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Alcohol Use Disorders And Antiretroviral Therapy Among Prisoners With Hiv/aids In Argentina

Michael Drake Alpert
Yale School of Medicine, mdalpert@gmail.com

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ALCOHOL USE DISORDERS AND ANTIRETROVIRAL THERAPY AMONG
PRISONERS WITH HIV/AIDS IN ARGENTINA

A Thesis Submitted to the
Yale University School of Medicine
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

By
Michael Drake Alpert

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ABSTRACT

While Argentina has significantly improved access to HIV care and antiretroviral therapy (ART) for both the general population and prisoners, the prevalence of alcohol use disorders (AUDs) among HIV-infected prisoners and their relationship to accessing ART in Argentina is currently unknown. This study aims to characterize the substance abuse patterns of HIV-infected prisoners in Argentina and to assess the independent correlates of receipt of pre-incarceration ART.

An anonymous, cross-sectional survey of 100 HIV-infected federal prisoners was conducted in the Buenos Aires municipality from July-December 2010. AUDs were assessed using the AUDIT scale.

A majority (63 per cent) of participants met criteria for AUDs, 45 per cent of subjects were diagnosed with HIV in prison and one-quarter had initiated ART during the current incarceration. In addition, over one-third (35 per cent) of participants did not receive ART during the pre-incarceration period despite receiving it upon incarceration. This correlated significantly with the presence of having an AUD (AOR 0.20, 95 per cent CI 0.06-0.74, $p = 0.016$).

AUDs are prevalent among HIV-infected prisoners in Argentina and are significantly related to not receiving ART in the community among those who meet treatment criteria and receive ART in prison. While Argentina has provided an exemplary model of HIV-related health care reform within its prisons, future efforts to provide

screening and treatment for AUDs are needed to improve the health of the nation's incarcerated population.

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INTRODUCTION

Similar to the global pandemic, HIV and incarceration are closely intertwined in Argentina. While 0.6% of Argentina's general population are estimated to be people living with HIV/AIDS (PLWHA), HIV is more than seven times more prevalent within its prisons compared to the general population (Oficina de las Naciones Unidas Contra la Droga y el Delito (ONUDD) 2009). As HIV testing is not mandatory, this represents the minimum prevalence of HIV among prisoners. In the past ten years, the number of known PLWHA in Argentina's federal prisons has ranged from 364 to 747, with approximately ten deaths from AIDS each year (ONUDD 2009). As of May 2008, there were approximately 260 people living with HIV and 93 people living with AIDS in federal prisons in Argentina, and approximately half were reported to have received antiretroviral therapy (ART) (ONUDD 2009).

Over the past decade, Argentina has greatly increased both *de jure* and *de facto* access to health care for PLWHA. These improvements in health care have been well characterized within the general population. By providing universal free ART to PLWHA who meet international treatment guidelines, Argentina has dramatically improved access to ART for HIV-infected patients in the general population from <10% in 2005 to 70% in 2007, and access to ART has remained steady through 2010 (Joint United Nations

Programme on HIV/AIDS (UNAIDS) 2008; World Health Organization (WHO), UNAIDS et al. 2010).

In addition to these recent improvements in health care access within the general community, the Ministry of Justice, Security, and Human Rights has worked over the past ten years in order to improve access to primary health care and psychosocial services within prisons in the Argentine Federal Penitentiary Service (FPS). As recently as 2003, federal prisons in Argentina were plagued by overpopulation and recurring violence. Since that time, the prisons have raised their standards for basic medical care, upgraded their medical equipment, and launched a number of successful health campaigns such as mass vaccinations for influenza, yellow fever, and tetanus. Argentina has also created rehabilitation centers within several federal prisons for people who use illicit drugs, as well as ambulatory treatment programs for individuals with dual diagnoses. Furthermore, Argentina has developed programs that allow mothers to care for their children while in prison, including powdered formula distribution and parenting workshops for inmates (Arcuri 2010).

As part of this blanket improvement in prisoner healthcare over the past decade, Argentina has greatly expanded the services offered to inmates living with HIV/AIDS. This expansion of care is enshrined in national legislation that mandates the right to psychosocial and medical services for incarcerated populations and includes provisions guaranteeing access to HIV treatment throughout the duration of incarceration (Arcuri

2010; El Senado y Cámara de Diputados de la Nación Argentina 1996). Voluntary, confidential HIV testing is provided for new prisoners, as well as for those who show clinical symptoms of AIDS or are diagnosed with HIV-associated medical co-morbidities (Arcuri 2010). Those with HIV receive special diets, and pregnant inmates with HIV have universal access to ART to prevent vertical transmission (ONUDD 2009).

In spite of these remarkable efforts, however, there remains room for improvement in the delivery of health care for PLWHA within prisons and communities in Argentina. Specifically, there is an unmet need for interventions focusing on the treatment of alcohol use disorders (AUDs) among prisoners living with HIV/AIDS in Argentina, owing to a dearth of research on the subject. This is an important line of investigation, given both the prevalence of alcohol use among the general population in Argentina, as well as the well-documented relationship in other countries between AUDs and adverse health outcomes (Azar 2010).

Alcohol consumption is widespread in Argentina. A survey of the general population found that greater than 80% of respondents had consumed alcohol in the past year, greater than 50% of respondents had consumed alcohol in the past month, 11.6% of respondents met criteria for harmful drinking using the alcohol use disorders identification test (AUDIT), and 34.5% of male respondents between the ages of 18-29 had had alcohol-related health problems in the past year (Munné 2005). Similarly, a survey of 500 MSM in Buenos Aires found that 78% of participants had consumed

alcohol in the previous two months, while 25% of participants were considered to be “heavy drinkers” (defined as consuming alcohol at least once per week and usually to the point of “feeling it a lot”, “getting drunk” or “feeling like they might pass out”) (Balan, Carballo-Diequez et al. 2013).

