


Women of Reproductive Age Living with HIV in Argentina: Unique Challenges for Reengagement in Care

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Abstract

This study evaluated the reasons for not taking antiretroviral treatment (ART) among women of reproductive age who are disengaged from HIV care (have missed pharmacy pickups and physician visits), with the goal of identifying strategies for reengagement in HIV care. Participants were cisgender women ($n = 162$), 18 to 49 years of age, and who completed sociodemographic, medical history, reasons why they were not taking ART, mental health, motivation, and self-efficacy assessments. Latent class analysis was used for analysis. Women who reported avoidance-based coping (avoid thinking about HIV) had higher depression ($U = 608.5$, $z = -2.7$, $P = .007$), lower motivation ($U = 601$, $z = -2.8$, $P = .006$), and lower self-efficacy ($U = 644.5$, $z = -2.4$, $P = .017$) than those not using this maladaptive strategy. As women living with HIV experience a disproportionate burden of poor health outcomes, interventions focused on the management of depression may improve HIV outcomes and prevent HIV transmission.

Keywords

HIV, South America, women

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Introduction

There are almost 40 million people living with HIV worldwide,¹ and it is estimated that over half of them are women. AIDS-related illnesses are the leading cause of death among women of reproductive age (defined as 15-49 years of age by the World Health Organization [WHO])² globally, and women have higher rates of adverse events and discontinuation of commonly prescribed antiretroviral therapy (ART). Although rates of engagement in care and viral suppression are higher among women of reproductive age during pregnancy, reproductive-age women living with HIV who are not pregnant are highly vulnerable to poor HIV outcomes and ART side effects.³⁻⁵ Despite the importance of controlling HIV among women of reproductive potential, women in this age-group are underrepresented in HIV research, due to issues such as limited child care services, lack of home support, pregnancy, and

difficulty with multidrug management.^{6,7} Finally, as women living with HIV are most likely to have condom-less sex, strategies to improve retention in care and adherence to ART

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What Do We Already Know about This Topic?

Reproductive-age women living with HIV are highly vulnerable to poor HIV outcomes and depression, which is associated with nonadherence to treatment and poor engagement in HIV care. In a previous study of men living with HIV, avoidance-based coping (avoiding thinking about having HIV) was linked with depression, low self-efficacy, and reduced odds of serostatus disclosure.

How Does Your Research Contribute to the Field?

This study examined reasons for nonadherence to treatment, including avoidance-based coping, among reproductive-age women in Argentina who were disengaged from HIV care. Nonadherent women who reported avoidance-based coping as a reason for nonadherence had lower motivation, lower self-efficacy, and higher depression than nonadherent women who did not report avoidance-based coping.

What Are Your Research's Implications toward Theory, Practice, or Policy?

The results of this study emphasize the importance of integrating the identification and treatment of depression into HIV care for women of reproductive age, especially those facing difficulties in coping with HIV, to optimize health outcomes.

among women of reproductive potential are essential to reduce sexual and perinatal transmission of HIV.

In Argentina, as in other Latin American countries, although HIV prevalence among women is lower than among men, it is estimated that there are about 40,000 women of reproductive age living with HIV. Argentina has met significant milestones in its response to HIV with the goal of achieving the Joint United Nations Programme on HIV/AIDS/WHO 90-90-90 objectives.⁸ Access to ART is the highest in Latin America and an adapted test-and-treat approach has been utilized since 2015. Although ART prescription rates among people diagnosed with HIV are almost 90% and similar between men and women, rates of viral suppression are significantly lower for women due to the lack of engagement in HIV care and nonadherence to ART.⁹

Mental health conditions, particularly depression, are common among women with HIV, and depression has been associated with poor engagement in HIV care and nonadherence to ART.^{10,11} Depression in women has also been associated with HIV serostatus nondisclosure to new and existing sexual partners.^{12,13} Avoidance-based coping is a maladaptive, anxiety-producing coping strategy used to avoid dealing with HIV-related stressors. Among men, coping with HIV infection

by avoidance has been found to mediate the relationship between depression and self-efficacy (one's belief in one's own ability to complete tasks and reach goals) and is associated with a decreased likelihood of HIV status disclosure.¹⁴ As such, avoidance-based coping may also be a pathway by which depression is associated with nonadherence to HIV care among women.¹⁵

