

Reducing Mortality of People Who Use Opioids through Medication Assisted Treatment for Opioid Dependence

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Abstract

Background: Globally, in countries of all income levels, people who inject drugs (PWID) are at high risk for premature mortality due to acute and chronic diseases related to injection drug use, including trauma, bacterial infections, viral infections, opioid use disorder, suicide and drug overdose. MAT is the use of medications, in combination with behavioral therapies, to provide a whole-patient approach to the treatment of substance use disorders. Addressing the needs of the whole-patient, including the risk of drug overdose with medications, can not only occur in the clinic but also in the community as part of community-based care.

Methods and findings: Literature review of published cohorts studies and reviews. MAT impacts public health through the reduction of opioid use, opioid overdose mortality and transmission of infectious diseases and can be provided in both clinical and community settings.

Conclusion: MAT is an important treatment paradigm, in clinical settings and in the community, for the reduction of premature mortality in PWID and who are opioid-dependent. HIV primary care and pharmacies provide health service delivery venues for MAT that can substantially reduce the risk of premature mortality of people living with HIV. As part of medical care, as well as, part of community-based care for PWID, providing medications to reduce the risk of opioid overdose is an emerging health care practice that can reduce fatalities from opioid overdose.

Keywords: Methadone; Buprenorphine; Medication assisted treatment; Opioids; Prescription opioid; Abuse; Heroin; Mortality; Overdose; HIV primary care

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Mortality in PWID

PWID are at high risk for premature mortality when compared to the data on mortality in populations that do not inject drugs [1-4]. For both high income countries and low or middle income countries cohort studies have shown higher, as much as 13 times higher, mortality rates and standardized mortality ratios for PWID. The causes of mortality are related to acute and chronic diseases associated with injection drug use, including trauma, bacterial infections, viral infections, opioid use disorder, suicide and drug overdose. Another factor related to the risk of death in PWID is the type of drug injected. People who use opioids have higher mortality risk than stimulant users. For PWID and who are living with HIV (PLWHIV), the risk of premature mortality is elevated above PWID who are not living with HIV. In cohort

studies of PLWHIV, both HIV infection and drug overdose have been reported as the leading causes of premature mortality [3]. Mortality due to HIV/AIDS appears to be more prevalent in males compared to females and may result from being disengaged from the general health care system, as well as, specifically lacking access to anti-retroviral therapy. Thus, health interventions that reduce drug use and promote access and entry into health care are important public health measures to reduce the mortality in PWID, both with and without HIV infection.

Reducing Mortality in PWID with MAT

Injection drug use is a serious public health issue and PWID are at high risk for co-occurring medical disorders, mental health disorders and social problems [5]. The use of illicit opioids or

prescription opioids can lead to opioid use disorder and the high-risk of premature mortality, particularly through unintentional drug overdose [6]. However, premature mortality can be reduced because opioid dependence is a chronic, relapsing disease that can be successfully medically treated [7, 8]. An effective treatment paradigm for opioid dependence is to provide comprehensive substance abuse treatment using MAT that addresses the complex medical, physiologic, psychiatric and social needs of the patients [9]. MAT is also an effective paradigm to incorporate into the medical management of co-morbid medical infectious diseases such as the HIV, hepatitis virus infection or tuberculosis for PWID [10, 11]. MAT impacts public health through the reduction of opioid use, opioid overdose mortality and transmission of infectious diseases [12].

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 [13]. MAT regulations establish policy and procedures to determine which health practitioners are qualified to dispense or prescribe medications, as well as, the clinical treatment setting. In the United States, federal regulations restrict the dispensing of methadone to Opioid Treatment Programs, but allow other pharmacotherapies, such as buprenorphine and naltrexone, to be provided in an office base, primary care setting. Such regulations promote the use of medications to treat opioid dependence and maximize access to MAT, as well as, time in treatment while addressing diversion of controlled medications. Maximizing access to MAT and retention in care and treatment are important characteristics in designing comprehensive MAT programs to promote good clinical and public health outcomes [14]. Barriers to access include requiring a certain number of drug detoxifications prior to the receipt of MAT, full capacity treatment programs resulting in wait times for treatment entry, registration of patients prior to treatment access, and a limited number of treatment programs providing MAT [15-17]. Barrier free access to MAT is important because the relative risk of mortality in out-of-treatment clients has been estimated to be 2.4 times higher than patients receiving treatment [18]. In addition, studies have shown that the more time patients remaining in treatment, the better the treatment outcome [19]. Thus, MAT programs as part of the continuum of care for opioid dependence has been shown to reduce all-cause mortality for those in long-term treatment and thus promote individual improved decision-making and well-being, as well as, community health [20, 21]. Specifically for women, long-term treatment for opioid dependence can reduce mortality by addressing poly-substance use; while in men, long-term treatment can reduce mortality by reducing overdose risk and increasing protective factors, such as employment and housing [22].