Although alcohol is legal in Argentina as in most other countries worldwide, excess alcohol consumption can result in serious negative consequences for both individuals and for society. Multi-criteria decision analysis modeling has shown alcohol to be the most harmful drug of abuse worldwide when accounting for its consequences to both individual users and society at large, and it ranks as the fourth most-harmful substance to individual users behind heroin, crack cocaine, and methamphetamine (Nutt, King et al. 2010). Further research has found alcohol to be causally linked to both acute and chronic disease outcomes affecting nearly all of the body’s organ systems (Rehm, Baliunas et al. 2010).

Along with health problems directly caused by alcohol consumption, AUDs are associated with numerous negative secondary HIV prevention outcomes. AUDs are associated with decreased ART adherence in prospective and cross-sectional research among the general population of PLWHA (Azar, Springer et al. 2010; Hendershot, Stoner et al. 2009; Mellins, Havens et al. 2009), as well as among HIV-infected incarcerated populations (Springer, Azar et al. 2011).

In addition to their association with decreased ART adherence, AUDs have been shown to accelerate liver disease in PLWHA, owing to both the hepatotoxic effects of alcohol as well as the increased hepatotoxicity in conjunction with ART (Springer, Azar et al. 2011). The hepatotoxic effects of alcohol on PLWHA are of particular concern as death from liver disease is the most frequent non- AIDS-related cause of mortality among PLWHA in the United States (Weber, Sabin et al. 2006). Furthermore, 30% of PLWHA in the United States are co-infected with HCV (Soriano, Sulkowski et al. 2002), and even low levels of alcohol consumption among individuals with HCV-associated hepatic steatosis significantly increases their risk of progression to hepatic fibrosis (Serfaty, Poujol-Robert et al. 2002).

Along with its deleterious effects on secondary HIV prevention, alcohol use is also strongly associated with factors related to primary HIV prevention as well (Springer, Azar et al. 2011). Specifically, alcohol use increases high-risk HIV transmission behaviors, as shown by research in both the United States and throughout Latin America. Among male inmates aged 18-29 in the United States, those who drank heavily were at greater risk to report unprotected sex with multiple partners in the three months prior to incarceration than those who did not (odds ratio [OR], 1.68, 95% confidence interval [CI], 1.11-2.54). (Ludford, Vagenas et al. 2013; Margolis, MacGowan et al. 2006; Springer, Azar et al. 2011; Vagenas, Ludford et al. 2013). Similarly, a recent systematic literature review of thirty articles pertaining to alcohol use and high-risk sexual behavior in Latin

America found that fourteen of the articles demonstrated direct associations between alcohol use and unprotected sex, while another thirteen provided indirect links between the two (Vagenas, Lama et al. 2013). Furthermore, research conducted among seropositive, sexually-active MSM in Lima, Peru found that the presence of an AUD was independently correlated with high-risk sexual behaviors in the previous six months, including: >5 sexual partners, presence of an STI, being a sex worker, unprotected sex during last encounter, and having sex with a seronegative partner. The associations between these variables and AUDs significantly increased with severity of the AUD (Ludford, Vagenas et al. 2013). In addition, seropositive Peruvian MSM with an AUD were more than twice as likely as those who did not meet AUD criteria to be unaware of their HIV status (Vagenas, Ludford et al. 2013).

AUDs are chronic relapsing conditions that are seldom sufficiently treated by forced abstinence provided in criminal justice settings. As such, individuals with AUDs have a high likelihood of relapse soon after release, and effective treatment is crucial to maintaining the benefits of ART afforded within the structured settings of prisons and optimizing longitudinal health outcomes upon release to the community (Copenhaver, Chowdhury et al. 2009; Springer, Azar et al. 2011).

STATEMENT OF PURPOSE, SPECIFIC AIMS, AND HYPOTHESES

Statement of Purpose and Specific Aims

In order to address this knowledge gap regarding AUDs among HIV-infected prisoners in Argentina, this study characterizes their prevalence among 100 HIV-infected prisoners. Because prisons are structured settings that can effectively screen and treat chronic conditions, this study examine factors associated with receipt of ART within the prison setting compared to a lack of receipt in the period immediately before incarceration where such structure may not have existed.

Hypotheses

- Given the widespread prevalence of alcohol use in Argentine society, there will be a high prevalence of AUDs among prisoners with HIV/AIDS in Buenos Aires.
- Given the recent efforts to improve the quality of medical care within Argentina's prison system, the controlled nature of the prison environment, and prior research that demonstrates decreased adherence to ART among individuals with AUDs in other settings, there will be a positive association between AUDs and improved receipt of ART within prisons in Buenos Aires.
- Factors that will relate to accessing HIV/AIDS-related care in the community will include: HIV/AIDS-related stigma, substance use disorders, mental health, and level of social support.

METHODS

Study Design

Data were collected from July 2010-January 2011 through an anonymous, cross-sectional study conducted at federal prisons near Buenos Aires, Argentina. A comprehensive study questionnaire was designed to assess the following parameters using standardized metrics:

- Drug abuse severity using the DAST-10 (Skinner 1982; Gavin, Ross et al. 1989). This is a brief instrument designed to quantitatively evaluate severity of substance use through a set of twenty-eight self-reported questions. Initial research found that it maintained internal consistency and reliability, and it has subsequently become a widely used metric in addiction research. 20- and 10-item versions of the DAST have also been developed, both of which maintain high internal consistency and reliability, as well as strong correlation with the original 28-question metric. The Spanish-language version of the DAST-10 metric used for this study was developed by a team of researchers from the Yale School of Medicine's Clínica Hispana and Nova Southeastern University and was validated among native Spanish-speakers in South Florida. Like the original English version, the Spanish version of this assessment was found to maintain internal reliability and to accurately differentiate users of illicit

drugs from non-substance users and from individuals with AUDs

(Bedregal, Sobell et al. 2006).