This study examined reasons for nonadherence to prescribed ART among reproductive-age women in Argentina who were disengaged from HIV care with the goal of identifying strategies for reengagement. Reengagement in care in this group is essential for prevention of sexual and perinatal transmission of HIV. Based on previous research in the United States,¹⁵ it was hypothesized that avoidance-based coping would be related to increased depressive symptoms, as well as decreased motivation and self-efficacy, and would be an underlying reason for ART nonadherence. It was anticipated that findings from this study could inform psychosocial interventions for reproductive-age women living with HIV to enhance engagement in HIV care in settings where rates of viral suppression were low, thereby reducing the likelihood of sexual and perinatal transmission of HIV.

Methods

Data for this cross-sectional study were collected at baseline from Conexiones y Opciones Positivas en la Argentina 2 (COPA2), a cluster randomized clinical trial of physician-delivered motivational interviewing to improve retention in care and treatment adherence among challenging patients living with HIV in Argentina¹⁶ (ClinicalTrials.gov ID: NCT02846350). Before study procedures, approval was obtained from the institutional review board of University of Miami (20160313) in the United States and Argentine study sites (Fundacion Huesped FH-22). All patients provided written informed consent prior to enrollment in the study.

Participants were recruited from 7 outpatient settings (4 public hospital-based clinics and 3 private clinics) providing HIV care in 4 Argentine urban centers (Buenos Aires, Neuquén, Rosario, and Cordoba). All but one site that also serves as a maternity center (Rosario) had patient populations that were more than 50% male. The COPA2 inclusion criteria included: (1) 18 years old or older, (2) diagnosed with HIV for at least 6 months, (3) HIV viral load of more than 500 copies/mL in the previous 3 months following at least 6 months of receiving prescription for ART, and (4) disengaged from HIV care based on information collected from medical and pharmacy records (defined as 3 missed pharmacy pickups in the last 6 months *or* had not attended a physician visit in more than 12 months). Potential candidates were identified by study recruiters from clinic records and invited to return to the clinic to enroll in the study. Candidates provided signed informed consent at enrollment. Consent included approval for medical record abstraction and review of pharmacy records. The COPA2 study enrolled both men and women living with HIV; the current study presents data obtained from cisgender women of reproductive age (18-49 years old) enrolled in the study (n = 162)

and presents baseline data prior to receiving any study-related intervention.

Demographic and psychosocial data were collected using an audio computer-assisted self-interview (ACASI) system. All measures had been translated into Spanish and adapted to the local context in previous research.¹⁷ Laboratory results and medical history were extracted from medical records; pharmacy pickup information was obtained from pharmacy records.

Measures

Sociodemographics and HIV history. Demographic information collected included age, relationship status, living situation (alone versus with others), educational attainment, employment, and health coverage. Time since HIV diagnosis, history of an AIDS-related event, number of prior ART regimens, HIV viral load prior to enrollment, last CD4 count before enrollment, and the last regimen in the treatment history (in particular the use of efavirenz [EFV] and lopinavir/ritonavir (LPV/r) as are commonly included in ART regimens for women of reproductive age in Argentina and may be associated with low adherence due to toxicity or pill burden) were extracted from the medical record. Mode of HIV infection and number of daily pills in the prescribed ART regimen were self-reported by participants. The number of times since diagnosis that the participant had not gone to the doctor for more than 12 months and the number of times since ART initiation that the participant stopped taking ART for more than 3 months were assessed from medical records or patient self-report, if not available from medical records.

Currently taking ART and reasons for not taking ART. Participants self-reported their current ART use (yes/no). Those who reported they were not currently taking ART were asked to indicate the reasons why not. Available responses included: “The doctor asked me to wait,” “I don’t want to think about having HIV,” “I’m worried about my ability to be adherent,” “I’m using drugs or alcohol,” “I’m taking alternative or complementary medicines,” and “other, please specify.” Responses were not mutually exclusive.

