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# Substance Abuse Treatment Utilizing Medication Assisted Treatment as HIV Prevention

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## 1. Introduction

International guidelines have been developed for the use of medications in the treatment of substance use disorders (WHO, 2008; WHO, 2009). Medications used in the detoxification from drug abuse and dependence provide symptomatic relief of drug and alcohol withdrawal. For long term treatment or medical maintenance treatment, medications eliminate the physiological effects of drug use by blocking drug-receptor binding in the brain and are an important part of the recovery process. The use of medication assisted treatment (MAT) is part of a comprehensive treatment plan for drug and alcohol dependence that addresses the medical, social, and psychological needs of the patient (SAMHSA, 2005; SAMHSA, 2009). An effective long term treatment paradigm for the successful treatment of alcohol or opioid dependence is the concomitant use of medications that block the effects of drug use in concert with behavior change counseling and psychotherapy. Medications which have demonstrated effectiveness in the long term treatment of opioid dependence are methadone, buprenorphine (subutex®, suboxone®), and naltrexone (Revia®, Depade®) or extended release injectable naltrexone (vivitrol®). Pharmacotherapies used in the treatment of alcohol dependence include acamprosate (Campral®), disulfiram (antabuse®, antabus®) and naltrexone (Revia®, Depade®) or extended release injectable naltrexone (vivitrol®).

Time in treatment is a reliable indicator for successful treatment of drug dependence. Patients remain in treatment for longer periods of time when they perceive that their health care environment is supportive and non-stigmatizing, have a good patient-provider relationship, and feel that their needs are identified and met. Access to community-based substance abuse treatment that includes MAT is fundamental to achieving broad service coverage. Given that substance abuse treatment is Human Immunodeficiency Virus (HIV) prevention and the frequent co-morbidity of substance abuse and HIV infection, the provision of prevention, care and treatment for both need to be addressed in a coordinated manner for ideal patient outcomes. There are several models to achieve excellent patient outcomes for both HIV infection and the treatment of substance abuse (Proeschold-Bell et al 2010; Weiss et al, 2011). The highest level of coordinated care model has MAT and HIV services fully integrated with both the same medical record and health providers for both

services. Alternatively, MAT and HIV services can be separately managed but co-located to allow convenient utilization of both MAT and HIV services in another form of “one stop shopping”. A third approach is coordinated care and treatment where MAT and HIV services are provided at distinct locations, and case managers, peer facilitators, or others promote coordination of referrals. This third model can pose significant barriers to substance users who are heavily stigmatized and medically disenfranchised and who have multiple competing medical, psychological and social needs that limit access to care. MAT programs that offer comprehensive services and care options can best contribute to improving the health of these individuals thereby reducing HIV infection in the community.

## **2. Drug and alcohol use and their linkage to HIV infection**

Exposure to the HIV can result in a patent viral infection. HIV infection can occur via two transmission routes: direct injection of the virus through the use of injection equipment infected with HIV and through sexual contact with an infected individual. There is a direct linkage between these disparate behaviours and drug and alcohol use.

For people who inject drugs, there is a risk of HIV infection when the injection equipment is reused and not sterilized after use or when there is direct sharing of the injection equipment with individuals who may be infected with HIV. Drug users who are under the influence of drugs may engage in risk behaviours for HIV that they would not while sober. In addition, for drug users who develop dependence, withdrawal induced drug cravings may result in the exchange of sex for money or drugs or other behaviours that increase risk of HIV acquisition. Similarly, alcohol consumption increases sexual risk-taking including high risk behaviors (Figure 1). That includes sexual acts without the use of condoms and an increased number of sexual partners. Concurrent sexual partnerships are a significant risk factor for the transmission of HIV (Epstein & Morris, 2011). Alcohol can also be an important contributor in the progression of HIV infection to acquired immune deficiency syndrome (AIDS) (Hahn & Samet, 2010). Alcohol consumption is an important consideration in the medical management of patients with HIV infection, particularly those co-infected with the hepatitis C virus (HCV) (Edlin et al 2001). Studies have also shown that alcohol consumption can modify drug metabolism in the liver, and thereby potentially influence the effectiveness of HIV antiretroviral therapy. Alcohol-induced cirrhosis can result in changes in drug metabolism in the liver through compromised liver function. Research has shown that alcohol consumption greater than 50 g/day (4–5 drinks) is a risk factor for disease progression for patients with HIV/HCV co-infection.

All substance abuse, whether the use of opioids, stimulants, or excessive alcohol, can negatively influence the course of HIV disease progression when the use results in low antiretroviral adherence or facilitates missed medical appointments. Substance abuse has been associated with less access to antiretroviral medications, lower medication adherence, and increased mortality among HIV infected patients.

### **2.1 Alcohol abuse, medication assisted treatment and HIV infection**

Alcohol abuse and dependence are global problems of major medical importance with high societal impact (WHO, 2010). In determining the global burden of disease, the World Health Organization (WHO) has noted that a leading cause of disability is alcohol and drug use disorders. Alcohol consumption is estimated to cause 4% of the total of Disability-Adjusted

Life Years and 3.2% of deaths, globally. The WHO estimates that about 2 billion individuals worldwide consume alcoholic beverages.