- AUDs using the AUDIT (Saunders, Aasland et al. 1993). The AUDIT is a ten-item questionnaire developed through a six-country World Health Organization collaborative project that assesses alcohol consumption, alcohol-related behaviors, and alcohol-related problems. The Spanish-language version of the AUDIT used in this study was previously validated among adults in Spain and was found to maintain high criterion-related validity when compared to clinical diagnoses of alcohol abuse or dependence as defined by DSM-IV and ICD-10 (de Torres, Rebollo et al. 2009). Of note for clinicians, this is a useful research tool that can be used to screen for alcohol dependence but is not a diagnostic instrument.
- Social support using the Multidimensional Scale of Perceived Social Support (MSPSS). This is a twelve-item questionnaire that subjectively assesses support from family, friends, and significant others, which has good internal and test-pretest reliability along with moderate construct validity (Zimet, Powell et al. 1990). Since its initial validation among a largely homogenous group of college students, its validity as a metric of social support has been confirmed among a broad range of populations (Canty-Mitchell and Zimet 2000).

- HIV-related stigma experienced by subjects using the Berger HIV Stigma Scale (Berger, Ferrans et al. 2001). This is a forty-question scale designed by Berger and colleagues that assesses perceived levels of HIV-related stigma. In addition to assessing global HIV-related stigma, this metric also contains four subscales focused on specific aspects of HIV-related stigma, namely: Disclosure Concerns, Personalized Stigma, Negative Self-Image, and Concern with Public Attitudes towards People with HIV. This survey utilized a Spanish-language version of the Berger Stigma Scale that was validated among a population of native Spanish-speakers in Peru (Franke, Munoz et al. 2010)
- Major Depressive Disorder using the Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer et al. 2001). This is a nine-item questionnaire on which patients provide a score of “0” (not at all) to “3” (nearly every day) for the 9 DSM-IV criteria of Major Depressive Disorder: depressed or irritable mood; decreased interest or pleasure; significant change in weight or appetite; change in sleep; change in activity; fatigue or energy loss; guilt/worthlessness; diminished concentration; thoughts of suicide/active suicide plan (Association and DSM-IV. 1994). Criterion validity was established by comparing this metric to structured mental health professional (MHP) interviews of 580 patients. Based on the MHP

interviews as gold standard, a score of PHQ-9 ≥ 10 was found to have 88% sensitivity and 88% specificity for Major Depressive Disorder. Subsequent research on young mothers in Honduras found that the Spanish-language version of the metric had a sensitivity of 77% and a specificity of 100% for diagnosis of Major Depressive Disorder compared with findings from structured clinical interviews (Wulsin, Somoza et al. 2002).

In addition to the standardized metrics above, the subjects were asked a series of questions written specifically for this survey to assess the following: background demographics, criminal justice history, substance use history, barriers to community re-entry upon release (Choi, Kavasery et al. 2010), medical co-morbidities, access to medical services, HIV-related risk behaviors in the period prior to incarceration, and access to HIV-related medical and social services both prior to and during the current period of incarceration.

This questionnaire was created in English and then translated into Spanish, using previously validated Spanish-language versions of the study metrics when available. The remainder of the study form was translated and back translated (Brislin 1970) by bilingual research assistants in the United States and further modified for the local context by research staff at the Fundación Huésped in Buenos Aires.

Data Collection

After receiving ethical approval from both the Yale University School of Medicine Human Investigations Committee in New Haven, CT, USA and the Committee of Bioethics at the Fundación Huésped in Buenos Aires, Argentina, subjects were sequentially selected for participation in the study. The study was conducted at the federal prison complex in Florencio Varela, Buenos Aires, Argentina in all five on-site units. All inmates with documented HIV-positive status and sufficient mental capacity to provide informed consent were eligible for participation in the study. HIV-positive status was determined using lists maintained in the medical office of the incarceration facility. Prison medical staff aware of a prisoner's HIV status asked if they were interested in participation. Interested inmates were then approached by research staff who explained the informed consent and enrollment procedures. Subjects were provided with both a written and oral explanation of the research study and were informed that there were no incentives or disincentives for their participation. In addition, subjects were informed that their individual response forms would be coded anonymously without any identifying information and that their answers would not be shared with the staff at the prison. After providing oral consent, subjects were interviewed individually in private offices by trained research assistants. All interviews were conducted in Spanish without the use of a translator, with the exception of one subject who had spent his childhood in North America and preferred to complete the interview in English.

Data Analysis

In total, all eighty-two individuals on the HIV registry at the Florencio Varela prison during the months of July and August 2010 were considered for participation in the study. Two individuals were excluded due to misidentification of their HIV status on the official registry, fourteen chose not to participate in the study, and five others were not able to participate as they were not on location at the prison facility at the time the interviews were conducted. A total of sixty-one individuals were enrolled in the study at the Florencio Varela prison, one of who subsequently chose not to complete the interview. Subsequently, forty more individuals from units within the federal prison in La Plata, Berisso, and Ensenada were enrolled in the study from October-December 2010 for a total of one hundred participants [Figure].

Individual survey responses were then coded and analyzed using SPSS v.19.0 (SPSS Inc., Chicago, IL) with the assistance of a trained biostatistician, Jeffrey Wickersham, Ph.D. Summary statistics of demographics, prevalence of substance abuse, and high-risk HIV behavior were assessed through variable count functions. In addition, a bivariate regression was performed using receipt of ART upon incarceration but not in the 30 days pre-incarceration as the dependent variable. For this study, these subjects were considered as having not received appropriate ART therapy in the period immediately prior to incarceration because they did not receive ART during that period

despite having been found to meet ART treatment guidelines upon incarceration. This group was compared to the remaining subjects, who were either on ART pre-incarceration or who had never initiated on ART in either setting because they did not meet the ART treatment guidelines used within the prison.