Lifetime history of mental health and depressive symptomatology. Participants were assessed for recent (last 30 days) or lifetime history of several mental health symptomatology, including anxiety, depression, hallucinations, cognitive difficulties, suicidal ideation, and suicide attempts. Participants were also asked if they were receiving treatment for any emotional problems. In addition to mental health history, depressive symptomatology was assessed using the Beck Depression Inventory–IA (BDI-IA, Spanish),¹⁸ which has been previously validated in Argentina.¹⁹ Current suicidal ideation (past week) was assessed using item 9 of the BDI. As in previous research,^{20,21} scores of 0 (“I do not have any thoughts of killing myself”) on this item were considered nonsuicidal and scores of 1, 2, or 3 were considered suicidal. The BDI demonstrated excellent internal consistency in this study, $\alpha = .9$. The ACASI system

alerted study staff if the participant’s BDI score indicated moderate to severe depression (BDI total ≥ 17) or active suicidal ideation (BDI item 9 score = 2 or 3) or a recent suicide attempt; these participants were further evaluated by a health-care provider and referred to outpatient treatment or hospitalization as needed.

Adherence. Self-reported adherence to ART was assessed using a visual analog scale (VAS²²), a validated tool for this population. Participants indicated what proportion of their medication they had taken over the past 4 weeks, using a scale of 0 (0%) to 10 (100%). If the participant indicated that they were prescribed more than one pill per day, they were asked about each pill individually (for up to 3 pills), and an average VAS adherence score was calculated from the VAS responses for each pill. Information regarding adherence to pharmacy pickups (number of pharmacy pickups in the last 3 months) was obtained from pharmacy records.

Motivation for adherence. Motivation for ART adherence was assessed using the motivation subscale of the LifeWindows Information–Motivation–Behavioral Skills Adherence Assessment Questionnaire (LW-IMB-AAQ).²³ The scale consists of 10 statements that participants respond to using a scale of 1 (strongly disagree) to 5 (strongly agree). For analyses, average motivation (average of all 10 items) was used. This scale demonstrated adequate internal consistency in this study, $\alpha = .73$.

Self-efficacy. Self-efficacy was assessed using the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES).²⁴ The HIV-ASES consists of 12 statements related to the participant’s perceived self-efficacy in adhering to HIV treatment; participants respond to each statement using a scale of 0 (cannot do at all) to 10 (completely certain can do). For analyses, average self-efficacy (average of all 12 items) was used. This scale demonstrated excellent internal consistency in this study, $\alpha = .92$.

Statistical Analyses

Prior to analyses, data were screened by examining descriptive statistics. To examine potential patterns of reasons for not taking ART, items were analyzed using latent class analysis in R 3.6 with the package “poLCA.”²⁵ Between 1 and 5, class solutions were examined, and the solution with the lowest sample size–adjusted Bayesian Information Criteria (ADBIC) would be retained following recommendations from Kim.²⁶ Conditional item response probabilities were used to elucidate patterns of ART nonadherence, and differences between the clusters on key study variables were examined using χ^2 tests of association for discrete variables and nonparametric Mann-Whitney *U* tests for continuous variables in SPSS version 24.

Table 1. Sociodemographics, HIV History, Mental Health, Motivation, and Self-Efficacy of Study Participants (N = 162); and Class Analysis and Differences on Key Study Outcomes among Participants Who Were Not Currently Taking ART (n = 90).

