

The Impact in Low and Middle Income Countries of Screening and Management of Substance-Related and Addictive Disorders in HIV Care

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Abstract

Illicit drug use, as reported by the World Drug Report, impacts public health globally and can lead to the development of substance-related and addictive disorders. Substance-related and addictive disorders comprise a family of related individual disorders along with an operational set of diagnostic criteria, with the most significant contributor to HIV/AIDS being opioid-use disorders (OUDs). Screening individuals for OUDs, followed by management of these disorders, are core interventions in HIV care and treatment in developed countries. For people living with HIV (PLHIV) in developed countries, interventions for OUDs improve the HIV –related outcomes of mortality, quality of life (QoL), retention in care, and anti-retroviral treatment (ART) adherence. This review examines the interventions: screening for and management of OUDs in HIV care and treatment in low and middle-income countries (LMIC), to determine the impact of the interventions on HIV-related outcomes in the areas of morbidity and mortality, retention in care and adherence to ART, QoL, and prevention of ongoing HIV transmission. The body of evidence regarding screening, diagnosis and management of OUDs in HIV care in LMIC suggests that these interventions impact ART treatment adherence as well as mortality, morbidity, retention in care, QoL, and prevention of ongoing HIV transmission.

Keywords: HIV primary care; Prevention; Substance use; Alcohol use disorder; Health services integration; Retention; Cost-effectiveness; Screening; Treatment and Care.

Introduction

Addressing substance-related and addictive disorders are fundamental components of personal health and well-being as defined by the World Health Organization (WHO) [1]. Substance-related and addictive disorders comprise a family of related alcohol-, caffeine-, cannabis-, hallucinogen-, inhalant-, sedative-, hypnotic-, anxiolytic-, stimulant-, opioid-, tobacco and other substance-related disorders, with individual disorder definitions and diagnostic criteria [2]. Substance-related and addictive disorders account for at least 10% of the global burden of disease [3]. In the United States, screening of a nationally representative population of people living with HIV (PLHIV) showed that 40% used illicit drugs and 12% screened positive for drug dependence [4]. Treatment of PLHIV in HIV care who receives medication assisted treatment (MAT) for opioid dependence show improved HIV-related outcomes of mortality, quality of life (QoL), retention in care, and anti-retroviral treatment (ART) adherence [5]. WHO suggests that substance-related and addictive disorders are highly prevalent and burdensome and that the gap between providing treatment that is urgently needed and what is available to reduce the burden of disease is still very wide [6]. WHO guidelines underscore that that HIV care settings provide the opportunity to screen for and manage common substance-related and addictive disorders through a range of care and treatment options that include counseling and pharmacotherapy and urges that that these services should be part of national HIV/AIDS programs, and integrated into primary care programs for PLHIV [6,7].

When screening of PLHIV who use and inject illicit drugs, opioid use is dominant followed by stimulant (amphetamine-type stimulants, ATS) [8-10]. Thus, opioid-use disorders and stimulant-use disorders are important comorbidities for PLHIV who need HIV care and support services. However, stimulant-use disorders are not routinely screened for in HIV care settings although highly prevalent in key populations seeking care [11-13]. Alternatively, OUDs are recognized as a significant HIV risk factor for people who inject drugs and has been shown to be the largest contributor to disability-adjusted life years (DALYs) for PLHIV due to substance-related and addictive disorders [7, 10, 14,15].

WHO guidance also recommends the promotion of well-being, and the treatment and rehabilitation of people with substance use disorders. The WHO guidelines indicate that substance abuse treatment, particularly methadone maintenance treatment (MMT) for opioid dependent PLHIV, is an essential HIV prevention intervention and recommends the integration of substance abuse treatment

within HIV care and treatment programs [15]. Recently, the WHO released consolidated guidelines on HIV that contain a comprehensive package of interventions for key populations [14]. Implementation and integration of these interventions, including screening, diagnosis and treatment of substance use disorders, particularly for opioid dependence and the use of MMT as part of MAT for PLHIV in HIV care, can substantially impact public health and the HIV epidemic [16, 17].

The purpose of this review is to provide an examination of the cumulative data to date on the interventions comprising screening for and management of OUDs as part of HIV care in LMIC for the HIV outcomes of morbidity and mortality, retention in care, quality of life (QoL) and HIV transmission.