AUDs, drug abuse severity, HIV-related stigma, age, duration of present incarceration, previous diagnosis of tuberculosis, and mental illness were used as independent variables. Statistical significance was defined as two-tailed $P < 0.05$. Alcohol use disorders were assessed with the AUDIT, and scores were stratified for bivariate analysis into two categories [Low Risk or sensible drinking (score < 8 for men or < 4 for women) vs. Hazardous Drinking or Alcohol Dependence (score of ≥ 8 for men or ≥ 4 for women)] (Miller, Zweben et al. 1992). This is in keeping with the stratification used by the initial validation study of the AUDIT metric, which found that 92% of individuals who received a clinical diagnosis of hazardous or harmful patterns of alcohol use had an AUDIT score ≥ 8 , while 94% of individuals found clinically to exhibit non-hazardous patterns of alcohol use had AUDIT scores < 8 (Saunders, Aasland et al. 1993). Drug abuse severity was assessed with the DAST-10. Given the relatively small sample size, responses were stratified for bivariate analysis into two categories [No-Moderate Reported Problem (score < 6) vs. Substantial or Severe Problem (score of ≥ 6)]. Major depressive disorder was screened for using the PHQ-9 and defined as a score of ≥ 9 . Subjects were also asked specifically if they had received prior treatment for mental

illness. Social support and HIV-related stigma were assessed using the Berger HIV Stigma Scale and the Zimet Social Support Scale, respectively, and the resultant scores were used as continuous variables in the bivariate analysis.

Correlations with appropriate ART in the thirty days before incarceration were examined using logistic regression modeling with all variables that met threshold of <0.2 at the bivariate level in a multivariate model examining the correlates associated with the dependent variable.

RESULTS

The characteristics of the sample are detailed in Table 1. Consistent with the demographics of the general prison population, the study participants were predominantly male. Of note, the study did include one transgender participant. In general, study subjects were serving multi-year sentences for non drug-related crimes. All subjects had some degree of formal schooling, although half had not completed secondary education.

Many of the subjects also had significant medical and psychological comorbidities. There was a significant prevalence of Hepatitis B and C among the study participants, and nearly one third had been diagnosed with tuberculosis. The anonymous nature of the study precluded a medical chart review, so this information was obtained via self-report.

AUDS and illicit substance use were widespread among the study participants. Nearly 2/3 of study participants met criteria for hazardous drinking or alcohol dependence per AUDIT screening guidelines. In addition, nearly half of the study participants had used cocaine in the 30 days prior to incarceration, and 1/5 of participants had used benzodiazepines recreationally during that same period. Of note, while nearly half of the study participants reported having a lifetime history of IDU, only 2% of study participants reported IDU in the period immediately prior to the current incarceration.

In general, participants reported widespread access to HIV-related medical services in prison. Nearly half of the subjects were diagnosed with HIV in prison, either previously or during the present incarceration, and one-quarter of the study participants had initiated ART during the current incarceration. In addition, nearly all participants felt confident they could continue to receive HIV-related medical care upon release. In spite of this, approximately one third (35%) of participants did not receive ART in the month prior to their incarceration despite meeting criteria for ART used within the prison setting and receiving ART during the current incarceration. Of note, three subjects who received ART in the 30 days prior to incarceration reported that it was not continued in prison.

Bivariate correlations with appropriate ART in the thirty days before incarceration were examined in order to create a multivariate model [Table 2]. In the final model, only the presence of AUDs (AOR=0.20, 95% CI 0.06-0.74, p=0.016) and duration of present incarceration (AOR=0.98, 95% CI 0.97-0.99, p=0.047) were significantly associated with receiving ART after incarceration, but not in the 30 days before. Specifically, presence of an AUD per AUDIT screening guidelines or increased duration of present incarceration correlated positively with inappropriate ART in the 30 days prior to incarceration. Lower social support, however, approached statistical significance in the final model (AOR=0.95, 95% CI 0.91-1.00, p=0.054).

DISCUSSION

Prevalence of AUDs among PLWHA within Argentina's Prisons: Implications for Prevention and Treatment

This study is the first to illustrate the widespread prevalence of alcohol use disorders (AUDs) among HIV-infected prisoners in Argentina and provide evidence showing the significant relationship between AUDs and secondary prevention of HIV in this population. The prevalence of AUDs among this sample is over five times that of the general Argentine population (Munné 2005). Furthermore, AUDs correlated significantly with decreased ART use prior to incarceration in multivariate logistic regression. This potentially suggests a need for improved access to treatment for AUDs not only in the community before incarceration, but for this sample, treatment of AUDs during incarceration and part of post-release transitional programs in Argentina. Research from other countries suggests that there are insufficient substance abuse treatment programs in prisons despite a clear, overwhelming need (Chandler, Fletcher et al. 2009; Hendershot, Stoner et al. 2009; Meyer, Chen et al. 2011).

The high prevalence of AUDs among the HIV-infected Argentine prison population could potentially be addressed through increased routine screening for AUDs upon incarceration using previously validated instruments (Cremonte and Cherpitel 2008), as well as through the development of culturally appropriate AUD treatment programs within prisons. Since AUDs are chronic relapsing conditions seldom

sufficiently treated by the forced abstinence philosophy prevailing in criminal justice settings, effective treatment is crucial to maintaining the benefits of ART afforded within the structured settings of prisons and optimizing longitudinal health outcomes upon release to the community (Springer, Azar et al. 2011). Pharmacologic therapy with naltrexone is the AUD treatment modality best supported by current evidence (Anton, O'Malley et al. 2006; Altice 2010). Acamprosate, another pharmacological therapy used for AUD treatment, has been found to be less effective than naltrexone but equivalent to counseling alone (Anton, O'Malley et al. 2006; Mason, Goodman et al. 2006), and the use of disulfiram for treating AUDs is precluded by its hepatotoxic effects. By contrast, behavioral interventions have been found to have small to modest effects on treating AUDs.

