abacavir · Risperidone · Urinary acidifiers (e.g. vitamin C) · Nicotine	· Cimetidine · Erythromycin, clarithromycin, · Delavirdine · Fluvoxamine, sertraline, fluoxetine, Paroxetine · Ketoconazole, fluconazole, itraconazole · Ethanol (acute use) · Ciprofloxacin
Medications with Opioid antagonist activity are contraindicated with Methadone use	**Medications that potentiate sedative effects of Methadone**
· Buprenorphine · Naloxone except for treatment of Overdose · Naltrexone · Pentazocine · Tramadol	· Tricyclic antidepressants such as Amitriptyline, Imipramine, clomipramine · Benzodiazepine i.e Valium, clonazepam
Foods and herbs that lowers methadone blood levels	**Foods and herbs that increase methadone blood levels**
· Pepper · Citreous fruit (Lemon, lime, oranges)	· Coconut juice (madafu) · Grapes
Medications that interact with Methadone and prolong QT interval	
· Class 1 or Class 111 anti-arrhythmic agents such as Lignocaine or miodarone and Quinine respectively · Calcium Channel blocking agents such as Verapamil, Diltiazem, etc. · Antipsychotics such as Chlorpromazine · Anti-depressants such as Amitriptyline, Fluoxetine, etc. · Medical conditions that may result into electrolyte imbalance such as hypokalaemia, hypomagnesaemia, etc. · Medications that may result into electrolyte imbalance such as diuretics, laxatives, corticosteroid hormones, etc.	

Annex 3: COW scale

For each item, write in the number that best describes the patient's signs or symptom.

Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date: _____
MAT induction: Times: _____ _____ _____ _____

Enter scores at time zero, 30min after first dose, 2 h after first dose, etc.

Resting Pulse Rate: (record beats per minute)				
Measured after patient is sitting or lying for one minute				
0 pulse rate 80 or below				
1 pulse rate 81-100				
2 pulse rate 101-120				
4 pulse rate greater than 120				
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.*				
0 no report of chills or flushing				
1 subjective report of chills or flushing				
2 flushed or observable moistness on face 3 beads of sweat on brow or face				
4 sweat streaming off face				

Restlessness *Observation during assessmen*t				
0 able to sit still				
1 reports difficulty sitting still, but is able to do so				
3 frequent shifting or extraneous movements of legs/ arms 5 Unable to sit still for more than a few seconds				
Pupil size				
0 pupils pinned or normal size for room light				
1 pupils possibly larger than normal for room light				
2 pupils moderately dilated				
5 pupils so dilated that only the rim of the iris is visible				
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored*				
0 not present				
1 mild diffuse discomfort				
2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing *Not accounted for by cold symptoms or allergies*				
0 not present				
1 nasal stuffiness or unusually moist eyes				
2 nose running or tearing				
4 nose constantly running or tears streaming down cheeks				

GI Upset: *over last 1/2 hour* 0 no GI symptoms				
1 stomach cramps				
2 nausea or loose stool				
3 vomiting or diarrhea				
5 Multiple episodes of diarrhea or vomiting				
Tremor *observation of outstretched hands* 0 No tremor				
1 tremor can be felt, but not observed				
2 slight tremor observable				
4 gross tremor or muscle twitching				
Yawning *Observation during assessment*				
0 no yawning				
1 yawning once or twice during assessment				
2 yawning three or more times during assessment 4 yawning several times/minute				
Anxiety or Irritability				
0 none				
1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious				
4 patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin				
0 skin is smooth				
3 piloerrection of skin can be felt or hairs standing up on arms				
5 prominent piloerrection				
Total scores with observer's initials				

Annex 4: Modified Finnegan Scale

Modified Finnegan Neonatal Abstinence Score Sheet[1]																	
System	**Signs and Symptoms**	**Score**	**AM**							**PM**							**Comments**
Central Nervous System Disturbances	Excessive high-pitched (or other) cry < 5 mins	2															
	Continuous high-pitched (or other) cry > 5 mins	3															
	Sleeps < 1 hour after feeding	3															
	Sleeps < 2 hours after feeding	2															
	Sleeps < 3 hours after feeding	1															
	Hyperactive Moro reflex	2															
	Markedly hyperactive Moro reflex	3															
	Mild tremors when disturbed	1															
	Moderate-severe tremors when disturbed	2															
	Mild tremors when undisturbed	3															
	Moderate-severe tremors when undisturbed	4															
	Increased muscle tone	1															
	Excoriation (chin, knees, elbow, toes, nose)	1															
	Myoclonic jerks (twitching/jerking of limbs)	3															
	Generalised convulsions	5															
Metabolic/ Vasomotor/ Respiratory Disturbances	Sweating	1															
	Hyperthermia 37.2-38.3C	1															
	Hyperthermia > 38.4C	2															
	Frequent yawning (> 3-4 times/ scoring interval)	1															
	Mottling	1															
	Nasal stuffiness	1															
	Sneezing (> 3-4 times/scoring interval)	1															
	Nasal flaring	2															
	Respiratory rate > 60/min	1															
	Respiratory rate > 60/min with retractions	2															
Gastrointestinal Disturbances	Excessive sucking	1															
	Poor feeding (infrequent/uncoordinated suck)	2															
	Regurgitation (≥ 2 times during/post feeding)	2															
	Projectile vomiting	3															
	Loose stools (curds/seedy appearance)	2															
	Watery stools (water ring on nappy around stool)	3															
	Total Score																
	Date/Time																
	Initials of Scorer																

