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Antiretroviral Therapy Adherence Among Transgender Women Living with HIV

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Abstract

Despite disproportionate rates of HIV among transgender women and evidence that medication adherence is necessary for treatment success and increased likelihood of survival, there has been little investigation into antiretroviral treatment (ART) adherence issues among transgender women. This study examined rates of self-reported ART adherence among transgender women on ART (n = 35) and well-established correlates of nonadherence including depression, adherence self-efficacy, patient perceptions of interactions with their providers, and perceived adverse side effects of ART compared to other respondents (n = 2,770). Transgender women on ART were less likely to report 90% adherence rates or higher and reported less confidence in their abilities to integrate treatment regimens into their daily lives. When transgender women were compared to other respondents, regardless of the current medication regimen, they reported significantly fewer positive interactions with their health care providers. Training for providers and integration of hormone therapy into HIV care is recommended.

Keywords

adherence; AIDS; antiretroviral therapy; HIV; transgender; women

In recent years, evidence of the disproportionate rates of HIV among transgender women has been rapidly increasing (Herbst et al., 2008). However, there has been very little systematic investigation into HIV treatment and adherence issues for this highly marginalized population. In addition, research has documented a number of barriers to

health care utilization among transgender women, including negative experiences with providers, fear of discrimination and mistreatment, being denied medical care due to the transgender status, and lack of provider knowledge about transgender health issues, among others (Clements, Wilkinson, Kitano, & Marx, 1999; Garafalo, Deleon, Osmer, Doll, & Harper, 2006; Kenagy, 2005; Sanchez, Sanchez, & Danoff, 2009). Clinical observations also suggest that transgender women living with HIV are likely to face unique challenges in adhering to HIV care and treatment regimens (Tom Waddell Health Center Transgender Team, 2006; Vázquez, 2008b).

While antiretroviral therapies (ART) as HIV treatment options have improved dramatically over recent years, clinicians continue to struggle with how to maximize benefits for patients living with HIV. Evidence indicates that medication adherence is necessary for treatment success and increased likelihood of survival (Garcia de Olalla et al., 2002). Although recent research does not indicate a single cutoff level to measure ART adherence, data support using 90% adherence as a meaningful distinction (Johnson et al., 2003). Nonadherence is related to increased risk of developing drug-resistant viral strains (Vanhove, Schapiro, Winters, Merigan, & Blaschke, 1996) and transmitting resistant strains to others (Blower, Aschenbach, Gershengorn, & Kahn, 2001). Studies have reported conflicting findings regarding correlates of nonadherence, and interventions aimed at improving adherence have not shown overwhelming promise.

Factors associated with nonadherence are complex and often involve a dynamic interaction of cognitive, emotional, and behavioral variables (Remien et al., 2003; van Dulmen et al., 2007). Correlates of poor adherence can be categorized into patient factors such as younger age, depression, and lower adherence self-efficacy; medication characteristics such as side effects; and interpersonal variables such as poor patient-provider relationships and low levels of social support (Fogarty et al., 2002; Johnson et al., 2006; Simoni, Frick, & Huang, 2006). However, medication adherence and its correlates have not been specifically studied in transgender women.

The purpose of the current analysis was to examine the rates of self-reported ART adherence among transgender women as compared to other respondents. We further attempted to contextualize adherence by examining well-established correlates of nonadherence including depression, adherence self-efficacy, patient perceptions of interactions with their providers, and perceived adverse effects of ART.

Methods

Study Respondents

A total of 3,818 HIV-infected individuals in four cities (San Francisco, Los Angeles, New York City, and Milwaukee) were screened for recruitment into the Healthy Living Project (HLP), a clinical trial of a comprehensive cognitive-behavioral sexual risk-reduction intervention that included coping skills and treatment adherence intervention modules. Recruitment and screening of potential respondents were undertaken in community agencies and health care clinics that served HIV-infected clients. Brochures, posters, and project descriptions as well as direct contact by study staff in clinical and social service agencies, were used to recruit respondents. Media advertisements and word-of-mouth were also used for recruitment.