Methods

Relevant studies were identified through Medline, PubMed, Global Health, and Embase through Ovid; Cumulative Index to Nursing and Allied Health Literature (CINAHL) through EBSCO; Sociological Abstracts (SOCA) through ProQuest; and African Index Medicus (AIM) through the WHO. The databases were searched for all citations published between January 2004 and December 2015. Search terms used to perform the review were intentionally chosen to produce a broad scope of results relating to HIV/AIDS and the selected interventions in LMIC. The identified citations were reviewed by at least two researchers and potentially relevant articles were retrieved and read in their entirety. Articles were included in the review if they: (a) evaluated screening for opioid-use or stimulant-use disorders in PLHIV or screened for opioid-use or stimulant-use disorders, followed by management of MHD in PLHIV (b) were conducted in LMIC, (c) reported on at least one of the five outcomes of interest.

The included studies were assessed and summarized by study design, study period, country, and number of participants, key findings, internal and external validity, and overall quality of evidence, cost-effectiveness and additional comments. The overall quality of evidence for individual studies was rated as strong, medium or weak on the basis of these factors. Because of the heterogeneity of literature, we did not attempt quantitative synthesis of study results overall. Instead, the evidence from all studies that address each outcome were grouped with a summarization of the overall quality of evidence, expected impact of the intervention, and evidence from economic evaluations. The overall quality of the body of evidence for each of the key outcomes was rated as *good*, *fair* and *poor*, and the expected impact of the intervention was rated as *high*, *moderate*, *low* or *uncertain* based on the evidence base and the known clinical benefit of an established intervention on MHD.

Results

A majority of the meta-analyses, quantitative studies, qualitative studies, literature reviews, and reports came from Asia and Eastern Europe but this review also includes articles from other LMIC in South America, the Caribbean, Africa and South Asia. From 2,855 abstracts cited, a total of 180 full-text articles were read; 45 articles met the inclusion criteria, addressing at least one of the outcomes of interest: mortality, morbidity, retention in care, QoL or HIV transmission. The search of the literature identified studies in resource limited settings (RLS) which present data on the prevalence of opioid-use and/or stimulant-use disorders in PLHIV through screening utilizing validated screening tools. In addition, we present (an anticipated) impact of opioid-use and/or stimulant-use disorders on clinical

outcomes in PLHIV based on the identified study results and the global body of evidence comprising the impact of substance-use and addictive disorders on HIV infection. Overall, although studies were noted to address stimulants use in key populations, no studies in RLS providing data on screening or management of stimulant-use disorders in PLHIV in HIV care. Thus, stimulant-use disorders are not reported on as part of this evidence review. A larger cohort of studies was noted for OUDs in PLHIV applying MAT paradigms, and the impact of these treatments on specific HIV-related outcomes. Studies providing data on MAT of opioid-use disorders, predominantly utilized MMT in the treatment of opioid dependence in PLHIV. Thus, the data were analysed with consideration of global data on the impact of the other treatment options or intervention strategies on HIV care and support in the context of the noted HIV outcomes.

Table 1: Summary of the Review of the Impact of OUDs in HIV Care and Treatment in LMIC

HIV Outcome	Overall Quality of the Evidence Rating ^{1, 2}	Impact	Comments
Morbidity & Mortality	Good	High	MAT directly reduces injection drug use morbidity/ mortality from
Retention in Care	Fair	High	OUDsa factor in poor adherence & ARTexclusion
Adherence to ART			
Quality of Life	Fair	Moderate	reduced QoL due to medical & social factors
HIV Transmission	Fair	Moderate	reducing both injection behaviors & risky sexual behavior
<i>Intervention</i>			
SBIRT & MAT	High	High	MAT&counseling is effective in reducing drug use for PLHIV in care

1.The expected impact of the intervention was rated as; **High**=Intervention expected to have a high impact on the outcome, **Moderate** =Likely to have a moderate impact on the outcome, **Low**=Intervention expected to have a low impact on the outcome and, **Uncertain**=Available information is not adequate to assess estimated impact on the outcome.

2.Note, assessment of the expected impact of the intervention was based on published evidence in both LMIC and high income countries. Additional considerations that would inform implementation decisions would have to take into account the cost effectiveness information and country specific contextual considerations.

In this review our categorization of studies resulted in two groups under each outcome: one grouping presented studies with data on opioid-use and/or stimulant-use disorders screening, that is, the occurrence of opioid-use and/or stimulant-use disorders among PLHIV and the given HIV-related outcome; a second grouping encompassed the studies that provide data on the management of opioid-use and/or stimulant-use disorders utilizing treatment and care options ranging from harm reduction strategies to pharmacotherapy in HIV care for the given HIV-related outcome.