Given these findings, naltrexone therapy offers much promise for improving the health and well being of PLWHA who meet criteria for AUD diagnosis. Studies examining the efficacy and safety of extended-release naltrexone are currently underway among HIV-infected men in Peru and among HIV-infected prisoners with AUDs transitioning to the community in the United States. Results from these studies could potentially serve as the basis for a similar program development in Argentina and elsewhere [Springer & Altice, www.clinicaltrials.gov, NCT01077310; Duerr, Lama, & Altice, www.clinicaltrials.gov, NCT01377168]. Such an intervention would likely have both primary and secondary preventative effects, given the strong association between

AUDs and high-risk sexual behavior throughout Latin America (Ludford, Vagenas et al. 2013; Vagenas, Lama et al. 2013; Vagenas, Ludford et al. 2013). Further research is also needed to characterize the connection between AUDs and insufficient treatment with ART within the community for PLWHA who are incarcerated in Argentine prisons.

In addition to the use of pharmacotherapy, there is growing interest in the use of complimentary and alternative medicine (CAM) for treating addiction. A review of evidence-based literature published in the past thirty years in English, Korean, Japanese, and Chinese on the use of acupuncture for treatment of AUDs, however, found that the results of these studies is equivocal and marred by poor adherence to the methodological criteria in the *Cochrane Handbook* (Cho and Whang 2009; Higgins, Green et al. 2008).

The use of randomized controlled trials as a gold standard, however, is based on several theoretical premises that are problematized in the study of acupuncture and other forms of CAM that have not yet been integrated into western clinical practice. The efficacy of some forms of CAM may be due to a number of synergistic factors that have each been shown to have strong effects on patients, thus problematizing the design of a true placebo. Furthermore, a true randomization of patients with a given medical diagnosis to either control or experimental arms of a CAM study would conversely work against the goal of minimizing bias, as this approach would fail to account for the *a priori* heterogeneity of expectations and beliefs regarding this treatment modality (Wayne and

Kaptchuk 2008; Wayne and Kaptchuk 2008; Wang, Schmid et al. 2010; Yeh, Kaptchuk et al. 2010).

Regarding acupuncture specifically, there is a wide degree of variation in its practice. Thus, research trials that attempt to standardize the acupuncture session by mandating factors such as loci of needle placement, and duration of stimulation do not accurately reflect acupuncture as practiced *in situ*. Furthermore, trials that utilize “sham” acupuncture involving the stimulation of “inactive” points or the use of retractable needles that do not penetrate the skin, remains controversial as a valid control (Lund and Lundberg 2006), as factors such as depth and location of needle placement, as well as the number of needles placed, vary greatly between styles of acupuncture and between different providers of the same style of treatment. There is even intra-provider heterogeneity of practice depending on the specific needs of a given patient (Langevin, Wayne et al. 2011).

Patterns of Substance Use: Implications for Harm Reduction Practices in Argentine

Prisons

The patterns of drug abuse among the study population are different than those found among incarcerated populations in other middle-income countries (Azbel, Wickersham et al. 2012; Dolan, Kite et al. 2007). Specifically, this study found an overwhelming predominance of cocaine abuse among the study population, as well as a

significant degree of benzodiazepine abuse. In contrast with previously reported studies of prisoners in other middle-income countries, however, hardly any of the subjects in this investigation reported using opioids. A study of 402 prisoners in Ukraine, for instance, found that in the thirty days prior to incarceration, 34.4% of participants had used opioids, 21.1% had used amphetamines, 20.5% had combined opioids with hazardous drinking, and 15.4% had combined opioid use with amphetamine use. Furthermore, 56.6% of the participants in the study met criteria for hazardous drinking and 48.7% had a lifetime history of IDU (Azbel, Wickersham et al. 2012). Another recent investigation of 97 HIV-infected persons recently released from prison in Ukraine found that 56.7% of study participants reported injection drug use while in prison, of whom 74.1% reported sharing injection equipment (mean of 4.28 sharing partners, mean of 4.43 uses per needle) (Izenberg, Bachireddy et al. 2013).

The substance use patterns found among our study participants are, however, consistent with nationwide patterns of drug abuse within Argentina. A study of 500 MSM in Buenos Aires, for instance, found that approximately 40% of participants reported a lifetime history of cocaine use and 30% reported using it in the previous two months, while approximately 20% of participants reported a lifetime history of *pasta base* or tranquilizer use and 15% reported using these substances in the previous two months. In contrast, less than 5% of study participants reported using the other substances assessed, including heroin/opioids, ecstasy, methamphetamines, hallucinogenics,

inhalants, and amyl nitrite (“poppers”) (Balan, Carballo-Diequez et al. 2013). Furthermore, cross-sectional research conducted in Buenos Aires, Argentina and Montevideo, Uruguay among individuals who had never injected drugs but had sniffed, snorted, or smoked illicit substances in the previous ninety days found that 91.7% of participants had used cocaine (80.4% via inhalation, 6.9% via smoking coca paste, and 1.1% via smoking crack), while only about 5% of participants reported using lysergic acid diethylamide (LSD), heroin, glue, or morphine during that same time period (Caiaffa, Zoccratto et al. 2011).

In addition, while injection drug use was initially the primary route of HIV transmission in Argentina at the outset of the HIV epidemic (Rodriguez, Marques et al. 2002) and nearly half of our research subjects reported a lifetime history of IDU, almost none of the subjects in this study had injected drugs in the month prior to the current incarceration. The high prevalence of remote drug injection and the long history of incarceration among this population likely explain the high prevalence of viral hepatitis in spite of little recent injection drug use. Lifetime history of IDU among our study participants was higher than the prevalence of IDU (31%) among seropositive inmates in a study conducted in 2001 within a federal penitentiary in Buenos Aires but was half that reported in prior research conducted among HIV-positive prisoners in Argentina in the 1990’s (Dolan, Kite et al. 2007; Troncoso, Palmero et al. 2004). This finding is consistent with patterns found among the Argentine population outside of prison,

namely that the prevalence of injection drug use (IDU) and the sharing of injection equipment have decreased since the 1990's (Cohen 2006; Rossi 2006), leading to a sharp decrease in the percentage of new HIV infections secondary to IDU in Argentina (Mendes Diz, Camarotti et al. 2008; Programa Nacional de Lucha contra el Retrovirus del Humano 2008).