Respondents were required to: (a) be at least 18 years of age, (b) provide written informed consent and medical documentation of HIV infection, (c) be free of severe neuropsychological impairment or psychosis, and (d) not currently involved in another behavioral intervention study related to HIV. All respondents were asked to self-identify as

male, female, or transgender, and they were then asked to report their sex as assigned at birth. Only transgender women were included in the current analysis, yielding a potential sample of 59 participants. Of the 59 transgender women in the sample, 35 reported that they were currently on ART. All other respondents (n = 3,759) comprised the comparison group (including 4 transgender men and 1 intersex person); 2,770 (73.7%) of these respondents indicated they were currently on ART.

Overview of Assessment Procedures

The data reported in this paper were from a baseline interview that also served as the screening determination for the HLP. All procedures and forms were reviewed and approved by the sites' institutional review boards (IRBs). After written informed consent was obtained, interviews were conducted in private settings in research offices, community-based organizations, and clinics in the four cities. Interviews were conducted over a period of 2 to 4 hours with regular breaks allowed to minimize respondent fatigue. Respondents were compensated $50 for completing the baseline interview, and individuals who required child care were eligible to receive an additional $10 to help defray child care costs.

Interviewer Training and Quality Assurance

Interviewers were centrally trained through the use of a detailed assessment manual, practice with the computer programs, participation in an intensive 3-day training program, and review and certification of audiotaped mock interviews based on standardized criteria. All interviews were audiotaped, and a systematic sample of tapes was reviewed for protocol adherence with feedback and correction provided to all interviewers on a regular basis.

Measures

Demographic characteristics and health status—Respondents were asked to provide personal information in a demographic questionnaire. Age, race/ethnicity, education, employment status, sexual orientation, time since HIV diagnosis, and self-reported HIV disease markers were assessed.

ART adherence—Recent self-reported ART adherence was assessed over a 3-day period using an adherence survey developed for use by the AIDS Clinical Trials Group (ACTG, Chesney et al., 2000). Respondents indicated how many antiretroviral pills they had skipped during each of the previous 3 days. This measure has been used widely with diverse samples. For the present study, we calculated percentage adherence based on number of pills actually taken divided by number of pills prescribed. Respondents were classified as 0 (*having achieved less than 90% adherence*) versus 1 (*90% or higher adherence*), consistent with current literature on minimum levels of adherence to achieve HIV viral suppression and clinical benefit (Garcia de Olalla et al., 2002; Paterson et al., 2000).

Frequency of ART-related side effects—Symptoms included in the ACTG symptom checklist (Justice et al., 2001) were adapted by asking respondents who were currently taking ART whether reported symptoms were thought to be due to their antiretroviral medications. Specifically, respondents were asked whether they experienced a given symptom (e.g., fatigue) over the previous 30 days. For each reported symptom, respondents were asked to indicate whether they thought it was "at all a side effect of your HIV medications." Total side effect burden was derived as a count of symptoms attributed to ART medications.

Affective symptoms of depression—The 21-item Beck Depression Inventory (BDI) assesses the severity of somatic, affective, cognitive, and behavioral symptoms of

depression during the previous week (Beck, 1967). Because many symptoms of depression and HIV disease are confounded (Kalichman, Rompa, & Cage, 2000), we calculated a modified BDI total score that excluded somatic depressive symptoms. This 12-item BDI-Affective subscale (i.e., sadness, future pessimism, failure, decreased satisfaction, guilt, punishment, disappointment, self-blame, thoughts of suicide, crying, irritation, and decreased interest in others) displayed adequate internal consistency reliability (Cronbach's $\alpha = .84$).

Adherence self-efficacy—Self-efficacy, or confidence in one's ability to perform specific behaviors such as complying with a treatment plan (Bandura, 1991), has been consistently linked to treatment adherence over time (Johnson et al., 2007; Kalichman et al., 2005). The HIV adherence self-efficacy scale (ASES; Johnson et al., 2007), developed at the University of California San Francisco, assesses patient confidence to carry out health-related behaviors associated with HIV treatment. This measure, which includes two subscales (i.e., Perseverance and Integration; Cronbach's $\alpha = .92$ and .90, respectively) was found to be related to enhanced adherence to ART in our previous research (Johnson et al., 2003). A sample item for treatment perseverance is: *How confident are you that you can continue with your treatment even when you are feeling discouraged about your health?* A sample item for treatment integration is: *How confident are you that you can integrate your treatment into your daily routine?*