Variable	Overall Sample (N = 162)	Participants Who Reported Not Currently Taking ART		P Value
		Don't Want to Think About HIV No (n = 58)	Don't Want to Think About HIV Yes (n = 32)	
Age	35.3 (37; 8.4)	36.1 (37.5; 8.3)	32.8 (31; 7.9)	.092
Education				.719
Less than high school	67 (41.4%)	24 (41.4%)	12 (37.5%)	
Complete high school or more	95 (58.6%)	34 (58.6%)	20 (62.5%)	
Employed				.263
No	92 (56.8%)	31 (53.4%)	21 (65.6%)	
Yes	70 (43.2%)	27 (46.6%)	11 (34.4%)	
Time since diagnosis (years)	11.9 (11.0; 6.6)	11.3 (9.9; 6.8)	11.1 (8.7; 7.4)	.768
AIDS-associated event				.054
No	109 (67.3%)	47 (81%)	20 (62.5%)	
Yes	53 (32.7%)	11 (19%)	12 (37.5%)	
Last CD4 count	328.2 (274; 265.2)	357.1 (266; 280.2)	302.7 (231.8; 222.2)	.448
Last log viral load	4.4 (4.4; 0.9)	4.6 (4.5; 0.7)	4.5 (4.4; 0.1)	.567
VAS adherence	3.5 (0.4; 4.2)	2.8 (0; 4.1)	1.5 (0; 3.4)	.251
Suicidality at baseline				.394
No	123 (75.9%)	43 (74.1%)	21 (71.1%)	
Yes	39 (24.1%)	15 (25.9%)	11 (34.4%)	
BDI total score (depression)	13.8 (10; 11.2)	11.9 (10; 9.2)	19.9 (16.5; 13.9)	.007
Average motivation	3.4 (3.4; 0.7)	3.5 (3.4; 0.8)	3 (3; 0.8)	.006
Average self-efficacy	7.3 (7.9; 2.1)	7.8 (8.2; 1.8)	6.3 (6.5; 2.7)	.017

^aContinuous variables are presented as mean (median; standard deviation [SD]), and categorical variables are presented as n (%). Percentages based on respective number of individuals in each class. Five responses missing for CD4 (3 in no, 2 in yes). P values compare yes/no on HIV avoidance (Mann-Whitney U for continuous measures and χ^2 for categorical).

Abbreviation: ART, antiretroviral therapy.

Results

Descriptive Statistics

Sociodemographic, HIV history, mental health, motivation, and self-efficacy of study participants are illustrated in Table 1.

Sociodemographics and HIV history. A total of 162 women were included in the subsequent analyses. Women were an average of 35.3 (median = 37; standard deviation [SD] = 8.4) years old and had been living with HIV for 11.9 (median = 11.0; SD = 6.6) years. The majority reported being single/divorced/widowed (n = 101; 62.3%); however, the majority reported not living alone (n = 152; 93.8%). About half of the women reported having at least completed high school (n = 95; 58.6%), were not currently employed (n = 92; 56.8%), and did not have private health insurance (n = 108; 66.7%). Regarding route of HIV acquisition, participants reported sex (with cis-gender men or transgender women) as the most common route of HIV infection (n = 92; 56.8%), followed by “don’t know” (n = 30; 18.5%), mother-to-child transmission (n = 18; 11.1%), blood transfusion (n = 7; 4.3%), intravenous drug use (n = 3; 1.9%), other (n = 2; 1.2%), or sex with a woman (n = 1; 0.6%). A total of 7 participants (4.3%) reported becoming infected with HIV through sex with a partner of an unspecified gender, and 2 responses to this question (1.2%) were missing.

One third of the women (n = 53; 32.7%) had a history of an AIDS-associated event, and women had a mean treatment history of 2.7 ART regimens (median = 2; SD = 1.9). The average log viral load was 4.4 (median = 4.4; SD = 0.9), and less than half of those participating (n = 74; 45.7%) had been virally suppressed (viral load < 200) the last time they were on treatment. The mean CD4 count was 328.2 (median = 274; SD = 265.21). Women reported they were prescribed a mean of 3.2 pills per day (median = 3; SD = 1.7), and under one quarter had been prescribed either EFV (n = 35; 21.6%) and/or LPV/r (n = 44; 27.2%) in the last regimen.