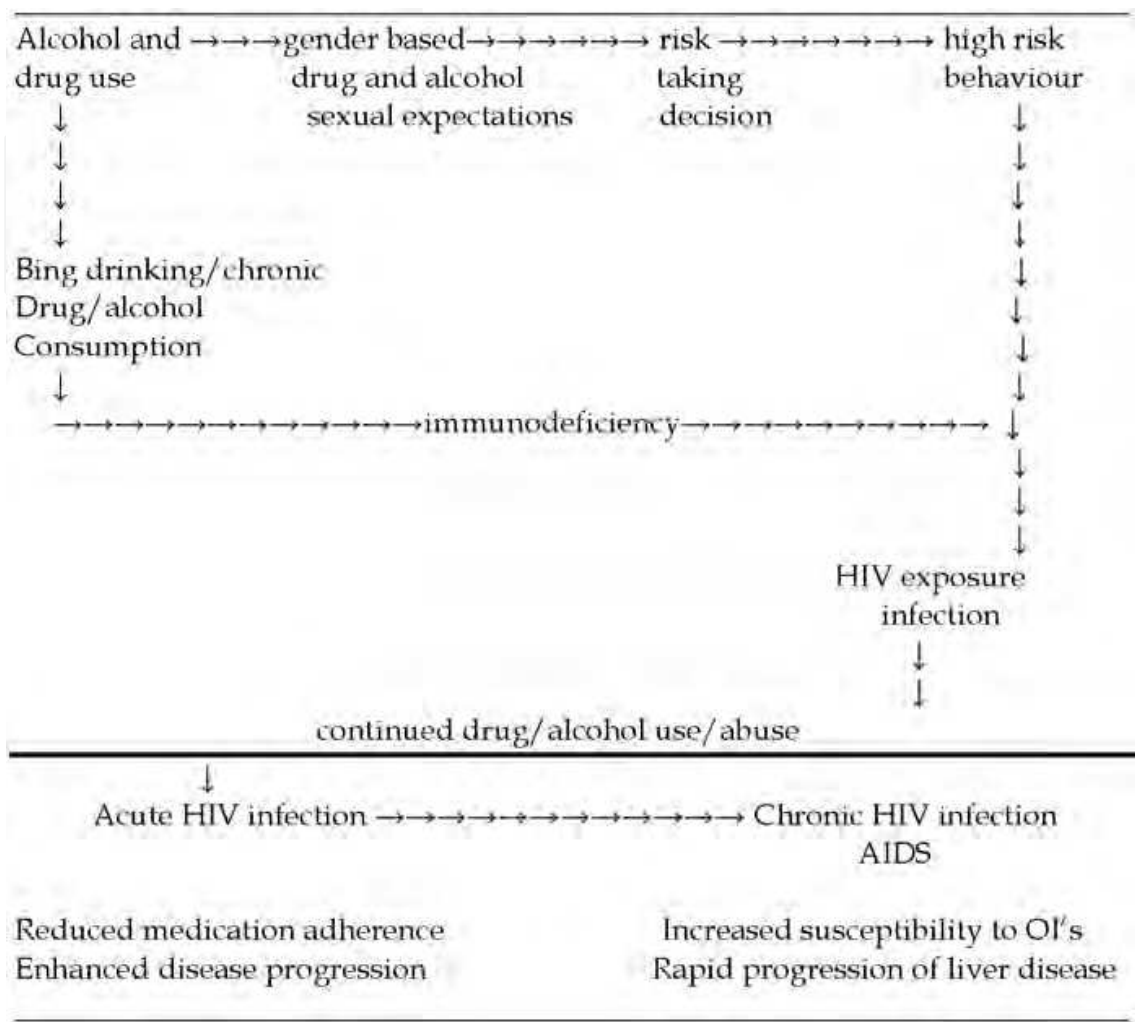


Fig. 1. Interactions and linkages between drug and alcohol use and abuse in the course of HIV infection and AIDS.

Alcoholic beverage consumption can be described based on quantity. Abstainers or light/occasional drinkers comprise roughly 40% of a general population while moderate drinkers comprise about 35% of the general population. Both groups comprise approximately 55–75% of a general medical practice. At-risk drinkers, those with hazardous drinking patterns or quantities, and alcohol abusers, those with harmful drinking (meeting the required clinical criteria) comprise approximately 20% of the population and 20–35% of a general medical practice. At-risk drinkers are males who drink more than two drinks a day or greater than four drinks per occasion. For females and individuals over the age of 65, at-risk drinkers are those who drink greater than one drink per day or greater than three drinks per occasion. These individuals consume alcohol at levels that place them at-risk for alcohol-related social and/or medical problems (Dufour, 1999). These at-risk individuals are best managed through the use of brief interventions that can be provided by primary care physicians, health care providers or specialists, upon training. Usually these brief interventions are outpatient interventions that include some form of counseling.

Approximately 76.3 million individuals have a diagnosable alcohol use disorder. Alcohol and drug use disorders are defined clinically as alcohol/drug abuse or dependence (WHO, 2004). Diagnostic and Statistical Manual of Mental Disorders-4<sup>th</sup> edition (DSM-IV) definitions of abuse and dependence are maladaptive patterns of alcohol or drug use that result in clinically significant impairment or distress as well as significant behavior modifications. Individuals with alcohol dependence comprise approximately 5% of the population and around 5-10% of a general medical practice. Alcohol abusers and alcohol-dependent individuals exhibit a varying degree of social and/or medical dysfunction. These individuals require intensive treatment, including structured counseling and/or pharmacotherapy (Fiellin et al., 2000). Severely involved dependent patients have been traditionally thought of requiring treatment in a specialty setting. However, studies (Fiellin et al., 2000a) have shown that primary care physicians may also have an important role in providing treatment to these individuals.

Pharmacotherapy for alcohol dependence is an important adjunct to behavioral therapies to reduce the risk of relapse to drinking after an initial period of abstinence (SAMHSA, 2009). Pharmacotherapy for alcohol consumption is also important for patients with co-occurring conditions such as patients with HIV and/or HCV infection(s) where alcohol consumption can augment disease progression. For these patients alcohol dependence treatment has been reported with either acamprosate, naltrexone, vivitrol or disulfiram (Collins et al, 2006). Acamprosate and naltrexone have different mechanisms of action and modify different behavioral aspects of alcohol dependence. Acamprosate is a long acting compound that prolongs periods of abstinence by normalizing glutamateric neurotransmission. Glutamateric neurotransmission in the brain is dysregulated during chronic alcohol consumption and withdrawal. Naltrexone is a fast acting opioid receptor antagonist that reduces heavy drinking through a decrease of the reward effects of ethanol. An evidence-based risk -benefits assessment can be used to inform health care providers on medication choice (Mason, 2003). However, the safety and efficacy of treatment using both medications for alcohol dependence has been shown in double blind studies (Kiefer & Wiedemann, 2004). Disulfiram, another pharmacotherapy option, blocks the oxidation of alcohol at the acetaldehyde stage of its metabolism. The increase in the levels of acetaldehyde resulting in a series of unpleasant symptoms (e.g., flushing, headache, and vomiting). Although disulfiram is widely used, particularly in the setting of opioid dependence, superior data of studies support the use of naltrexone and acamprosate as pharmacologic treatments of alcoholism (Kiefer et al 2005). For resource limited settings, a series of factors acting synergistically may be creating the "perfect storm" promoting alcohol availability, alcohol consumption, and reducing alcohol control policies, thereby increasing the need for public health efforts (Table 1) to reduce alcohol consumption beyond the use of medication-assisted treatment for alcohol abuse and dependence (Caetano & Laranjeira, 2006).