Ratings of overall quality of the body of evidence of articles reviewed ranged from “good” to “moderate”. The quality of the overall body of evidence for the screening for and management of OUDs rating was “good” for mortality and morbidity and retention in care and ART, and “fair” for the other outcomes: quality of life, and prevention of onward HIV transmission. The expected impact of screening for and management of OUDs based on the global evidence-based management strategies ranged from “high” to “low”: the rating for mortality was “high”, and “moderate” for the other four outcomes: morbidity, retention in care, QoL and prevention of onward HIV transmission. Multiple studies addressed the cost-effectiveness of the impact of screening for and management of OUDs: These studies showed that MMT is a cost-effective intervention for averting HIV infections and MMT increases retention in HIV care.

Results by Outcome

Mortality: Mortality in PLHIV who inject drugs has been addressed in three major reviews [18-20]. From these reviews, it can be noted that mortality rates for PLHIV who inject drugs are higher in low and middle income countries than in comparison cohorts from higher income countries. In addition, mortality rates for non-AIDS mortality in PLHIV and injecting drugs has been noted to be higher in low and middle –income countries than in higher income countries and highest when PLHIV were not receiving MAT for their opioid dependence. These reviews show that the level of care and treatment services for injection drug users is very low in low and middle income countries leading to higher mortality. Other reviews have shown that SUDs in PLHIV are associated with poorer health of the individual, poor health service quality, weak adherence to ART, and higher mortality rates than the general population [21, 22]. The level of HIV care and treatment services for patients with SUDs, including substance abuse treatment, is very low leading to reported high mortality [18, 20].

Studies also show, however, that integrating HIV care and MMT for opioid dependent PLHIV receiving ART resulted in decreased mortality [23, 25]. The overall rating for the quality of the body of evidence related to screening and the high impact of OUDs on mortality in PLHIV is good

and the rating for integrating MMT into HIV care to reduce mortality of opioid dependent PLHIV is good with high impact.

Morbidity: For LMIC as shown in the mortality studies, SUDs in PLHIV compromises adherence to ART and results in faster progression to AIDS. A common morbidity in PLHIV who inject drugs in low, middle and high income countries is malnutrition [26,27]. Malnutrition is a strong predictor of poor clinical outcomes for PLHIV, particularly for those who inject drugs and receive limited HIV care through drop-in centers [26]. The combination of injection drug use, malnutrition and poverty in PLHIV provides a setting for repeated opportunistic infections and Mycobacterium tuberculosis infection, as well as, other pulmonary diseases [28]. In a resource limiting setting, providing HIV care and treatment, including ART does not fully relieve the manifestations of malnutrition [29]. However, a study by Bachireddy [30] shows that care management through integrated HIV care and substance abuse treatment can result in good clinical outcomes, including reduced morbidity for people who inject drugs (PWID) when these patients receive ART, as well as, effective evidence-based drug treatment.

The rating for screening for SUDs and observed enhanced morbidity in PLHIV is also good and the rating for the intervention of integration of HIV care and treatment for SUDs to reduce morbidity in PLHIV is good with overall moderate impact for these disorders.

Retention in Care and ART: Studies that address the impact of retention in care as an outcome in PLHIV with SUDs show that PLHIV with untreated SUDs are frequently excluded from receiving ART based on a perceived provider bias of poor medication adherence [21]. In addition, SUDs have been shown to be associated with low rates of retention in care and ART adherence in PLHIV [21, 31]. Globally, studies also show that for opioid dependent PLHIV, MMT promotes retention in HIV treatment in closed care systems [32], and that MAT for opioid dependence increases retention in HIV care and ART in LMIC [21, 31, 33, 34]. As has been shown in high income countries, the dose of methadone PLHIV receive in low and middle income countries is an important factor in producing patient stability and retention in treatment [29, 35]. Also, both in high and low income countries, retention in MAT impact HIV outcomes including enhancing the number of PLHIV obtaining virologic suppression [36,37]. Viral suppression of HIV can also be enhanced by directly administered ART in a methadone treatment setting [38]. The rating for retention in care and ART for PLHIV with screening and management with MAT for OUDs is good for LMIC because of the evolving increase of MAT in low and middle income countries and the integration of MAT and ART programs as a best practice [16-18, 21, 23, 30, 31, 37].

