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Viral suppression among HIV-infected methadone-maintained patients: The role of ongoing injection drug use and adherence to antiretroviral therapy (ART)

Roman Shrestha[a,b,*], Michael M. Copenhaver[a,b]

[a] Department of Allied Health Sciences, University of Connecticut, Storrs, CT, USA
[b] Institute for Collaboration on Health, Intervention, and Policy, University of Connecticut, Storrs, CT, USA

HIGHLIGHTS

- Methadone maintenance therapy (MMT) is associated with improved virologic outcomes.
- No studies have explored factors associated with viral suppression in HIV-infected patients on MMT.
- We found that one in five participants was not able to achieve viral suppression.
- The benefit of MMT may be negated among a significant segment of methadone-maintained patients.
- These findings have important implications for the recently identified concept of HIV treatment as prevention.

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ABSTRACT

Introduction: Methadone maintenance therapy (MMT) is associated with improved virologic outcomes, yet no studies have explored factors associated with viral suppression in HIV-infected patients on MMT. Given the critical role of sustained viral suppression in maximizing benefits of antiretroviral therapy (ART), we sought to assess factors associated with viral suppression in patients stabilized on MMT.

Methods: A sample of 133 HIV-infected, methadone-maintained patients who reported HIV-risk behaviors were assessed using an audio-computer assisted self-interview (ACASI). Multivariable logistic regression was used to identify significant correlates of viral suppression.

Results: Among all participants, self-reported HIV risk behaviors were highly prevalent and over 80% had achieved viral suppression. Independent correlates of viral suppression were: having optimal adherence to ART (aOR = 4.883, $p = .009$), high CD4 count (aOR = 2.483, $p = .045$), and ongoing injection drug use (aOR = 0.081, $p = .036$). Furthermore, results revealed a significant interaction effect that involved optimal ART adherence and injection of drug use on viral suppression (aOR = 2.953, $p = .029$).

Conclusion: Overall, our findings highlight unaddressed HIV-related treatment challenges faced by certain group of methadone-maintained patients. These findings have significant implications for the HIV treatment as prevention efforts and, thus, indicate the need for comprehensive efforts to promote viral suppression in this risk population.

1. Introduction

Achieving optimal adherence to antiretroviral therapy (ART) and sustaining viral suppression are essential to reduce morbidity and mortality associated with HIV among people living with HIV (PLWH) (Mocroft et al., 2003; Rodger et al., 2013). Further, recent clinical trials have demonstrated that people who achieve and maintain an undetectable viral load effectively have no risk of sexually transmitting HIV. This has contributed to an increasing global consensus regarding the use of antiretroviral medications for HIV prevention, as HIV treatment-as-prevention (TasP) initiatives for PLWH (Bavinton et al., 2017; Cohen et al., 2016; Cohen et al., 2011; Rodger et al., 2016) and, hence, underscores the importance of viral suppression in improving health outcomes and preventing HIV transmission. Given this evidence, the US National HIV/AIDS Strategy has called for linking PLWH to high-quality HIV care and sustained viral suppression (The White House,

* Corresponding author at: 358 Mansfield Road, Unit 1101 Storrs, CT, 06269-1101, USA.
E-mail address: roman.shrestha@uconn.edu (R. Shrestha).

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2016).

Unfortunately, not all risk groups have benefited equally from scientific advancements in HIV care and treatment. Among HIV-infected people who use drugs (PWUD), in particular, serious gaps exist in the rates of engagement in HIV care services, uptake of ART, and viral suppression – a series of stages referred to as the "HIV care cascade" (Azar et al., 2015; Li et al., 2017; Meyer, Althoff, & Altice, 2013; Zhang et al., 2018). Despite these challenges, recent studies have demonstrated potential benefits of opioid substitution therapies (OST), such as methadone maintenance treatment (MMT), buprenorphine, or naltrexone, on optimal treatment outcomes – uptake and adherence to ART and viral suppression – among HIV-infected opioid-dependent individuals. For example, Low et al. showed that OST was associated with a 69% increase in recruitment onto ART, a 2-fold increase in adherence, and 45% increase in odds of viral suppression (Low et al., 2016). These findings support the use of OST as part of the integrated approach to improve HIV treatment and care continuum.

Opioid-dependent individuals stabilized on MMT are highly diverse and beyond the benefit of HIV TasP efforts. In the broader literature, several factors have been associated with viral suppression (Aibibula et al., 2018; Arthur et al., 2015; Bowen et al., 2017; Crepaz, Tang, Marks, & Hall, 2017; Ferrand et al., 2016; Socías et al., 2016). Despite substantial research in this area, prior studies have not explored theoretically informed correlates among HIV-infected opioid-dependent patients within drug treatment settings. Thus, given the critical role of sustained viral suppression in maximizing the individual- and population-level benefits of ART, the aim of this study was to assess factors associated with viral suppression in patients stabilized on MMT. Identifying subgroups at-risk for not achieving viral suppression and addressing factors causing the disparities could inform approaches to optimize HIV treatment outcomes and prevention efforts (e.g., HIV TasP).