Use of alcohol may impact the care and course of HIV infection for an individual patient (Baum et al, 2010; Hahn & Samet, 2010). Optimal management of HIV infected patients with alcohol problems requires recognition of the impact of alcohol on a number of issues: patient's linkage to medical care; adherence to anti-retroviral treatment, impact on co-morbid conditions (such as HCV infection), liver function, and the stage of HIV disease. Due to its many ramifications, the clinical approach to the HIV infected patient with alcohol problems takes on a high priority, yet it is similar in many ways to the standard optimal approach to any medical patient (Bogart et al., 2000). It requires the effective screening for



Public Health Educational Efforts to Prevent HIV Transmssion in the Context of Aclohol Consumption :	
	<ul style="list-style-type: none"><li>• Public education to inform youth and adults of the harms associated with at-risk alcohol consumption</li><li>• Education of women of the gender related issues regarding alcohol use and abuse</li><li>• Public education on changing societal norms for heavy drinking, and awareness of HIV related risk, including condom use</li><li>• Beverage industry collaboration to promote responsible drinking.</li></ul>
Integration of targeted alcohol information, education and interventions in HIV/AIDS prevention programs for persons at high risk for HIV/ AIDS:	
	<ul style="list-style-type: none"><li>• Women of child-bearing age</li><li>• HIV-positive persons and their partners</li><li>• Anti-retroviral treatment patients</li><li>• Sex trade workers and truckers</li><li>• Injection drug users</li><li>• MSM</li></ul>
Brief Interventions. Screening, brief advice & motivational interventions for at-risk drinkers	
	<ul style="list-style-type: none"><li>• By HIV healthcare workers</li><li>• By HIV peer outreach workers</li><li>• By VCT and anti-retroviral professionals</li></ul>
Detoxification	
	<ul style="list-style-type: none"><li>• Community-based detoxification for acute stabilization prior to outpatient or residential treatment</li><li>• Hospital detoxificaion - as medically required</li></ul>
Specialty treatment for alcohol abusers and dependent persons	
	<ul style="list-style-type: none"><li>• Inpatient or residential treatment</li><li>• Therapeutic Community Model</li><li>• Outpatient treatment and Aftercare- Community drop-in centers for alcohol-free activities and outreach, peer support</li><li>• Supportive Residential- Half-way or similar residential support post-discharge</li><li>• Treatment approaches- Motivational Interviewing, Cognitive Behavioral, and 12-step based treatmen, Relapse Prevention, and Peer Support</li><li>• Medications (Naltrexone, Acamprosate, Disulfiram, Vivitrol)</li></ul>
Peer Recovery Community Support	

Table 1. Approaches to Alcohol Use and Abuse in HIV/ AIDS

the prevalent condition of alcohol abuse, assessment of the severity of the alcohol problem, and skills to intervene effectively to reduce the harm associated with alcohol use/abuse. New strategies to target alcohol use/ abuse in HIV populations need to be implemented in the context of existing recommended HIV clinical approaches. Addressing alcohol problems in HIV-infected persons has the potential to improve the overall management of HIV disease in a substantial proportion of the population

## 2.2 Illicit opioid abuse, medication assisted treatment and HIV infection

Based on the 2010 World Drug Report (UNODC, 2010) from the United Nations Office on Drugs and Crime (UNODC), it is estimated that between 175- 250 million people from almost every country, or 5 percent of the global population age 15-64, have used illicit drugs at least once in the last 12 months. Cannabis is by far the most widely used drug, followed by stimulants, such as amphetamines and ecstasy, then cocaine use and then opioids. While most individuals occasionally use or have casually tried illicit drugs, UNODC estimates that there are between 18-38 million problem drug users. These individuals consume most of the drugs and likely fulfill the criteria for a diagnosis of drug abuse or dependence.

These medical co-occurring conditions are specifically prevalent in injection drug users (IDU). Estimates for IDU's are available for at least 130 countries with approximately 78% of the 13.2 million IDU's living in developing or transitional countries (Aceijas et al 2004). Forty-one countries have reported a high prevalence (>5%) of HIV infection in this high-risk population. Globally, IDU's now account for at least 10% of all new HIV infections which are estimated at 5 million per year (IHRDP, 2006). In chronic HIV infection, AIDS has been reported as the leading cause of death in IDUs (Chin, 2007). Epidemiological data of HIV infection show that generalized HIV epidemics can result from diffusion transmission of HIV from high risk groups, such as IDUs. Thus, it is important for countries and regions to undertake surveillance studies to identify current alcohol and drug use patterns and develop best practices for the treatment of individuals who use and abuse alcohol and illicit drugs.

Drug dependence is a chronic, relapsing neurophysiological disease resulting from the prolonged effects of drug(s) on the brain. The neurochemical abnormalities resulting from chronic use are the underlying cause of many of the observed physical and behavioral aspects of abuse and dependence. The brain abnormalities associated with addiction are wide ranging, complex, and long lasting (Chana et al 2006; Goodkin et al 1998; Langford et al 2003). They can involve abnormal brain signaling pathways, psychological conditioning or stress and social factors that result in cravings leading to a predisposition to relapse even months or years after drug(s) use cessation. Thus, substance abuse/dependence can be most effectively addressed in a multifaceted medical-based paradigm that comprises a comprehensive program of interventions that are delivered through the course of long term treatment. Such comprehensive treatment programs include behavioral, social rehabilitative components, as well as biological (pharmacological) components Table 2. Behavioral therapy interventions have been extensively researched and are critical components of the treatment of all drug addictions. Social rehabilitative components are also important and may prove suited to certain treatment environments.