These findings of minimal levels of IDU among study participants suggest that future efforts should focus on sexual transmission. Although our study did not inquire regarding high-risk behavior within the prison, prior research among seropositive inmates within a federal penitentiary in Buenos Aires found that 66% of subjects had had multiple sexual partners in the past year (of whom 60% never used a condom), and 27% reported being the victim of sexual assault. Furthermore, none of our study participants admitted to having same-sex relations before incarceration, but prior research focused on sexual behavior among seropositive inmates in an Argentine federal penitentiary found that nearly $\frac{3}{4}$ of the subjects had engaged in homosexual activity within the previous twelve months, of whom half had first engaged in this activity while in prison (Troncoso, Palmero et al. 2004). To that end, Argentine law stipulates access to condoms for all inmates regardless of whether or not they receive conjugal visits (Programa Nacional de Lucha contra el Retrovirus del Humano 2008). If universally available, such programs may prevent intra-prison HIV transmission. While few prison facilities have initiated

such programs themselves, several prisons have allowed for nongovernmental organizations (NGO's) to provide government-issued condoms to inmates.

Other Findings and Limitations

In addition to the presence of AUDs, increased duration of incarceration was significantly associated with receiving ART during the present incarceration but not in the 30 days beforehand. Though this particular study was unable to elucidate the reasons behind this association, one explanation is the improved access to ART in the community in Argentina over the past decade, which would have increased the likelihood that individuals who were incarcerated more recently would have received ART prior to incarceration. Another possible explanation is that the study subjects were at increased likelihood of meeting criteria ART initiation criteria after a prolonged period of incarceration. Further research is needed to explore the mechanism underlying this association.

This study did have a number of limitations. Ideally, we would have defined eligibility for ART use based on CD4+ lymphocyte counts, but the lack of available clinical data made this impossible, thus requiring us to construct the dependent variable based on the expectation that anyone who was eligible for and could tolerate ART would receive it in prison. In addition, the relatively small sample size could have potentially decreased the power to detect a larger number of significant associations, as well as the

applicability of the study results to all HIV-infected prisoners. Of note, the study did not find a significant relationship between the use of other substances and secondary prevention of HIV. This is potentially due to either the relatively small size of our sample or to the widespread prevalence of AUDs, which could have overshadowed the relationship between other substances and the dependent variable. Moreover, while social support was found to be associated with the primary outcome of accessing ART during incarceration but not beforehand, the relatively small sample size may have been insufficient to truly disentangle this association. Prior research has, however, demonstrated stronger correlations between social support and adherence to ART (Ammassari, Trotta et al. 2002; Gonzalez 2004; Gordillo, del Amo et al. 1999; Simoni, Frick et al. 2006), but its association on accessing ART remains undocumented. These findings here suggest a need for further research on the relationship between social support and access to and receipt of ART in community settings among a larger sample size in Argentina.

In addition, the data could not be stratified by gender owing to the small number of female subjects, which reflect the lower rates of incarceration of women. While women have traditionally had decreased access to ART, it was not possible to perform such analyses with the present data. Furthermore, the cross-sectional nature of the study precludes the inference of causality between AUDs and receiving ART upon incarceration but not in the pre-incarceration period. This can be addressed through further research

using a prospective, longitudinal design. Such a study could also examine the correlates with appropriate ART during the post-incarceration period of transition back into the community.

In order to maintain the anonymity of the subjects, the survey relied on subjective reports regarding access to HIV medication and was not verified with objective medical records that could have demonstrated the medical outcomes of ART initiation in prison, namely changes in CD4 counts and viral loads. Similarly, self-reported medical co-morbidities could not be verified by objective medical records. Assuming that there could be patients in our study who have either not been screened for hepatitis and TB, are not aware of their diagnoses, or do not care to share these diagnoses with others, the number of individuals with these co-morbidities reported in our sample could potentially be lower than the actual prevalence of these diseases in our study sample. This could be addressed in the future through a retrospective analysis of anonymized prison records in Argentina. Despite these limitations, this study does provide a unique insight into the substance abuse patterns and access to HIV medication among Argentine prisoners and provides a basis for future interventions.

Aligning Public Health with Public Safety: Healthcare and Criminal Justice

Consistent with prior research in prisons in the United States (Beckwith 2010; Springer, Pesanti et al. 2004) this study demonstrates the important role of criminal justice settings in the diagnosis and treatment of HIV (Altice, Mostashari et al. 2001;

Flanigan and Beckwith 2011) Though Argentina is a middle-income country, HIV treatment outcomes appear similar to those in high-income settings, likely due to its standardized treatment guidelines that are used in both correctional and community settings. Compared to other middle-income countries, these findings are markedly better than reported elsewhere (Azbel, Wickersham et al. 2012; Choi, Kavasery et al. 2010; Fu, Bazazi et al. 2012) and could potentially serve as a model for prison health care reform in other middle-income countries. Three of the subjects, however, reported that they had received ART in the 30 days prior to incarceration but had not received it in prison. The reason for ART discontinuation was not explored further. Since interruption of ART is associated with increased risk of HIV-related adverse events (Emery, Neuhaus et al. 2008), it is important that the prison system in Argentina work to ensure that all inmates who received ART prior to incarceration continue to receive treatment while in prison.