Discussion

Quality of Life: Providing MAT to PLHIV who are opioid depend in a HIV care and treatment setting improves the QoL of those patients [30, 38, 39]. A limited number of studies have addressed QoL as an outcome in PLHIV with SUDs. The studies suggest that disabilities are becoming increasingly important issues in the management of HIV and that the QoL of PLHIV is impacted by drug use. The studies in Vietnam show that PLHIV in HIV care with an SUD had reduced QoL and were noted to improve QoL measures the longer they receive MMT [40,41]. The rating for QoL for in the case of interventions for OUDs in LMIC the rating is fair because of the limited number of intervention studies addressing SUDs on QoL to-date.

HIV Transmission: Reducing HIV transmission risk for PLHIV with SUDs addresses access and entry into substance abuse treatment to reduce drug related HIV transmission risk, as well as, HIV prevention interventions to reduce sexual transmission risk. Evidence from LMIC suggests that the use of MAT in a HIV care setting can reduce HIV transmission via high-risk injecting behavior, while HIV counseling and testing can reduce risky sexual behavior. Successful introduction of ART at any CD4 count can have HIV transmission preventive benefit for PLHIV with SUDs, in that obtaining an undetectable viral load can prevent onward sexual transmission of HIV [42, 43].

The evidence rating for the screening for common MHD is fair with moderate impact because although there are a limited number of studies in this category. However, when implemented MAT is highly effective in reducing HIV transmission through a reduction in injection of opioids.

Cost-effectiveness: Studies in Asia and Europe have addressed the cost-effectiveness of treating PLHIV for opioid dependence with MMT [31, 33, 44-47]. Chen [33] determined that PLHIV who are opioid dependent were retained in care at a cost of U.S.\$2,749 per DALY averted when receiving MMT; Xing [44] determined that for MMT in China the cost was U.S.\$9.1-16.7 per month; MMT averted 8.4-87.2 HIV infections with a cost-effectiveness of U.S.\$2509.3-4609.3 per HIV infection averted. Wolfe [31] determined that in areas with concentrated HIV epidemics, the savings ration could be as high as 7:1 for provision of treatment with MMT, compared to the social and medical costs of drug use. Other studies have shown cost effectiveness of providing MAT in hospital settings in LMIC and still others have performed mathematical modeling showing the highly cost –effectiveness of MAT for PLHIV with OUDs.

This review of the literature for the interventions comprising screening for and management of OUDs in HIV care in LMIC for PLHIV resulted in the assessment of screening studies which demonstrate the consequences of SUDs in PLHIV and a limited number of studies which provide data on the clinical management in HIV care programs. All studies showed a negative impact of OUDs on all five patient outcomes. Studies addressing the screening for and treatment of OUDs provide evidence of improved clinical outcomes, with the use of counseling and pharmacotherapy in the treatment of opioid dependence integrated into HIV care and treatment programs to enhance HIV-related outcomes and ultimately reduce morbidity.

WHO documents, other summary review articles by experts in the field, and this evidence-based literature review show that the prevalence of substance-use and addictive disorders is substantial in LMIC, particularly in PLHIV [6, 7]. However, resources in LMIC to address this major health issue are minimal, and where available, there is substantial variation in regional and national services [18]. There is a treatment gap of roughly 90% [31] which can ultimately compromise good clinical outcomes for PLHIV, as well as increase HIV transmission risk behaviors [30]. Furthermore, in areas with concentrated epidemics, addressing opioid dependence with MMT has shown a savings ratio as high as 7:1 for provision of drug treatment compared with social and medical costs of drug use [31].

Substance-related and addictive disorders are a growing health problem particularly for key populations in need of HIV clinical care [11-13]. For key populations, including people who inject drugs, sex workers and men who have sex with men (MSM), substance use disorders are particularly prevalent. There is a growing knowledge framework in LMIC on evidence-based best practices to address illicit drug use through substance abuse treatment and HIV care and support. The Lancet series of articles in 2010 provide an excellent global summary of studies addressing PLHIV, injection drug use and HIV care [18, 21, 31]. This review and other studies show that PLHIV who inject drugs do not routinely access and receive HIV care and substance abuse treatment. Good clinical outcomes occur when these patients access integrated HIV care and substance abuse treatment early in the course of their HIV infection, resulting in reduced HIV morbidity and mortality [21]. Individuals who receive evidence-based substance abuse treatment are more likely to be retained in care and adherent to ART. In such scenarios, substance abuse treatments in HIV care are cost-effective interventions [31].