MAT and HIV Primary Care

Opioid users are less physically and psychiatrically healthy than nonusers and, thus, are frequent users of medical services [5, 23]. Providing care and treatment for the multiple comorbidities in a primary care setting and creating a medical home for opioid dependent patients is an important venue into which MAT could

be integrated. This is particularly important for PWID who are living with HIV infection. For opioid dependent PLHIV, all-cause mortality is very high with the leading causes of death being drug overdose and HIV/AIDS [3, 24]. HIV primary care becomes an important venue to address both HIV/AIDS and risk of overdose due to opioid use. The provision of MAT in a primary care setting versus referral for treatment is roughly twice as likely to result in entry into drug treatment [25]. For PLHIV, receiving MAT along with appropriate dosing of medication for opioid use disorders, enhanced time in treatment, and initiation of anti-retroviral treatment results in decreased mortality [26-28]. In combination, MAT and anti-retroviral treatment can increase survival through reductions in overdose deaths and AIDS-related mortality. In addition, the provision of MAT to PLHIV can also reduce the transmission of HIV by roughly 50% [28, 29]. This reduction in HIV transmission can be augmented by the obtainment of an undetectable viral load in PLHIV through the use of anti-retroviral therapy [30]. Thus, the integration of MAT with anti-retroviral treatment for PLHIV, who are opioid dependent, represents a best practice model where both MAT services and anti-retroviral care and treatment can be provided with optimal clinical outcomes [31].

Integrating anti-retroviral treatment into primary care-based addiction treatment has been shown to be effective for PLHIV when services included a comprehensive substance use assessment, individual and group counseling, MAT comprising buprenorphine pharmacotherapy and case management [32]. In this study, receipt of MAT was associated with engagement in care and a driver for acceptance of comprehensive substance abuse treatment. Patient preferences have been shown to be positive for the convenience and efficiency of integrated care; supportive for team-based care; positive toward the offered needed structure; valuing the importance of counseling and education; and an improved overall well-being and quality of life [33]. While viewed as efficacious, integration of MAT with HIV primary care has been met with system barriers, particularly when integrating anti-retroviral treatment into methadone treatment in Opioid Treatment Programs. Results have been mixed with some successes and other results showing no benefit for HIV outcomes using directly administered anti-retroviral treatment [34-38]. Directly administered anti-retroviral treatment has been recommended for PWID by the International Association of Providers of AIDS Care [39]. A recent study, addressing issues that may influence HIV outcomes, has shown that the receipt of methadone doses greater than 100 mg/day was associated with optimal anti-retroviral adherence [40]. In addition, this study showed a dose-response relationship between increasing methadone dose and ante-retroviral adherence. Another study performed in China points out the importance of national anti-retroviral treatment guidelines for PWID in the integration of MAT with anti-retroviral treatment [41]. In this study, patients who entered MAT after becoming eligible for anti-retroviral treatment had less favorable treatment outcomes than patients who entered MAT regardless of anti-retroviral treatment eligibility. The new recommendations of implementing Test and Treat for PWID may reduce barriers to accessing anti-retroviral treatment, but a recent study has shown that that for PLHIV who are opioid

dependent, free anti-retroviral treatment reduces HIV-related mortality but not drug-related mortality [42].