Positive provider interaction—Adapted from previous studies (Johnson et al., 2006), an 8-item scale was used to assess patients' perceptions of positive interactions with their providers. Respondents were asked how often certain things occurred during recent contacts with health care providers, such as: (a) getting help from providers to solve problems in taking medications or to deal with symptoms or side effects, (b) feeling helped by talking with or seeing a provider, and (c) leaving visits thinking that she and her provider had agreed upon a treatment plan that the patient could really follow. A sample item is: *How often during your recent contacts with your health care providers did you get your providers to really listen to your concerns?* Response options were 0 (*never*), 1 (*some of the time*), 2 (*most of the time*), and 3 (*every time*). Scores on each item were averaged, with higher scores indicating more positive provider interactions. The scale demonstrated adequate internal consistency reliability (Cronbach's $\alpha = 0.84$).

Data Analysis

Primary analyses for the present study compared transgender women on ART ($n = 35$) and other HIV-infected persons on ART ($n = 2,770$). We began by comparing the demographic characteristics of transgender women to those of other HIV-infected persons using chi-square analyses for categorical variables and independent samples *t*-tests for continuous variables. Then, we used binary logistic regression to determine whether transgender women were less likely to report achieving adequate levels of adherence (i.e., ≥ 90%). Next, using independent samples *t*-tests, we examined whether or not transgender women reported more ART-related side effects, higher affective symptoms of depression, lower levels of adherence self-efficacy, and decreased positive interaction with health care providers than their nontransgender counterparts. Informed by these analyses, we examined the extent to which significant differences in these psychological factors accounted for lower rates of ART adherence among transgender women in a mediation analysis using binary logistic regression.

Results

Respondent Demographics

Most of the 2,805 respondents who reported being on ART self-identified as gay (*n* = 1,218; 43.4%) or bisexual (*n* = 322; 11.5%). The majority of respondents were African American (*n* =1,348; 48.1%), but sizeable proportions were Caucasian (*n* = 730; 26.0%) or Hispanic/Latino (*n* = 552; 19.7%). The mean age of the respondents was 42.0 (*SD* = 7.6) years. The sample was largely well-educated with almost half (*n* = 1,344, 47.9%) having completed at least some college. More than 10% (*n* = 302, 10.8%) reported being homeless in the previous year, and 1,455 (51.9%) were currently single. Almost one half (*n* =1,309, 46.7%) of the respondents reported being convicted of a crime in the past, and 1,418 (50.6%) had served time in jail or prison. The mean self-reported CD4+ T cell count for the sample was 428 cells/mm^3 (*SD* = 292), and 1,428 (50.9%) of the respondents reported having a detectable HIV viral load. As shown in Table 1, transgender women were significantly younger on the average ($t(2801) = -2.82$, $p < .01$) and more likely to describe their sexual orientation as bisexual or other/unsure (χ^2 (3) = 112.06, $p < .001$). We also observed that transgender women were significantly more likely to report ever having been convicted of a crime (χ^2 (1) = 10.84, $p < .01$) and to report having previously served time in jail or prison (χ^2 (1) = 17.53, $p < .001$). The finding that transgender women living with HIV were less likely than other HIV-infected respondents to report currently taking ART has been reported elsewhere (Melendez et al., 2006).

Differences in Dependent Variables

As shown in Table 2, transgender women who reported that they were currently on ART were significantly less likely to report taking at least 90% of their prescribed ART medications during the previous 3 days (*OR* = 0.49, 95% CI = 0.25–0.97). Using independent samples *t*-tests, we also observed that transgender women had significantly lower scores for the Integration subscale ($t(2,802) = 2.99$, $p < .05$) but not the Perseverance subscale ($t(2801) = 0.62$, $p > .05$) of the HIV adherence self-efficacy measure. Transgender women on ART reported marginally lower positive provider interactions ($t(2,798) = 1.71$, $p = .09$). However, when we examined the full sample, irrespective of whether respondents were currently prescribed ART, transgender women (*M* = 2.1, *SD* = 0.7) reported significantly lower positive provider interactions compared to other HIV-infected respondents (*M* = 2.3, *SD* = 0.6; $t(3,405) = 2.00$, $p < .05$).