Current ART use and reasons for not taking ART. Ninety participants reported not currently taking antiretroviral medications; reasons for not taking ART are described in Table 2. The most common reason was avoidance-based coping—the participant did not want to think about having HIV. Many participants indicated the “other, please specify” option; their results were reviewed, and common responses were identified and grouped as described in Table 2.

Lifetime history of mental health and depressive symptomatology. Less than half of the participants (n = 71; 43.8%) reported ever having experienced major depression, more than half (n = 87; 53.7%) reported having experienced anxious symptomatology,

Table 2. Reasons Why Participants Reported They Are Not Currently Taking ART (n = 90).

Why Are You Not Taking ART at the Moment?	n
I do not want to think about having HIV	32 (35.5%)
Intolerance/toxicity/makes me sick/side effects	10 (11.1%)
The doctor asked me to wait	8 (8.9%)
Depression	4 (4.4%)
Family/relationship problems	4 (4.4%)
Personal problems/reasons	4 (4.4%)
I am worried I won't adhere to the medication	3 (3.3%)
Problems with coverage	3 (3.3%)
Tiredness/tired of taking medication	3 (3.3%)
Problems with adherence	2 (2.2%)
Live far away (from health center)	2 (2.2%)
Other health problems	2 (2.2%)
Work-related problems	2 (2.2%)
Moved	2 (2.2%)
I forget	2 (2.2%)
Problems with taking the pills (eg, integrating them into routine or swallowing them)	2 (2.2%)
Apathy/Indifference/Did not want to take them	2 (2.2%)
I am consuming drugs or alcohol	1 (1.1%)
I am taking alternative or complimentary medication	1 (1.1%)
Because I felt good	1 (1.1%)
Other (did not fit into any previous category)	9 (10%)

Abbreviation: ART, antiretroviral therapy.

and 22 (13.6%) reported having experienced hallucinations. Less than half of the women (n = 71; 43.8%) reported difficulty understanding/concentrating/remembering, one-third (n = 57; 35.2%) reported experiencing suicidal ideations, 34 (21%) reported having attempted suicide, and a quarter (n = 39; 24.1%) reported a history of treatment for emotional problems. Almost half of the women (n = 75; 46.3%) reported experiencing emotional problems (anxiety, depression, or thoughts of suicide) in the last month. Depression scores on the BDI were an average of 13.83 (median = 10; SD = 11.19), indicative of mild depression. About one quarter of participants (n = 39; 24.1%) reported suicidality at baseline as assessed by the BDI.

Adherence. The mean adherence score was 3.5 (median = 0.4; SD = 4.2), indicating low adherence. Participants had an average of 0.5 (median = 0; SD = 0.9) pharmacy pickups within the 3 months prior to enrollment, had missed going to their doctor for more than 12 months after being diagnosed with HIV ~1.5 times (median = 1; SD = 1.6), and stopped their ART for more than 3 months since diagnosis ~2.2 times (median = 2; SD = 1.7).

Motivation and self-efficacy. Average motivation was 3.4 (median = 3.4; SD = 0.7), indicating moderate levels of motivation. Average self-efficacy was 7.3 (median = 7.9; SD = 2.1), indicating moderate levels of self-efficacy.

Latent Class Analysis

Participants' responses for not taking antiretroviral medications fell into 21 categories (see Table 2). A latent class analysis was performed on the 90 participants reporting not currently taking ART using 5000 iterations and 100 replications per class solution. The 2-class solution was found to have the lowest ADBIC of 654.1 (1 class = 684.2, 3 classes = 658.1, 4 classes = 669.0) and was retained as the model of choice. In examining the conditional item responses, it was found that the classes were perfectly separated by the response "I do not want to think about having HIV."

Class Differences

Using the response "I do not want to think about having HIV" as the class indicator, Mann-Whitney *U* tests were performed to examine potential differences on key study variables between individuals endorsing and not endorsing the response "I do not want to think about having HIV." Mann-Whitney *U* tests revealed that participants differed on their item response pertaining to depressive symptomatology ($U = 608.5, z = -2.7, P = .007$), motivation ($U = 601, z = -2.8, P = .006$), and self-efficacy ($U = 644.5, z = -2.4, P = .017$). The group endorsing not wanting to think about HIV had lower median motivation and self-efficacy, as well as higher depressive symptomatology (see Table 1). Participants did not differ with respect to age ($U = 728, z = -1.7, P = .092$) or time since diagnosis ($U = 893, z = -0.3, P = .768$).