MAT and Incarceration

The World Health Organization document, Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations, provides guidance on HIV prevention, care and treatment for all individuals detained in criminal justice and prison [43]. These guidelines provide a comprehensive package of services for closed settings that included the provision of MAT for those with opioid dependence in detention. The guidelines stress the need for medical services, such as MAT, to be uniformly available both in the detention and in the community. Access to MAT is required in both settings due to the high mortality rate of persons who opioid dependent and release from the detention [44-47]. The highest risk is death for these individuals is from opioid overdose during the post-release period. Implementation of MAT prior to release from the closed setting reduces illicit opioid use and risk behaviors in in the closed setting, as well as, the risk of death due to overdose on release while promoting access to community-based drug treatment [48-50]. A study performed almost a decade ago has shown that only 29 countries or territories offer MAT in prisons and 37 countries offer MAT in the community [51]. Only 1-14% of the prison population in these countries with MAT has access to this life saving treatment. This underutilization is global, with use of MAT in the United States in prison settings limited largely to pregnant women and individuals experiencing withdrawal [52]. Those reentering the community from detention were not likely to receive MAT. Barriers that reduce the use of MAT include the criminal justice system preference for drug-free treatment, limited knowledge of the benefits of MAT in the criminal justice system, security concerns related to medications, regulations prohibiting use of MAT for certain agencies, and lack of qualified medical staff [52]. These barriers can be overcome through innovative treatment paradigms that utilize MAT with non-opioid agonist pharmaceuticals as part of treatment programs during incarceration and in post-release programs [53, 54].

MAT and Unintentional Drug Overdose

An unintentional drug overdose results from drug misuse, drug abuse, and taking too much of a drug for medical reasons. Unintentional drug overdoses can occur with licit prescription opioids or illicit street opioids, such as heroin. With the increasing abuse of opioid pain medications, in the United States more deaths have occurred due to unintentional drug overdoses than automobile accidents [55]. This major threat to public health has resulted in a call for more patient education, opioid prescription monitoring, physician-patient pain management contracts, as

well as, increased distribution of naloxone in the community and drug treatment settings [56].

Community-based programs have offered opioid overdose prevention services to laypersons who might witness an overdose, including persons who use drugs, their families and friends, and service providers [57]. From 1996-2014, this distribution has resulted in the reporting of over 26,000 overdose reversals. Retail pharmacies are a community venue that can provide opioid overdose prevention services through their universal presence in communities across the nation, easy access, and extended hours [58]. Pharmacists currently can provide services for PWID, such as over-the-counter needle sales and opioid agonist therapy counseling. In addition through prescription drug monitoring programs, pharmacists currently identify individuals who doctor shop for opioid medications and are thus at-risk for a drug overdose [59]. Pharmacists are well-positioned to provide additional services to opioid users that include but are not limited to overdose education, stocking and distribution of naloxone, and promoting naloxone co-prescribing where permissible by law [60]. In a number of health care delivery models, pharmacists are not only dispensing prescriptions written by a physician, but also dispensing naloxone via collaborative practice agreements [60], standing order legislation [61], or self-prescribing without involvement of a physician as allowed by state law [62]. Through these pilot programs, pharmacists have demonstrated a successful increase in community-based naloxone distribution efforts [60]. These programs address the barriers to health care service delivery to and access by PWIDs that include crime, ethical consideration, time and legal constraints. As these programs are adopted and scaled-up with community acceptance, barriers are overcome and pharmacists can extend additional services with increased exposure to PWID [63]. Thus, pharmacists can also help fill a growing need to provide overdose education and naloxone distribution to reduce mortality of people who use and misuse opioids.

Drug treatment programs that provide MAT are also important venues for the distribution of naloxone to reduce the mortality due to opioid overdose. Patients, with opioid use disorder, are most vulnerable to overdose during the induction phase of MAT, after dropping out of MAT before completion, or upon completion of detoxification [64]. In addition, since opioid dependence is a chronic relapsing disease, the risk of relapse and overdose remains real throughout the course of and after the completion of treatment. With access to naloxone, all health care providers involved in the treatment continuum can enhance their medical management of patients with opioid use disorders and patients can benefit from receiving an additional supportive tool as part of MAT. Extending the distribution and educational trainings to clinical settings that provide all forms of treatment for opioid use disorders can augment the reduction in overdose deaths [65].

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