In the United States, opioid abuse/dependence can be treated in two differing medical paradigms. In the highly regulated and structured environment, methadone is dispensed daily at Opioid Treatment Programs (OTPs). These OTPs are increasingly providing "wrap-around" services to address important patient needs, enhance time in treatment, and promote recovery. Alternatively, buprenorphine can be prescribed in a primary care health care setting similar to other illnesses to reduce the stigma/discrimination of drug dependence. Both medical paradigms need to address the reduced quality of life, physical and mental functioning, compared to the general population that is associated with drug abuse/dependence (Millson et al. 2006). In addition, multiple comorbidities are associated with substance abuse and dependence that also contribute to the lower quality of life

Drug Use, Abuse and Dependence

- (1)PREVENTION OF DRUG INITIATION
- Individual targeted interventions through the life span
- Family targeted interventions
- Community interventions
- (2)IDENTIFICATION OF SUBSTANE USE CONDITIONS
- Screening for drug use
- Case finding
- Assessment & Diagnosis
- (3)INITIATION AND ENGAGEMENT IN DRUG TREATMENT
- Brief intervention
- Promoting Engagement, case management/ care navagators
- Detoxification/ Withdrawal Management
- Assessment of social, co-morbid medical conditions and co-occurring disorders
- (4) LONG TERM TREATMENT OF SUBSTANCE USE ILLNESS
- Psychosocial
- Pharmacotherapy
- Treatment of co-morbid medical conditions and co-occurring disorders
- Promotion of treatment engagement & social stability through legal, social, educational, financial support
- (5) PRIMARY CARE AND POST TREATMENT MANAGEMENT OF PATIENT
- Recovery
- Relapse prevention
- Rehabilitation
- Medical Home

Table 2. Elements of the Continuum of Care in the Treatment of Opioid Abuse/Dependence experienced and documented by opioid dependent individuals. Life priorities of opioid users have been reported as concern about HIV and treatment of infection with HIV, housing, money, and protection from violence (Mizuno et al, 2003). Substance abuse is a complex medical disorder composed of multiple physiologic, social and behavioral problems often interrelated with psychological illness. Health care providers need to screen substance misusing patients for psychological illness (Schuckit, 2006). Although it can be difficult to ascertain whether substance abuse, psychological illness, or infectious comorbidities should be addressed first, an initial focus on the medical treatment of drug abuse is often necessary to create sufficient patient stability from which other treatments can begin. Stability is further increased with both mental health services and substance abuse treatment, subsequently enhancing the medical outcomes of treatment for comorbidities.



In the United States, multiple pharmacological treatments, including both agonists and antagonists have been developed and approved by the Food and Drug Administration for specific drug dependence. Currently, medications and evidence-based treatment paradigms utilizing these pharmacotherapies are available for the treatment of nicotine, alcohol, and opioid substance use disorders. Although none are available for stimulants, such as cocaine and methamphetamine, many potential medications are now being developed for these drugs of abuse and are expected to be available over the next few years. An effective treatment strategy for drug abuse and dependence is to match a comprehensive treatment plan to the individual's particular substance abuse problems and needs. Desired treatment outcomes should: a) reduce dependence on drugs of abuse, b) reduce morbidity and mortality of and associated with drugs of abuse, and c) maximize the patients' abilities to access services and achieve social integration.

### **2.2.1 Medication assisted treatment utilizing methadone**

In most countries that utilize MAT for the treatment of opioid dependence, methadone is the pharmacotherapy of choice. Methadone is usually the least expensive medication and when used in evidence-based treatment paradigms is cost effective and can result in abstinence from illicit drug use over time and the achievement of recovery (Connock et al 2007; Skinner et al 2011). Methadone is a synthetic  $\mu$ -opioid receptor agonist with pharmacological properties qualitatively similar to morphine and was originally used to treat the painful symptoms of withdrawal from heroin and other opioids (Gowing et al 2006; Payte & Zweben, 1998). Administered daily as an oral dose for the treatment of opioid dependence, an individual therapeutic dosage is determined to maintain an asymptomatic state and stabilize a patient, without episodes of opioid overmedication or withdrawal. The therapeutic dosage for a patient is a function of many factors including: absorption, metabolism, drug-drug interactions, physiology, diet and the use of alternative medications. Minimum retention time in treatment varies for residential and outpatient methadone treatment programs. The National Institutes of Health consensus panel on opioid-addiction treatment (NIH, 1997) concluded that individuals treated for fewer than three months with methadone do not show substantial medical gain. As time in treatment progresses, study outcomes have reported partial reductions of illicit opioid use progressing to abstinence. Relapse to opioid use is common when methadone is discontinued without further support or behavioral treatment. In the United States, OTPs or methadone maintenance treatment programs, MMTP, under the certification of the Substance Abuse and Mental Health Services Administration (SAMHSA), dispense methadone and can provide a comprehensive therapeutic milieu comprised of primary medical care, psychosocial counseling, vocational rehabilitation, HIV testing and counseling, hepatitis C education and testing and other vital medical and social services. Methadone treatment is effective as both primary and secondary HIV prevention (Kerr et al 2004) and cost-effective to society (Barnett et al 2001; Doran et al 2003). In addition to improving health outcomes, methadone treatment also substantially improves the quality of life of patients over the course of methadone treatment (Giacomuzzi et al 2005).

Barriers to retention in methadone treatment include the severity of drug, medical and social problems at initiation of treatment, as well as patient readiness for treatment and motivation. Integrating multiple components of the drug treatment program is fundamental to successful treatment outcomes. Treatment programs that offer a broader array of "wrap-around" services and a greater frequency of services have reported improved retention in

treatment and treatment outcomes (Fiellin et al 2003). Programs responsive to the severity of drug abuse during initial stages of drug treatment have been shown to produce positive treatment outcomes based on greater retention time in treatment and patient satisfaction with treatment services. Maximum retention time in methadone treatment is associated with comprehensive treatment, provision of frequent health service, as well as appropriate methadone dosing (Litwin et al 2001).