If the baby has three consecutive scores averaging more than eight (8), the child should be treated for NAS

1. Finnegan LP. Neonatal abstinence syndrome: assessment and pharmacotherapy. In: Nelson N, editor. Current therapy in neonatal-perinatal medicine. 2 ed. Ontario: BC Decker; 1990.

References

1. United Nation Office on Drug and Crime World Drug Report of 2018
2. National Aids Control Program consensus report, 2014
3. United Nation Office on Drug and Crime World Drug Report of 2017
4. The integrated Methadone Program in Tanzania: A five Year Report July, 2009 – June, 2014 (unpublished)
5. Principles of Drug Addiction Treatment-A research based Guide, NIDA 2012
6. The Drug Control and Prevention of Illicit traffic in drug act 1995
7. The United Republic of Tanzania. Drug Control and Enforcement Act, 2015
8. Nyandindi, C. L. 2011. "HIV Serostatus, Hepatitis C and Depression Among Injection Drug Users in Kinondoni Municipality, Dar es Salaam, Tanzania". Dar es Salaam, Tanzania: Muhimbili University of Health and Allied Sciences
9. Unpublished, Msami, (2004) HIV prevalence Among Injecting Drug Users in Kinondoni Municipality.
10. Williams ML, McCurdy SA, Bowen AM, Kilonzo GP, Atkinson JS, Ross MW, Leshabari MT. HIV seroprevalence in a sample of Tanzanian intravenous drug users. AIDS Education & Prevention. 2009 Oct;21(5):474-83.
11. Ubuguyu O, Tran OC, Bruce RD, Masao F, Nyandindi C, Sabuni N, McCurdy S, Mbwambo J, Lambdin BH. Improvements in health-related quality of life among methadone maintenance clients in Dar es Salaam, Tanzania. International Journal of Drug Policy. 2016 Apr 1; 30:74-81.

12. Minimum Standard for Health facility providing medically assisted treatment of Drug Dependence, Drug Control Commission. 2010.

13. Unpublished, Mwankemwa S, Perceived Quality of Life among Opioid dependent individuals attending methadone clinic in Dar es Salaam, Tanzania (2015)

14. Guideline for Medically Assisted Treatment for Opioid dependence in Tanzania. MoHSW, Oct 2010.

15. Bruce RD, Lambdin B, Chang O, Masao F, Mbwambo J, Mteza I, Nyandindi C, Zamudio-Haas S, Buma D, Dunbar MS, Kilonzo G. Lessons from Tanzania on the integration of HIV and tuberculosis treatments into methadone assisted treatment. International Journal of Drug Policy. 2014 Jan 1;25(1):22-5.

16. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013 May 22.

17. Thomas R. Kosten, Tony P. George. The Neurobiology of Opioid Dependence: Implications for Treatment. Sky PractPerspect. 2002 Jul; 1(1): 13–20.

18. U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. Washington, DC: HHS, November 2016

19. Comer SD, Sullivan MA, Yu E, Rothenberg JL, Kleber HD, Kampman K, Dackis C, O'Brien CP. Injectable, sustained-release naltrexone for the treatment of Opioid dependence: a randomized, placebo-controlled trial. Archives of general psychiatry. 2006 Feb 1;63(2):210-8.

20. Ward J, Hall W, Mattick RP. Role of maintenance treatment in Opioid dependence. The Lancet. 1999 Jan 16;353(9148):221-6.

21. Comer SD, Sullivan MA, Yu E, Rothenberg JL, Kleber HD, Kampman K, Dackis C, O'Brien CP. Injectable, sustained-release naltrexone for the treatment of Opioid dependence: a randomized, placebo-controlled trial. Archives of general psychiatry. 2006 Feb 1;63(2):210-8.

22. Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance Use Disorders. American Journal of Psychiatry. 2008 Feb; 165(2):179-87.

23. World Health Organization. Department of Mental Health, Substance Abuse, WHO, INCB, UNODC. Guidelines for the psychosocially assisted pharmacological treatment of Opioid dependence. World Health Organization; 2009.