As nearly half of the study participants were diagnosed with HIV within prisons settings, this research suggests that enhanced routine HIV testing in Argentine prisons has succeeded in detecting a significant number of previously undiagnosed HIV cases and demonstrates a need for increased HIV testing of the adult population outside of the prison setting. Given the near-universal access to ART both within and outside of the prison system in Argentina, increased HIV testing would likely result in significant numbers of previously undiagnosed individuals with HIV receiving necessary HIV care, as occurred with this study population (de Voux 2012). Widespread voluntary testing of

the adult population would likely decrease rates of HIV transmission, as providing this previously undiagnosed population of PLWHA with access to ART would decrease viral loads and subsequently infectivity (Granich, Gilks et al. 2009). Furthermore, while nearly all participants in the study felt confident that they could continue to receive HIV care upon release, further research is needed to determine the degree to which recently released HIV-infected inmates are actually able to access HIV-related services and adhere to ART upon release. Other studies elsewhere have suggested that this process may be much more difficult than our subjects anticipate (Baillargeon, Giordano et al. 2009; Springer, Pesanti et al. 2004)

The findings from this study indicate that HIV-infected Argentinian prisoners not only have a high prevalence of AUDs but much greater access to ART than their counterparts in prisons located in other middle-income countries throughout the world. A survey conducted in Ukrainian prisons among 402 individuals being released within six months, for instance, found that half of those who were infected with HIV were unaware of their HIV status. Furthermore, 56% of these HIV-infected inmates had CD4 <350 cells/mL but only 11% of inmates eligible for ART were receiving it (Azbel 2013). Another recent study conducted in Ukraine of HIV-infected individuals who had been released from prison within the previous year found that 67.9% of individuals on opiate substitution therapy and 70.4% of individuals on ART experienced an interruption in medication during the detention process (Izenberg, Bachireddy et al. 2013).

Furthermore, a similar study conducted in Malaysian prisons of 102 HIV-infected inmates found that while about half of the subjects reported ≥ 7 HIV-related symptoms, only two of the subjects had ever reported receiving antiretroviral medications (Choi, Kavasery et al. 2010).

These findings were also confirmed by a literature review on access to ART in prisons in five low- and middle-income countries – China, Vietnam, Russia, Ukraine, and Malaysia – that found that all five countries provided either highly restrictive or no access to ART within their prisons. In Vietnam, prisoners were held without treatment and released if they were seriously ill. While such hard data is difficult to come by in Russia, interviews with individual patients released from a Russian prison in 2009 paint a harrowing picture of bureaucracy, stigma, incompetence, and poor sanitation that have disastrous consequences on the health and well-being of inmates infected with HIV (Wolfe, Carrieri et al. 2010):

“When they brought me to the prison, I said that I had HIV and AIDS and that I had started taking ART because my clinical condition called for it. When I got to prison, I explained my situation to all the doctors who saw me, I explained, that having the medicines was a matter of life and death for me, and that I can’t interrupt the treatment. They told me to calm down...And they didn’t give me anything. They told me they didn’t have those medicines, they didn’t have connections with the AIDS Center...Basically, they were out of the loop and they didn’t have anything. This is how it[treatment] looked: they opened the feeding bunk and threw in all the pills – here you are, take it...and that’s it! The nurse gave the same pills to everyone – and each inmate had a different diagnosis. She would give us all the same pill and said, “swallow it”. They didn’t check at all if people were treated or not. If you come to the doctor’s office, they give you pills

and look in your mouth to make sure you swallow them. If you don't swallow and you take a pill with you from there, you get 15 days in a punishment cell. So [one] guy kept eating the pills...In the end he got ascites, drum belly. And he died.

When I got there [medical correctional facility], I told all the doctors that I had advanced AIDS, told them everything, showed my last medical records...But nothing, no effect. When I came there in 2007, many inmates with HIV had been transferred there and they didn't know what to do with them. They hadn't even registered us as HIV patients – we were listed as TB patients. So they put all the inmates with HIV in one barrack and didn't let us out at all. I got very sick in spring of 2007 or 2008. I had a fever of 40°C for a whole week. The doctors couldn't do anything, they couldn't understand what was going on. At that time, all people with HIV had to be isolated. Even in the prison hospital, they put us in the isolation chamber in the basement. Can you imagine?! A punishment isolation chamber. The chamber I was put in was very small, about two meters long. There were two of us there. They didn't do anything. For two or three weeks I sat in the isolation chamber and then was just sent back. They didn't even list us people with HIV anywhere. Because an HIV patient in the prison means a certain diet, state subsidies, some additional money is supposed to be allocated for an inmate with HIV. And they didn't have it. We spent one year, even more, listed as TB patients, not HIV patients; there was no HIV.”

In contrast to such dire conditions, the prisons in Argentina play an important role in HIV diagnosis and delivery of HIV-related medical care. Despite the availability of ART both within and outside of prison in Argentina, however, this study finds that AUDs are a widespread problem associated with decreased use of these medications outside of prison among currently incarcerated HIV-infected inmates. As AUDs are medically-treatable conditions, it would thus be useful to design future interventions in Argentine prisons that provide addiction treatment services to include alcohol counseling

and potentially medication-assisted therapies in order to improve primary and secondary HIV prevention.