### **2.2.2 Medication assisted treatment utilizing buprenorphine**

In the United States and globally, primary care physicians can expand the accessibility of substance abuse treatment while mitigating the stigma associated with drug use and treatment through an outpatient treatment setting in primary care and the use of buprenorphine. However, in the United States, buprenorphine-only OTPs have been recently developed where buprenorphine is provided to opioid dependent patients under the highly regulated rules and regulations that apply to methadone. Buprenorphine, a partial mu-receptor opiate agonist (Ling & Smith 2002), differs significantly from full agonists. Most significantly, buprenorphine has a plateau of its agonist properties at higher doses. This results in an improved safety profile compared with a full agonist. Specifically, buprenorphine has a favorable 'ceiling effect' on respiratory depression precluding overdose potential (Walsh et al 1994). However, the abuse of other substances that may enhance respiratory depression (e.g., benzodiazepines) remains a contraindication with buprenorphine as with methadone. Improved safety and thrice weekly flexible dosing promotes patient acceptance. In addition, buprenorphine has two features that decrease street diversion. Buprenorphine can precipitate opiate withdrawal when buprenorphine is taken by an opiate dependent patient (Schuh et al. 1996) and buprenorphine can be marketed both alone (Subutex®) and in combination with naloxone (Suboxone®). In the latter formulation, if it is crushed and injected, acute opiate withdrawal symptoms will occur which are a potent disincentive for prescription opioid abuse (Yokell et al. 2011).

### **2.2.3 Medication assisted treatment utilizing naltrexone**

Naltrexone is a non-narcotic long-acting, opioid antagonist that blocks the euphoric effects of opioids binding the mu opioid receptor. Unlike methadone, there is no negative reinforcement (opiate withdrawal) upon discontinuation. Due to naltrexone's opioid antagonism, patients must abstain from opioids for a minimum of seven days prior to starting treatment to avoid the precipitation of opiate withdrawal. The effectiveness of naltrexone treatment depends upon patient motivation and social support system (Greenstein et al 1983). Thus, in cultures where there is strong family or social support for the patient in care, oral naltrexone has been shown to be effective in the prevention of relapse to heroin use (Krupitsky et al 2010). Because of a lack of positive reinforcing effects with naltrexone and low motivation on the part of many patients, as well as, poor clinician acceptability, it is not widely prescribed for the treatment of opioid dependence in the United States.

Vivitrol is an injectable extended-release formulation of naltrexone that has recently been approved for the treatment of opioid abuse and dependence. Vivitrol addresses the concern of medication adherence as a monthly injectable formulation and has been shown to be more effective than oral naltrexone (Krupitsky & Blokhina, 2010). This was also shown in a recent Phase 3 clinical trial that confirmed Vivitrol's safety and efficacy in the prevention of relapse to heroin use in a cohort of injection drug users. A higher retention in care and higher rates of

opioid-free urine screens were observed along with a significant reduction in opioid craving compared to placebo. Currently, studies are underway to determine the most efficacious service model(s) for the use of vivitrol in the treatment of relapse prevention to heroin use.

**3. Medication assisted treatment: Stages of treatment and recovery**

The stages or phase of MAT are shown in Table 3. The patient travels through these three stages of treatment, sometimes linearly and sometimes with oscillations between phases. The ultimate goal upon entering MAT is a good clinical outcome which includes the

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<ul style="list-style-type: none"><li>• <u>Induction</u><ul style="list-style-type: none"><li>○ Medication is chosen based on clinical and patient circumstances</li><li>○ MAT initiation where initial dosing of medication is observed and dosing titration is performed by a clinician</li><li>○ Dosing and dose titration is based on expression and control of withdrawal symptoms and is a critical period in terms of risk of opioid overdose in treatment</li><li>○ procedures for patient observation during and after dose titration are incorporated into the clinic setting</li><li>○ Induction can last 7-10 days with the goal of obtaining a therapeutic dose of opioid medication</li></ul></li><li>• <u>Stabilization</u><ul style="list-style-type: none"><li>○ stabilization phase occurs when the patient no longer exhibits drug seeking behavior or craving</li><li>○ The correct dosage of medication is critical (overdosing versus underdosing) as well as successful participation of the patient in behavioral therapies and rehabilitation services</li><li>○ MAT provider determines stabilization based on patient symptoms, not on opioid free urine samples</li><li>○ Individual patient health (e.g. pregnancy, liver disease, etc.), other medical treatments including HAART and TB treatments, and other drug use or alcohol consumption affects stabilization</li></ul></li><li>• <u>Maintenance</u><ul style="list-style-type: none"><li>○ Maintenance pharmacotherapy occurs when the patient is responding optimally to medication treatment and routine dose adjustments are not needed.</li><li>○ Patients at this stage have stopped using illicit opioid and resumed productive lifestyles away from the local drug culture.</li><li>○ It is also at this stage that patients should have minimal or normal medical needs and can move away from intensive drug treatment settings and receive their medications in a primary care/community setting.</li><li>○ Typically take home medication of controlled medications is allowed for patients</li><li>○ If maintenance phase cannot be reached, other drug dependence treatment approaches should be explored to complement MAT</li></ul></li></ul>
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Table 3. Stages or Phases of MAT

recovery from opioid abuse and dependence and social reintegration back into society. The individual in recovery is a functioning member of the community and contributes to the social fiber and health of the community. Thus, a foundation of MAT is the obtainment of Recovery from opioid abuse and dependence (Davidson & White, 2007).

The recovery process is the individual way in which a person actively manages their substance use disorder with efforts to reclaim full functional and meaningful lives in the community. Recovery is personal process of growth and change which embraces hope, autonomy and the elements that result in establishing a satisfying and productive life. MAT is a recovery oriented system of care when integrated with other medical, social and rehabilitative services in support of the individual's and family's long term efforts to reclaim full and meaningful lives in the community. Important in recovery is the provision of comprehensive services in the context of MAT but also a supportive, enabling environment that fosters individual responsibility over one's health and empowerment to change to a healthy lifestyle (Sowers, 2005).