Programmatic considerations

- **Training of HIV care providers in proper screening and treatment of substance-use and addictive disorders:** Services, such as counseling services and pharmacotherapy programs have been put in place and studied in LMIC, but they are limited and not as developed as in high-income countries [1, 6, 7]. Instead, according to a meta-analysis by AIDSTAR-Two (48), in many LMIC, HIV service providers who are not appropriately trained to recognize and/or treat substance-use and addictive disorders, may view these disorders as a morality issue rather than a medical disorder -citing a study done in South Africa which revealed that many HIV service providers classify excessive alcohol use as “bad character” of patients rather than a medical disorder [48]. Thus, training health care workers in the screening for and management of substance-use and addictive disorders is an important component to consider for improving HIV outcomes.

The WHO recommends that HIV programs provide screening, diagnosis and treatment for PLHIV with common substance use disorders as important elements of HIV care to obtain good HIV clinical outcomes in LMIC [1, 6, 7, 14,15]. To do this, countries need to build and sustain the capacity of health-care providers to recognize and treat common mental health disorders, and determine the kinds of services and referral processes to be offered through various HIV care systems.

There are several validated screening tools that are validated for use in LMIC as well as for specific populations within these countries to identify alcohol use disorders and illicit drug use [6, 7]. Managing these as co-morbidities in a chronic care model for HIV care in LMIC includes basic, standardized regimens and formularies, standardized supervision and patient monitoring approaches, as well as integrated delivery of care at decentralized primary health centers [49] and referring to specialized care as needed: Recent pilot projects in LMIC have shown the feasibility and acceptability of screening for SUDs in outpatient HIV care clinics [50].

- **Enhanced access to treatment of substance use and addictive disorders in LMIC:** Recent studies have shown that the integration of services for substance-use and addictive disorders into HIV care is an effective strategy to address the co-morbidities of PLHIV [21, 51, 52].
- **Integration of evidence-based effective interventions for substance use and addictive disorders in HIV care and ART programs along with concurrent HIV testing:** There is a growing understanding of substance-use and addictive disorders as they relate to HIV care and treatment in LMIC.

However, as noted in this review even where programs exist, services are often limited, have not been well integrated into routine HIV care with no imminent plans to scale up [15]. This review supports improving utilization of screening and management of substance-use and addictive disorders, and the inclusion of interventions within the context of comprehensive HIV care programs, especially as there is evidence that demonstrates the cost-effectiveness of integrating interventions for OUDs into routine HIV care.

- **Address barriers to HIV care experienced by PLHIV:** This analysis provides the evidence-base for the integration of substance-use and addictive disorders services into routine HIV care in order to improve clinical outcomes in PLHIV. These services comprise an array of interventions that address common substance-related and addictive disorders. While it is important to identify evidence-based interventions, it is equally important to address the barriers to MHD care experienced by PLHIV as they attempt to access services when in place [43].

As the screening and management of substance-use and addictive disorders in HIV care is considered by policy makers and program planners, attention needs to be paid to reduce the stigma and discrimination experienced by PLHIV, in particular key populations. The barriers to care presented by the criminalization of behaviors, such as injection drug use, sex work and same sex behaviors must be addressed. Specifically, integration of ART with opioid substitution, increased peer engagement in treatment delivery, and reform of harmful policies are needed to improve ART coverage with people who inject drugs [42]. Eliminating barriers in the context of HIV care and substance-use and addictive disorders must be taken into consideration during the development, piloting and implementation of evidence-based HIV care interventions, having been identified in this review as fundamental components to improving HIV outcomes.

Conclusion

There is a modest evidence base detailing screening for and management of substance-use and addictive disorders utilizing various interventions and treatment paradigms in HIV care in LMIC. Although limited, evidence suggests that integrating services to address substance-use and addictive disorders enhances clinical outcomes for PLHIV. However, more studies in LMIC are necessary to further develop evidence-based HIV care programs integrated with screening and management programs for common disorders. The data to date indicate that integrated services focused on HIV care and treatment and the screening and management of substance-use and addictive disorders can result in improving client social status and overall treatment outcomes for PLHIV. This is a cost-effective way of improving HIV outcomes.

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