Mediation Analysis

Among the psychological factors related to ART adherence that were examined in the current analysis, the Integration subscale of the HIV-adherence self-efficacy measure was the only variable where significant differences were found. Using hierarchical binary logistic regression, we examined whether lower integration accounted for the lower rates of ART adherence among transgender women. The Integration subscale for the adherence self-efficacy measure was centered (*M* = 0, *SD* = ± 1) to facilitate interpretation of the adjusted odds ratio (*AOR*). As shown in Table 3, after adding integration in the second block, transgender women no longer reported significantly lower rates of ART adherence (defined as taking ≥ 90% of doses prescribed during the previous 3 days). For every one standard deviation increase in integration, the odds of reporting adequate levels of ART adherence were more than two-fold higher.

Discussion

Consistent with observations from clinicians working with transgender women living with HIV, we found significantly lower ART adherence among transgender female respondents,

who were less likely than their nontransgender counterparts to report adherence rates that were 90% or greater. This finding has clinical significance for the management of HIV among transgender women. Evidence from other investigations found that, depending on specific regimen characteristics and baseline levels of adherence, a 10% increase in adherence may have been associated with as much as a halving of viral loads and a 20% to 30% decreased risk of progression to AIDS, suggesting that the magnitude of the effect observed in our study has potentially important clinical ramifications (Bangsberg et al., 2000; Hogg et al., 2002).

Transgender women reported significantly lower self-ratings on the Integration subscale of the adherence self-efficacy measure than comparison respondents. Failure to integrate treatment into one's life has been identified in prior research as a consistent obstacle to medication adherence (Chesney, 2000; Johnson et al., 2003). Given the multitude of reports that transgender people often avoid seeking health care due to previous negative experiences in interactions with providers (Clements et al., 1999; Kenagy, 2005; Lombardi, 2007; Sanchez et al., 2009), it makes sense that transgender female respondents would report less confidence in their ability to keep appointments and adhere to treatment plans, especially when medication regimens interfere with daily life.

No differences in depression were found between transgender women and the comparison group. Because a majority of respondents in the comparison group identified as gay or bisexual (55%), it may be the case that both transgender women and gay and bisexual men and women have significantly elevated rates of depression when compared to the general population. This finding has been reported in the literature on depression in lesbian, gay, and bisexual populations (Cochran, Mays, & Sullivan, 2003) as well as among transgender adults (Israel & Tarver, 1997), and may account for the lack of difference between the groups in this study.

Although we did not find differences in reports of side effects attributed to HIV medications, transgender women may present a more complicated side effect profile due to hormone use, which was not assessed in the present study. There have been some preliminary discussions among clinicians who serve HIV-infected transgender women regarding possible interactions between ART and hormone treatment (Vázquez, 2008a), but the studies that have examined these drug interactions have all been conducted with nontransgender female participants who were taking oral contraceptives (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2009). Several antiretroviral medications have been shown to alter the levels of estrogen in the blood, thus requiring adjusted levels of hormones to achieve the same treatment effect and/or to avoid unnecessary risks and side effects (Connolly & Kohler, 2006). It is unclear whether transgender women in our study perceived any interactions between their hormone treatment and ART or how their perceptions may have influenced rates of adherence or reporting of side effects.

Some evidence has suggested that transition-related health care, especially hormone treatment, is more highly prioritized by many transgender women than primary care, including HIV-related care and treatment (Kammerer, Mason, Connors, & Durkee, 2001). Many transgender women are unable to access hormone treatment through a health care provider and must pay large sums of money to obtain hormones from street markets. They often desire quick results, especially individuals who are in early transition and, because they self-administer hormones without medical supervision, they often take higher doses of estrogen than is considered safe (Sanchez et al., 2009). Considering the multiple barriers to obtaining and monitoring hormone treatment, transgender women would likely consider an ART-related drug interaction that lowers estrogen levels as highly undesirable. In addition, the combination of ART and hormone use may mean that additional monitoring of blood

levels is needed to determine whether dosages need to be adjusted. Given the pervasiveness of transgender women's aversion to seeking health care services due to fear or previous negative experiences (Transgender Law Center's Health Care Access Project, 2004; Lombardi, 2007), further medical attention may not be readily accepted by many patients.

Limitations and Future Directions

The small number of transgender women in the sample limited our study. The method of determining gender identity may have inadvertently excluded some respondents who either did not wish to identify as transgender due to fear of stigma or other reasons or did not feel that their gender identity was adequately represented by the options provided. Future studies should include more substantive sample sizes and more comprehensive and sensitive assessments of transgender identities.