MAT, as a recovery orientated system of care, has four phases as shown in Table 4, along with a set of recovery oriented goals, strategies, and services (White & Mojer-Torres, 2010). An important consideration in phase four, long term sustained recovery, is the personal decision to continue with medical maintenance of pharmacotherapy or to taper the medication. In either case, the home or living environment is critical to the prevention of relapse to opioid use. To prevent relapse of opioid use the individual in recovery needs a drug free environment. While significant gains have been made through national prevention programs such as "Drug Free Communities", it remains a Herculean task to keep a community entirely free of illicit drug use. Thus, for long term recovery the home or living environment is where recovery is nucleated (Ashcraft et al, 2008). Local peer recovery programs as well as recovery oriented systems of care that link to or provide individualized, quality long term supportive care are critical (Jason & Ferrari, 2010). These settings provide a network of people to support abstinence as well as a low risk environment to support recovery. Receiving abstinence support, guidance and information from a recovery home, that is committed to long term sobriety, reduces the risk of relapse to illicit opioid use. These homes need to be considered as a fundamental component in the development and maintenance of the public health of communities.

#### **4. Service models for medication assisted treatment**

Health service programs deliver MAT in a regulatory environment where both the federal government and state/local government provide a regulatory framework for the access to and delivery of medications that are controlled by international convention (Kresina et al, 2009). In the United States, state and local regulation can enhance the federal regulations but they can not negate the federal regulations. The MAT federal regulations can be found in the Code of Federal Regulations (CFR, 2002) and establish procedures to determine if a health practitioner is qualified to dispense methadone in the treatment of opioid abuse and dependence in opioid treatment programs, as well as, the quantity of methadone that can be provided for unsupervised use by patients. Thus, the federal regulations address the balance needed in the use of controlled medications for treatment versus the restrictions to limit diversion of the controlled medication (Yokell et al 2011).

The MAT federal regulations do not regulate the health service models that can be used to maximize access to MAT as well as time in treatment. These are two important

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<ul style="list-style-type: none"><li>• <i>Recovery initiation and stabilization</i><ul style="list-style-type: none"><li>○ <u>Major goal</u>- eliminate use of illicit opioid use for at least twenty-four hours as well as other drug of abuse<ul style="list-style-type: none"><li>▪ Educate the patient about the risk and benefits of pharmacotherapy</li><li>▪ Provide a choice of alternate/supplemental therapeutic approaches</li><li>▪ Identify patient’s treatment needs and engage early</li><li>▪ Minimize sedative and side effects of medication</li><li>▪ Asses safety and adequacy of each dose after administration</li><li>▪ Discourage self medication of withdrawal symptoms</li><li>▪ Assess and initially address medical, social, legal, family and other problems</li><li>▪ Develop initial coping and craving strategies</li></ul></li></ul></li><li>• <i>Early recovery and rehabilitation</i><ul style="list-style-type: none"><li>○ <u>Major goal</u>- empower individuals to cope with life problems, medical needs co-occurring disorders vocational and educational needs, family problems, legal issues and develop long term goals for education, employment and family reconciliation<ul style="list-style-type: none"><li>▪ Insure medication dose promotes daily comfort</li><li>▪ Link patient to family and peer-recovery support</li><li>▪ Develop recovery plan</li><li>▪ Assess and initially address personal strengths and needs</li></ul></li></ul></li><li>• <i>Recovery Maintenance</i><ul style="list-style-type: none"><li>○ <u>Major goal</u>- patient assumes primary responsibility for their life<ul style="list-style-type: none"><li>▪ Patient receives needed integrated services</li><li>▪ Patient is active in community recovery support programs</li><li>▪ Patient receives take home medication from an OTP</li><li>▪ Decision on medical maintenance or tapering of pharmacotherapy</li></ul></li></ul></li><li>• <i>Long-term Sustained Recovery</i><ul style="list-style-type: none"><li>○ <u>Major goal</u>- continued primary responsibility for life<ul style="list-style-type: none"><li>▪ Taper from pharmacotherapy- quarterly or biannual check-up from substance abuse treatment program</li><li>▪ Continuing pharmacotherapy- continued regular check-up with substance abuse treatment provider</li><li>▪ Continued engagement with peer-based recovery support program</li><li>▪ Patient becomes a recovery support for other patients</li></ul></li></ul></li></ul>
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Table 4. Phases and Goals of MAT Recovery Oriented Systems of Care



characteristics to maximize as one designs model MAT programs to ensure good clinical and public health outcomes. Barrier free access to MAT is important for obtaining maximal public health impact and reaching all opioid abusing individuals seeking treatment. Research studies have shown that the more time in MAT the better the treatment outcome. Thus, MAT programs providing comprehensive services as part of the continuum of care (see Table 2) in an enabling environment result in quality and effective substance abuse treatment services that promote individual well-being and improved community health.

#### **4.1 Integrated models of medication assisted treatment**

Health service models for MAT that provide comprehensive services interface substance abuse treatment services with primary medical care and social/rehabilitation services. That interface can be comprehensive through the integration of substance abuse treatment services, primary medical care, infectious disease prevention, care and treatment and social/rehabilitation services. An integrated care and treatment model, where MAT services are provided within primary care using a single medical record, minimizes the stigma and discrimination associated with drug treatment services while improving overall health outcomes in a cost-effective manner (Collins et al 2010).

For OTPs dispensing methadone, primary medical care and social/rehabilitation services are integrated on-site in the structured environment where methadone is dispensed (Freidman et al 1999; Kresina et al 2008). Based on patient needs, various types of health services can be integrated into OTP MAT services including primary care, mental health, and infectious diseases. Specific limiting factors for the integration of services have been shown to be the organizational structure of the OTP and cost.

Buprenorphine, a less regulated opioid agonist medication, is approved in the United States for office based opioid treatment. An office based setting provides enhanced treatment access to MAT using buprenorphine in a less stigmatized environment enabling integrated medical care of infectious diseases and co-morbid conditions (Gunderson & Fiellin, 2008). Multiple models have been piloted for the integration of MAT using buprenorphine within HIV primary care (Sullivan et al 2006). These include an on-site combination of addiction treatment/HIV specialist treatment; a HIV primary care physician prescribing buprenorphine; a non-physician health care provider integrating medical care and substance abuse treatment services using buprenorphine; and a community outreach model where buprenorphine is provided along with medical services in a mobile van. These pilot projects have uncovered barriers to integrating MAT using buprenorphine within HIV primary care that are both financial and regulatory. Regulatory challenges include licensing and training restrictions imposed by the Drug Addiction Treatment Act of 2000 and confidentiality regulations for alcohol and drug treatment records (Schackman et al 2006). A recent study has shown that in a primary care setting that used buprenorphine, prescription opioid dependent patients showed better clinical outcomes compared to patients who were dependent on heroin (Moore et al, 2007).