24. National guideline for comprehensive package of HIV interventions for key and vulnerable populations, April 2017

25. WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users, 2009

26. Kreek MJ. Methadone-related Opioid agonist pharmacotherapy for Heroin addiction: history, recent molecular and neurochemical research and future in mainstream medicine. Annals of the New York Academy of Sciences. 2000 Jan;909(1):186-216.

27. Inturrisi CE. Pharmacology of methadone and its isomers. Minerva anestesiologica. 2005 Jul;71(7/8):435.

28. Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opiate use, HIV risk behavior and criminality: a meta-analysis. Addiction. 1998 Apr;93(4):515-32.

29. Peles E, Bodner G, Kreek MJ, Rados V, Adelson M. Corrected-QT intervals as related to methadone dose and serum level in methadone maintenance treatment (MMT) patients—a cross-sectional study. Addiction. 2007 Feb;102(2):289-300

30. Wesson DR, Ling W. The clinical opiate withdrawal scale (COWS). Journal of psychoactive drugs.2003 Jun 1;35(2):253-9

31. Finnegan LP, Connaughton JJ, Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. Addictive diseases. 1975;2(1-2):141-58.

32. Sarkar S, Donn SM. Management of neonatal abstinence syndrome in neonatal intensive care units: a national survey. Journal of Perinatology. 2006 Jan;26(1):15

33. Farid WO, Dunlop SA, Tait RJ, Hulse GK. The effects of maternally administered methadone, buprenorphine and naltrexone on offspring: review of human and animal data. Current neuropharmacology. 2008 Jun 1;6(2):125-50.

34. Fudala PJ, Bridge TP, Herbert S, Williford WO, Chiang CN, Jones K, Collins J, Raisch D, Casadonte P, Goldsmith RJ, Ling W. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. New England Journal of Medicine. 2003 Sep 4;349(10):949-58.

35. Fischer G, Johnson RE, Eder H, Jagsch R, Peternell A, Weninger M, Langer M, Aschauer HN. Treatment of Opioid-dependent pregnant women with buprenorphine. Addiction. 2000 Feb;95(2):239-44.

36. Fudala PJ, Jaffe JH, Dax EM, Johnson RE. Use of buprenorphine in the treatment of Opioid addiction. II. Physiologic and behavioral effects of daily and alternate-day administration and abrupt withdrawal. Clinical Pharmacology & Therapeutics. 1990 Apr 1;47(4):525-34

37. Kim D, Irwin KS, Khoshnood K. Expanded access to naloxone: options for critical response to the epidemic of Opioid overdose mortality. American Journal of Public Health. 2009 Mar;99(3):402-7.

38. Wanger K, Brough L, Macmillan I, Goulding J, MacPhail I, Christenson JM. Intravenous vs subcutaneous naloxone for out-of-hospital management of presumed Opioid overdose. Academic Emergency Medicine. 1998 Apr 1;5(4):293-9.

39. Clarke SF, Dargan PI, Jones AL. Naloxone in Opioid poisoning: walking the tightrope. Emergency Medicine Journal. 2005 Sep 1;22(9):612-6.

40. Robinson A, Wermeling DP. Intranasal naloxone administration for treatment of Opioid overdose.American Journal of Health-System Pharmacy. 2014 Dec 15;71(24):2129-35.

41. Implementing HIV and HCV comprehensive programmes with people who inject drugs UNODC 2017

42. National Guideline for comprehensive package of HIV interventions for key and vulnerable populations 2017

43. Hines S, Theodorous s, Williamson A, Fong D, Curry K Management of acute pain in methadone maintenance therapy in-patients. Drug Alcohol Rev. 2008 Sep; 27 (5):519-23.

44. Diagnostic and Statistical Manual of Mental disorders: DSM 5 - 5th edition. ISBN 978-0-89042-554-1

45. International Covenant on Economic, Social and Cultural Rights

46. UNODC-WHO International Standards for the Treatment of Drug Use Disorders

47. Monitoring and Evaluation Framework March 2010

48. National Guideline for the Management of HIV and AIDS sixth edition October 2017

49. The Tanzania Quality Improvement Framework in Healthcare 2011-2016 pg.41, Implementation Guidelines for 5S-KAIZEN-TQM Approaches in Tanzania 3rd Ed March 2013-3

50. https://www.who.int/gpsc/ipc/en/ - reference – infection prevention and control

51. National Communication Strategy for Infection Prevention and Control 2012-2017

52. National Infection Prevention and Control standards on IPC 2012. Standards-Based Management and Recognition for Improving Infection Prevention and Control Practices – An Assessment Tool. June 2012

53. NHS (2015) Community infection prevention control Guideline for Health and social fair