Future studies of adherence among transgender women should also assess whether or not respondents are currently using hormones and their perceptions of interactions between their hormone treatment and HIV medications. Similarly, the measure of adherence used in this study was self-report and only inquired about medication adherence over the previous 3 days; longer timeframes and more objective measures of adherence may yield more robust findings. Finally, given the relatively small number of transgender respondents, there was limited statistical power to examine multiple predictors of adherence such as age, race/ethnicity, education, housing status, time on regimen, health care utilization patterns, history of incarceration, and substance use.

Clinical Implications

Findings from this study suggest that culturally appropriate interventions that address lack of adherence self-efficacy may facilitate higher rates of ART adherence and thereby result in better clinical outcomes for transgender women with HIV. Training for health care providers to increase cultural competency to work with transgender patients, increase patient trust, and promote positive interactions between patients and providers may help to cultivate an atmosphere that is more conducive to fostering greater adherence self-efficacy and medication adherence among transgender women living with HIV.

Clinicians who serve transgender women have found that hormone treatment can serve as an incentive for patients to seek and adhere to ART (Zevin & Martinez, 2007). Integration of hormone treatment into HIV care may augment adherence as well as decrease the prevalence of self-administered hormone use among members of this population (Grimaldi & Jacobs, 1998).

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Table 1

Respondent Characteristics (N = 2,805)

	Transgender Women on ART (n = 35)	**Other HIV-Infected Respondents on ART (n = 2,770)**	***p* Value**
Ethnicity	*n* (%)	*n* (%)	
Black/African American	22 (62.9)	1,326 (47.9)	
Hispanic/Latino	7 (20.0)	545 (19.7)	
Caucasian	3 (8.6)	727 (26.3)	
Other Ethnic Minority	3 (8.5)	170 (6.1)	
Sexual Orientation			$p \leq .001$
Heterosexual	7 (20.0)	1,197 (43.3)	
Homosexual	10 (28.6)	1,208 (43.7)	
Bisexual	9 (25.7)	313 (11.3)	
Other/not sure	9 (25.7)	47 (1.7)	
Education			
Did not graduate high school	15 (42.9)	693 (25.0)	
High school graduate	9 (25.7)	744 (26.9)	
Some college	9 (25.7)	916 (33.1)	
College graduate or greater	2 (5.7)	417 (15.0)	
Currently working	7 (20.0)	813 (29.5)	
Homeless (in the previous year)	2 (5.7)	300 (10.8)	
Currently single	18 (51.4)	1,437 (54.8)	
Ever convicted of a crime	26 (74.3)	1,283 (46.4)	$p \leq .001$
Ever served time in jail/prison	30 (85.7)	1,388 (50.1)	$p \leq .001$
Detectable HIV viral load (self-reported)	21 (63.6)	1,407 (52.4)	
	M (*SD*)	*M* (*SD*)	
Age	38.4 (5.6)	42.0 (7.6)	$p < .01$
CD4+ T cell count (self-report)	346.9 (209.0)	429.1 (292.4)	

Table 2

Outcome Measures

	Transgender Women on ART (*n* = 35)	**Other HIV-infected Persons on ART (*n* = 2,770)**	***p* Value**
≥ 90% ART Adherence	51.5%	68.4%	$p < .05$
	M (SD)	***M (SD)***	
ART Side Effect Count	6.2 (5.4)	6.5 (5.6)	
Depression (BDI-Affective)	7.1 (5.9)	7.1 (6.1)	
Adherence Self Efficacy			
Integration	6.5 (2.5)	7.5 (2.0)	$p < .05$
Perseverance	6.9 (2.2)	7.1 (2.3)	
Positive Provider Interaction	2.1 (0.7)	2.3 (0.6)	

Note. ART = antiretroviral therapy, BDI = Beck Depression Inventory

Table 3

Hierarchical Binary Logistic Regression of Correlates of ART Adherence (N = 2,805)

	***OR* (95% CI)**	***p* Value**
Block 1		
Transgender women	0.49 (0.25 – 0.97)	$p < .05$
	AOR (95% CI)	
Block 2		
Transgender women	0.71 (0.33 – 1.54)	
Adherence self-efficacy (Integration)	2.42 (2.20 – 2.65)	$p < .001$