Naltrexone is a non-narcotic and therefore non-controlled medication for the treatment of opioid abuse as well as alcohol abuse. Naltrexone integrated with mental health services, particularly psychosocial treatment has been shown to be an effective maintenance treatment for reducing heroin use after detoxification (Minozzi et al. 2006). In addition, using clonidine and naltrexone together has been shown to be successfully integrated into a primary care setting (O'Connor et al. 1997). In this study retention in care and successful

detoxification from opioid abuse was observed with MAT using either naltrexone or buprenorphine. In other care settings, treatment of alcohol use disorders using naltrexone has been successfully integrated into the treatment of patients who have tuberculosis (Greenfield et al. 2010). Current efforts are determining the optimum conditions to integrate vivitrol (extended release naltrexone) into HIV primary care programs. Additionally, how to integrate vivitrol into an OTP setting and in primary medical care as a relapse prevention intervention for patients following their completion of maintenance treatment with either methadone or buprenorphine, is currently moving forward.

#### **4.2 Coordinated care models of medication assisted treatment**

Health service models for MAT that provide comprehensive services can connect substance abuse treatment services with primary medical care and social/rehabilitation services in a non-integrated but coordinated fashion. Here, MAT services coordinate with primary medical care and social/rehabilitation services to promote good patient outcomes and enhance community health. MAT, health services and social/rehabilitation services can be separately managed with a different network of health care providers but co-located to allow convenient utilization of primary care, MAT and other services. An additional coordinated approach provides primary care, MAT and other services at distinct locations through a differing network of health care providers. As shown in a recent study where twice as many patients retained in MAT when the MAT services were provided at single location compared to referral of MAT to a distant location (Lucas et al 2010), providing needed health services at distinct locations is less than optimal. However, coordinated programs can be effective when case managers, peer facilitators, care navigators or others promote or support service utilization at the various locations. For example, a referral system intervention was modeled with linkages to treatment services for substance use, mental health and social services for HIV+ patients receiving HIV primary care (Zaller et al. 2007). Patients receiving the intervention were referred to MAT either at an OTP or in an office based setting that prescribed buprenorphine. An alternative model provided highly stable OTP patients with 28 days of methadone doses and required monthly check-ins. Successful patients were noted to have increased family and social activities and failed patients were provided stepped treatment intensification (King et al. 2006). Community -wide health service delivery programs also provide an alternative to integration through enhanced access to networked drug treatment and comorbidity health services (Neufeld et al 2010).

Unique to buprenorphine is the model that a substance abuse treatment specialist provides the initial treatment (induction) with buprenorphine until the patient is stabilized. Then the patient is transferred/referred to a primary care physician who can then provide maintenance buprenorphine treatment and medical primary care. This so called 'wheel and spoke model' allows for substance abuse treatment specialists to manage the more difficult portion of buprenorphine treatment (early treatment -or induction phase) while the primary care medical program manages the long term maintenance phase of buprenorphine treatment (BBI, 2008). This model is important in the United States since the Drug Addiction Treatment Act of 2000 limits the number of patients a qualified buprenorphine treatment provider can manage in their practice (DATA, 2000). This model has been adapted to HIV+ patients where the buprenorphine induction is performed by the substance abuse treatment specialist and then the patient is transferred/ referred to the HIV primary care physician (Basu et al. 2006).

Coordinated MAT for patients seeking relapse prevention interventions after detoxification from opioid use can be provided by naltrexone or the recently approved vivitrol. As noted earlier, naltrexone it is not widely prescribed for the treatment of opioid dependence in the United States, but is provided as an office based treatment for opioid dependence after detoxification. In addition, studies have shown that the extended release formulations are effective in reducing opioid use and retaining patients in care after detoxification (Comer et al 2006; Kunoe et al. 2010). Fishman et al 2010 has shown good clinical outcomes (retention in care and reduced opioid use) for adolescents receiving vivitrol over a four month period. This study is important because of the limited use of controlled pharmacotherapies in adolescent populations as part of national regulatory frameworks.

### **5. Preventing HIV infection by integration of medication assisted treatment into HIV prevention services**

Important HIV prevention interventions for people who inject drugs are the provision of clean needles and syringe through syringe service programs and associated HIV testing and counseling programs. These HIV prevention interventions, when integrated into MAT programs, maximize the enrollment in treatment programs for opioid and alcohol abuse, and thereby maximize HIV prevention efforts (Kidorf et al 2009; Lloyd et al 2005). Maximizing HIV prevention efforts targeting people who use drugs and those dependent on opioids and alcohol are critical to prevent HIV infection in these most-at-risk populations. Integrating drug abuse treatment and early HIV prevention interventions, particularly HIV testing and counseling, are important as components of the newly emerging “Seek, Test, Treat and Retain” strategy (Crawford & Vlahov, 2010; Taeghe, 2011). This is an engagement and retention strategy that outreach workers can employ with injection drug users to reduce their risk for HIV infection. By utilizing outreach workers to seek out most-at-risk people who inject drugs, establish their HIV status through HIV testing, followed by sexual risk reduction counselling, HIV risk behaviors can be addressed with subsequent emphasis on treatment for their substance use disorder.