There was a marginal association found between the response "I do not want to think about having HIV" and history of an AIDS-associated event, $\chi^2(1) = 3.7, P = .054$. No differences were found among any other sociodemographic or HIV history variables.

Discussion

This study evaluated nonadherence to prescribed ART among women of reproductive age in Argentina who were disengaged from HIV care and found that avoidance-based coping (not wanting to think about HIV) was the most frequent reason for not taking prescribed ART. Women utilizing avoidance-based coping had more depressive symptoms, lower motivation, and lower self-efficacy than those not using this maladaptive strategy.¹⁵ As such, this constellation of factors (depression, motivation, and self-efficacy) appears to act as a driver of nonadherence to ART and likely contribute to disengagement from HIV care, poor HIV outcomes, and sexual and vertical transmission of HIV.²⁷

Results from this study complement the understanding of previous research on the contribution of depression to poor HIV and health outcomes for women of reproductive age living with HIV and for infants of mothers living with HIV worldwide.²⁸⁻³⁰ This study is however unique as it the first to utilize cluster analysis to clearly define that avoidance, low self-efficacy, and low motivation are critical drivers likely

influenced by depression among women. The use of this novel statistical analysis allows to better understand the impact of exposure to multiple risks, so interventions can be targeted to subgroups that will benefit most, such as in this case, women with avoidance-based coping. Interestingly, our results using this approach indicate that when there is avoidance-based coping, depressive symptomatology negatively impacts ART uptake, even when depressive symptoms are low. However, isolation of the differences between those engaging or not engaging in avoidance-based coping clearly differentiated factors associated with the strategy of avoidance. Avoidance, while enabling the individual time to process a stressor, becomes a liability when it prevents resolution of the problem. Results highlight the importance of the integration of routine assessment and treatment of depression in HIV care³² before the patient comes to rely on avoidance as a coping strategy. Therefore, targeting avoidance-based coping, likely with acceptance- and commitment-based therapies, may help promote reengagement in care and may, in turn, help prevent the sexual and perinatal transmission of HIV in this group of women.^{31,32} Further research is needed to explore the mechanism behind avoidance-based coping and depression, and how these factors together may impact motivation and self-efficacy, which have been shown to be important for adherence and reengagement in care.¹⁷

Interventions to improve HIV health outcomes among women living with HIV in Argentina and other regions have primarily focused on provision of ART in clinical settings and have neglected comprehensive reproductive and mental health treatment. Women represent over 50% of the population living with HIV worldwide and face unique challenges and barriers to HIV care.³³ Clearly, strategies for improving retention in care and ART adherence are essential to achieve the goal of controlling the HIV epidemic, and there is a need to understand barriers to care among the vulnerable population of women of reproductive age.³³

Despite the importance of our findings and the need to address depressive symptoms in this population, this study had several limitations. The primary limitation was the small sample size and the use of a cross-sectional analysis. In addition, the study relied on self-report, and though using a valid and reliable measure of depressive symptoms (the BDI), a depression diagnostic tool was not used. Additionally, some information related to HIV history (number of times they did not see a physician for more than 12 months and number of times they stopped taking ART for more than 3 months) was sometimes unavailable in the medical record and in those cases was self-reported, which may be subject to recall bias.

This study highlights the importance of integrating mental health care into HIV care for women facing difficulties in coping with HIV, with the aim of increasing motivation and self-efficacy and reducing depression, to optimize the benefits of ART. As women living with HIV experience a disproportionate burden of poor health outcomes and mental illness, gender-specific interventions focused on the treatment of

depression could be the gateway to improving HIV outcomes and preventing HIV transmission.


Declaration of Conflicting Interests

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