FIGURE AND TABLES

Figure: Participant disposition

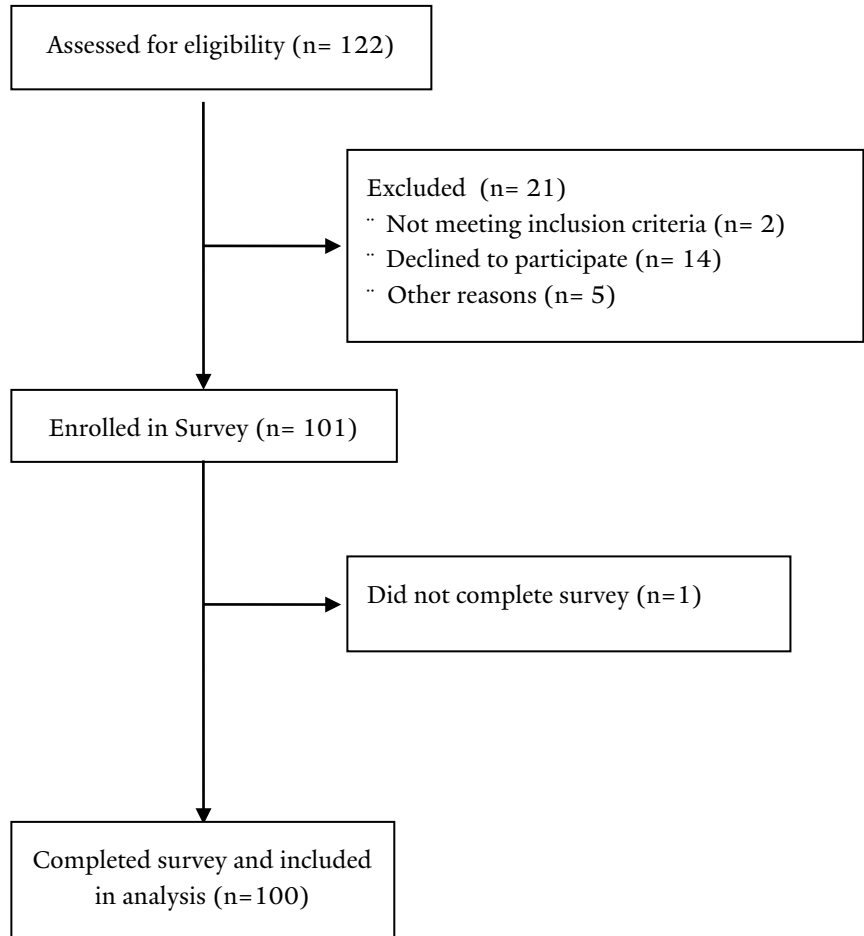


Table 1: Study Participant Characteristics

Background Demographics	N=100
Mean Age, years	37.6
Gender	
Male	93
Female	6
Transgender	1
Did not complete secondary education	45
Criminal Justice History	N=99
Mean duration of present incarceration (months)	38
Mean time remaining until release (months)	22
Mean number of adult incarcerations	3
Mean total lifetime spent incarcerated (years)	10.5
Medical Comorbidities	N=96 (%)
Tuberculosis	30 (31%)
Received treatment during current incarceration	12 (12.5%)
Hepatitis	
Hepatitis B (n=93)	20 (22%)
Hepatitis C (n=93)	37 (40%)
Hypertension (n=93)	23 (25%)
Co-Morbid Drug Use and Mental Illness	
Ever diagnosed with mental illness (n=93)	6 (7%)
Major Depressive Disorder (PHQ-9 >9) (n=95)	41 (43%)
Alcohol Use Disorders (n=92)	
Hazardous Drinking (AUDIT: Men 8-14; Women 4-12)	21 (23%)
Alcohol Dependence (AUDIT: Men ≥15; Women ≥13)	36 (39%)
Hazardous Drinking OR Alcohol Dependence	57 (62%)
Other drug use in thirty days prior to incarceration (n=100)	
Cocaine	46 (46%)
Crack/Paco	17 (17%)
Opioids	2 (2%)
Benzodiazepines	19 (19%)
HIV transmission behavior	N=93
Injection drug use	
Lifetime	42 (45%)
In 30 days before present incarceration	2 (2%)
Mean number of unprotected sex partners in 30 days before present incarceration (n=92)	2

Partner known to be HIV-infected	1
Partner not infected with HIV or serostatus unknown	1
Mean number of unprotected sexual encounters in 30 days before present incarceration (n=62)	22
Partner known to be HIV-infected	9
Partner not infected with HIV or serostatus unknown	11
HIV Care and Treatment	
Mean time since HIV diagnosis, years (N=100)	11
First diagnosed with HIV in prison (N=100)	45
Diagnosed during current incarceration	15
Ever saw HIV doctor or nurse (N=99)	91
Felt they could easily see HIV doctor after release (N=98)	95
Received ART upon incarceration but not in the 30 days pre-incarceration (N=75)	26 (34.7%)

Table 2: Correlates of receiving ART during present incarceration, but not receiving it in the 30 days before incarceration

Covariate	Bivariate			Multivariate		
	UOR	95% C.I.	P-value	AOR	95% C.I.	P-Value
Alcohol use disorders*						
None	Referent					
Hazardous or Dependent Drinking*	0.21	0.06-0.71	0.012	0.20	0.06-0.74	0.016
Duration of present incarceration	0.98	0.97-0.99	0.018	0.98	0.97-0.99	0.047
Social Support**	0.97	0.93-1.01	0.145	0.95	0.91-1.00	0.054
Number of years since HIV diagnosis	1.00	0.99-1.01	0.776			
Major Depressive Disorder (PHQ-9 >9) ⁺	0.75	0.28-2.01	0.565			
Moderate to severe substance abuse severity ⁺⁺	0.73	0.27-1.98	0.536			
Age, years	1.04	0.97-1.11	0.291			
HIV-Related Stigma ⁺⁺⁺	0.99	0.98-1.01	0.577			
AIC = 132.00, BIC = 277.51						

Legend:

UOR = Unadjusted Odds Ratio, AOR = Adjusted Odds Ratio

*Alcohol use assessed with AUDIT scale and stratified as Low Risk (men <8, women <4); Hazardous Drinking or Alcohol Dependence (men ≥8, women ≥4)

**Social Support assessed with Zimet Social Support Scale

⁺Mental Illness assessed with PHQ-9 Scale

⁺⁺Drug use assessed with DAST-10 scale and stratified by "no" (0), "low"(1-2), "moderate" (3-5), "substantial" (6-8), and "severe" (9-10) problem

⁺⁺⁺HIV stigma assessed with Berger HIV Stigma Scale

AIC=Akaike Information Criterion; BIC=Bayesian Information Criterion

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