Unfortunately, there is not significant integration of HIV testing and counseling in OTPs. In the US, while approximately 90% of opioid treatment programs provide some form of federally mandated HIV/AIDS education, only 74% of opioid treatment programs offered HIV testing (Kresina et al 2005). These services appear underutilized in that approximately one-in-three persons receiving substance abuse treatment also received HIV testing and counselling (Pollack & D'Aunno, 2010). Globally, although substantial efforts are being made to increase the availability of HIV testing, most-at-risk populations remain underserved with regard to HIV prevention service utilization. It is estimated that only 10% of persons at-risk for HIV infection receive HIV testing. Thus, strategies such as opt-out testing, home-based testing, door-to-door testing as well as providing dedicated HIV testing counselors at point-of-service locations are being utilized to enhance the uptake of HIV testing for people who use alcohol and inject drugs. Studies have shown that most-at-risk populations prefer point-of-service HIV testing, however, this intervention requires additional measures to support HIV positive individuals entering into HIV care and treatment (Keller et al 2011).

### **6. Preventing HIV transmission by integration of medication assisted treatment into HIV care and treatment**

A significant factor in not reducing the global HIV epidemic is the lack of entrance into HIV care and treatment by most-at-risk populations. These populations, which include illicit

drug users and alcohol abusers, encounter numerous barriers in accessing HIV care and treatment. In addition, once in treatment these individuals often suffer stigma and discrimination as they receive their needed medical care. The result is an increase in the prevalence of medical and psychiatric co-morbidities as well as social issues and high risk behaviors, in addition to worse clinical outcomes with a higher mortality rate compared to the non-drug and non-alcohol using populations infected with HIV (Altice et al 2010).

The increased mortality rate noted in people who inject drugs is related to their late presentation for HIV care. Patients who present late for care and treatment of HIV/AIDS are at a higher risk of significant clinical complications and are thus more difficult to clinically manage. Late presentation for treatment of HIV/AIDS is a common scenario leading to death (Moreno et al 2010). A recent study has documented a highly lethal neurological syndrome found in HIV-infected drug abusers (Newsome et al 2011). Although rare, the newly described syndrome is highly lethal with a mean survival time of 21 days after diagnosis. The authors suggest that access and initiation of antiretroviral therapy may provide a better outcome for these patients. In addition, substance abuse treatment, particularly MAT, which has been shown to enhance the health status, reduce mortality and quality of life of injection drug users, would be an important adjunct to anti-retroviral treatment for these patients. Thus, as noted earlier integrating both MAT with anti-retroviral treatment in a HIV primary care setting is a paradigm to optimize health outcomes and the health status of HIV-infected injection drug users.

How MAT is integrated in HIV primary care programs depends on the country's regulatory framework. In the United States, all medications except methadone, can be prescribed to patients in a HIV primary care or outpatient HIV clinical care setting. The federal regulations in the United States require methadone to be dispensed in OTPs. However, in this setting studies have shown that HIV care and anti-retroviral treatment can be effectively prescribed either as directly observed therapy or as routine care. Other countries, such as Australia, have less stringent federal regulations for prescribing controlled medications and all medications comprising MAT can be provided in a primary care setting. In either case, the important aspect of providing integrated MAT and HIV primary care is the single location/clinic. In that case, the patient can receive all the needed services to support their recovery from drug/alcohol dependence as well as care and treatment for HIV infection.

## **7. Essential health interventions for the prevention of HIV infection in people who inject opioids**

The WHO, UNODC and UNAIDS has approved and advocates for a package of essential interventions for the prevention, treatment and care of HIV for people who inject drugs (WHO, 2009a). These evidence based intervention, shown in Table 6, need three important characteristics in their implementation to maximize effectiveness. These interventions need to be part of a public health policy that is human rights based, gender responsive, and community owned.

As noted earlier, no single intervention alone will prevent or reverse the growing national HIV epidemics due to injection drug use and abuse. However, the greatest impact will be obtained when the interventions are provided through an integrated services platform in a comprehensive fashion. And in order to reach all of those seeking HIV prevention, care and treatment services, health service platforms need to provide an enabling environment that establishes confidentiality. In addition, they also need to develop patient-provider trusting



relationships. Both community outreach and peer –to-peer services can promote full service utilization. The national Ministries of Health need to embrace and support these health services and interventions through a supportive legal and policy framework validating their place in the public health area and in society as they improve community health.

Prevention, Care and Treatment for People Who Inject Drugs
1. Needle and Syringe Programmes (NSP)/Syringe Service Programs (SSP)
2. Drug dependence treatment including Medication Assisted Treatment (MAT) and Opioid Substitution Treatment (OST)
3. HIV Testing and Counselling
4. Antiretroviral Therapy (ART)
5. Prevention and Treatment of Sexually Transmitted Infection (STI)
6. Condom distribution programs for People Who Inject Drugs and their sex partners
7. Targeted information, education and communication (IEC) for People Who Inject Drugs and their sex partners
8. Vaccination, diagnosis and treatment of viral hepatitis infection
9. Prevention, diagnosis and treatment of tuberculosis

Table 5. Listing of Internationally Accepted Essential Interventions for HIV

8. Conclusion

Substance abuse treatment is HIV prevention. The use of medication assisted treatment as a component of a comprehensive treatment plan for those individuals who abuse opioids and/or alcohol is an effective, evidence-based treatment paradigm that results in good medical outcomes including a reduction in HIV transmission as well as a reduction of incident infections in opioid and alcohol abusing populations.

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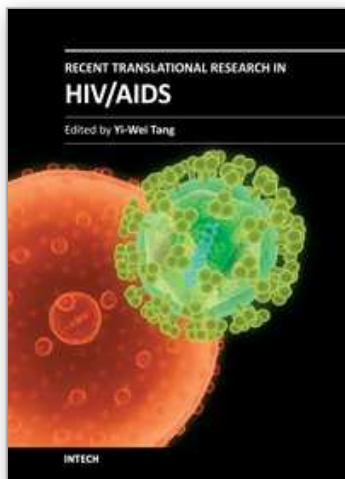
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The collective efforts of HIV/AIDS research scientists from over 16 countries in the world are included in the book. This 27-chapter Open Access book well covers HIV/AIDS translational researches on pathogenesis, diagnosis, treatment, prevention, and also those beyond conventional fields. These are by no means inclusive, but they do offer a good foundation for the development of clinical patient care. The translational model forms the basis for progressing HIV/AIDS clinical research. When linked to the care of the patients, translational researches should result in a direct benefit for HIV/AIDS patients.

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