2. Methods

2.1. Participants

Participants were HIV-infected, opioid-dependent individuals enrolled in a community-based methadone maintenance drug treatment facility in New Haven, Connecticut. Between September 2012 and January 2018, 133 individuals were recruited if they were a) 18 years or older, b) HIV positive, c) reported drug- or sex-related risk behavior (past 6 months), d) met DSM-V criteria for opioid use disorder and stabilized on methadone, and e) able to provide informed consent.

2.2. Study design and procedures

Data for the current study was derived from the Holistic Health for HIV (3H+) project, a randomized controlled trial designed to improve HIV risk reduction and medication adherence among high-risk HIV-infected PWUD. The study design has been described previously (Shrestha, Karki, Huedo-Medina, & Copenhaver, 2016; Shrestha, Krishnan, Altice, & Copenhaver, 2015). Participants were recruited through clinic-based advertisements and flyers, word-of-mouth, and direct referral from counselors in the methadone clinic. Individuals who met inclusion criteria and expressed interest in participating provided informed written consent and were administered a baseline assessment. Participants were assessed using an audio computer-assisted self-interview (ACASI) program. We utilized data collected at the baseline assessment.

The study protocol was approved by the Institutional Review Boards at the University of Connecticut and Yale University, and received board approval from the methadone clinic. Clinical trial registration is available at www.ClinicalTrials.gov (NCT01741311).

2.3. Measures

General demographic variables including age, gender, sexual orientation, ethnicity, marital status, educational status, employment status, annual income, living arrangement, methadone dose (mg), HIV diagnosis duration, and ART status were collected.

We collected chart abstracted viral load and CD4 cell counts from medical records. Viral suppression, which was defined as clinic-recorded HIV-1 RNA test value < 200 copies/mL whereas high CD4 count was defined as CD4 count ≥ 500 cells/mm^3 (Bowen et al., 2017; Crepaz et al., 2017).

Other variables included participants' adherence to ART (in the past 30 days), which was assessed using an empirically validated, self-report visual analog scale (VAS) approach (Giordano, Guzman, Clark, Charlebois, & Bangsberg, 2004). We used a standardized cut-off, adherence of 95% or greater, as optimal adherence (Paterson et al., 2000). We assessed participants' motivation to adhere to ART using the 18-item Motivation for ART adherence scale. Items were rated in a 4-point scale ranging from not at all (0) to extremely (Azar et al., 2015), with higher score indicating greater motivation for adherence ($\alpha = 0.72$).

Measures of the information-motivation-behavioral skills (IMB) model constructs related to HIV risk reduction (Huedo-Medina, Shrestha, & Copenhaver, 2016) were also collected. Domains of the IMB constructs included: (a) Information – HIV risk-related knowledge (range: 0–4); (b) Motivation - readiness to change and intentions to change HIV risk behavior (range: 0–32); and (c) Behavioral Skills - risk reduction skills (range: 0–16).

We used a validated HIV Stigma Mechanism Measure to assess participants' internalized, anticipated, and enacted HIV-related stigma (Earnshaw, Smith, Chaudoir, Amico, & Copenhaver, 2013). Internalized HIV stigma ($\alpha = 0.91$) was measured with 6 items including "*I feel ashamed of having HIV*." Anticipated HIV stigma ($\alpha = 0.90$) was measured with 9 items including "*Healthcare workers will treat me with less respect*." Enacted HIV stigma ($\alpha = 0.91$) was measured with 9 items including "*Family members have avoided me*." Items were rated on 5-point Likert-type scales. Items were averaged to create composite scores, with higher scores indicating greater stigma.

Disclosure of HIV status, which was defined as having any sex with disclosure of HIV-positive status to the partners in the past six months. Serostatus disclosure to partners was measured by asking, *"In the past six months, did you have sex with anyone who you told your HIV status sometime before you had sex?"* Responses were reported using a "yes" or "no".

The HIV risk assessment, adapted from NIDA's Risk Behavior Assessment (Dowling-Guyer et al., 1994) was used to measure several aspects of HIV risk behaviors in the past 30 days, including a measurement of "any" high risk behavior (sexual or drug-related) as well as measurements of event-level (i.e., partner-by-partner) behaviors.

2.4. Data analysis

We computed descriptive statistics, including frequencies and percentages for categorical variables, and means and standard deviations for continuous variables. After conducting bivariate analyses to examine significant associations with the dependent variable (i.e., viral suppression), we conducted multivariable logistic regression analyses on any bivariate associations found to be significant at $p < .10$. Additionally, we examined the interactive effect of pairs of variables in the main effects model to determine the moderated effect on viral suppression. Stepwise forward entry and backward elimination methods both showed the same results when examining the independent correlates ($p < .05$) expressed as adjusted odds ratios (aOR) and their 95% confidence intervals. Model fit was assessed using a Hosmer and Lemeshow Test (Hosmer, Hosmer, Le Cessie, & Lemeshow, 1997). Analyses were conducted using SPSS version 23 (IBM Corp., 2015).