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Self-Reported Medication Adherence and Symptom Experience in Adults with HIV

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Abstract

Symptom burden has been identified as a predictor of medication adherence, but little is known about which symptoms are most strongly implicated. This study examines self-reported adherence in relation to demographic, clinical, and symptom characteristics among 302 adults living with HIV. Only 12% reported missing medication during the 3-day assessment, but 75% gave at least one reason for missing medication in the prior month. Poor adherence was associated with higher viral load and greater symptom burden. Trouble sleeping and difficulty concentrating were strongly associated with poor adherence. Given that “forgetting” was the most common reason for missing medication and nearly one third reported sleeping through dose time, future research should examine the influence of sleep disturbance on adherence. Effective management of

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common symptoms, such as sleep disturbance, fatigue, and gastrointestinal side effects of medications may result in better adherence, as well as improved clinical outcomes and quality of life.

Keywords

adherence; fatigue; HIV; sleep; symptoms

Treatment advances for HIV infection have resulted in lower rates of mortality for those affected by the disease. With these advances, greater attention has been given to co-morbidity and quality of life issues, and the effective management of symptoms has emerged as an important factor in enhancing the lives of persons with HIV (Côté et al., 2009). Treatment adherence has also been a topic of interest, as near-perfect adherence to medication regimens is needed to achieve optimal clinical outcomes. A multitude of demographic and clinical factors have been examined as predictors of treatment non-adherence, and one of the most consistent correlates of poor adherence is high symptom burden (Ammassari et al., 2002). Symptom burden has been described as the sum of the severity and impact of symptoms associated with a given disease or treatment (Cleeland, 2007).

Early studies of predictors of medication adherence identified symptoms, particularly depression, as significant correlates of poor adherence among adults living with HIV (Holzemer et al., 1999). The total number of symptoms has been found to be predictive of medication adherence as measured by both self-report and electronic monitoring (i.e., MEMS cap), with concerns about antiretroviral therapy (ART) serving as a mediator of this relationship (González et al., 2007). Recent evidence suggests that the relationship between symptoms and adherence is not simply one of association but that symptom burden and adherence directly affect each other. A clinical trial of a 3-week symptom management program, administered either individually or in group format, determined that the program significantly increased self-reported adherence and quality of life, as well as improved measures of CD4+ T cell and viral load, compared to a wait-list control (Chiou et al., 2006). Furthermore, a recent prospective study found that highly adherent patients experienced a decrease in symptoms over a 6-month follow-up period, while less adherent patients did not (Cooper, Gellaitry, Hankins, Fisher, & Horne, 2009). Moreover, those whose symptoms did not improve began to question the necessity of ART. These findings suggested a vicious cycle whereby poor adherence could exacerbate symptoms, which in turn could interfere with regimen adherence.

The complex interaction of symptom experience, beliefs about treatment, and adherence has been described in a number of conceptual models. The UCSF Symptom Management Model (Dodd et al., 2001) is a general model for understanding the relationships between symptom experience, management strategies, and outcomes. The model addresses the recursive relationships between HIV symptom management, adherence to ART, and clinical outcomes. This conceptual model informed the current study to better understand the complex and bidirectional relationships between symptom experience and adherence.

Despite the abundance of studies documenting the relationship between adherence and symptoms, little is known about which symptoms experienced by those living with HIV are most associated with poor adherence. The aim of this study was to explore this issue further by examining demographic, clinical, and symptom characteristics of adults grouped by level of self-reported adherence to their medication regimen. The study involved a diverse cohort

of adults living with HIV in the San Francisco Bay Area, and both global measures of symptom burden as well as ratings of individual symptoms were included in the analysis.

Method

Participants and Procedure

Participants were recruited as part of the Symptoms and Genetics Study, a longitudinal study aimed at identifying biomarkers of symptom experience among HIV-infected adults (Lee et al., 2009). This analysis addressed self-reported adherence and its demographic, clinical, and symptom-related correlates in a community-dwelling sample of adults with HIV. The Committee on Human Research at the University of California, San Francisco (UCSF) approved the study protocol. All participants provided written informed consent and were paid for their participation. A convenience sample of adults with HIV was recruited from 2005 to 2007 using approved flyers posted at local HIV clinics and community sites and through referrals from other study participants. Eligible subjects were English-speaking adults, at least 18 years of age, who had been diagnosed with HIV at least 30 days prior to enrollment. Exclusion criteria included current use of illicit drugs (as determined by self-report or urine drug test), shift work (i.e., at least 4 hours between 12 a.m. and 6 a.m.), report of a diagnosed sleep disorder, bipolar disorder, schizophrenia or dementia, or pregnancy within the prior 3 months. The baseline assessment occurred over a 72-hour period, and participants were screened for illicit drug use by a urine drug test at the beginning and end of the 3-day assessment. A positive drug test at either time point resulted in exclusion from subsequent data analysis.

Measures

Demographic and clinical characteristics—Self-report demographic questions assessed gender, age, education, employment, and race/ethnicity. Given the low number of participants self-identifying as being of either mixed race/ethnicity or Asian, Pacific Islander, Native American, or other race/ethnicity not listed in the questionnaire, these groups were treated as a single subcategory for analysis. Participants also reported the length of time since their HIV diagnosis, their medication regimen, and any history of AIDS diagnosis. CD4+ T cell count and viral load were obtained from the most recent medical lab report for each participant. Viral suppression was defined as a viral load of < 400 copies/mL.

Medication adherence—The AIDS Clinical Trials Group (ACTG) Adherence Questionnaire has been used extensively to measure adherence to antiretroviral medications (Chesney et al., 2000). Although investigators have modified this measure in various ways, the scale used in this study included 9 of the original 14 reasons why people miss taking their medications (see Table 1). Holzemer and colleagues (2006) used the same 9 items based on factor analysis and reliability estimates, and the Cronbach's alpha coefficient was .89. The shorter scale is more sensitive to participant burden, while retaining validity and reliability. The alpha for the 9-item scale was .85 in the current sample. Respondents are asked to rate on a 4-point scale (*never, rarely, sometimes, often*) how often each of the 9 reasons applied to them within the previous month. A total score is calculated as the sum, with a range of 9 to 36. Holzemer and colleagues (2006) dichotomized their sample as adherent (scores 9–20) and non-adherent (scores 21–36). To more specifically examine level of adherence we also grouped our sample into approximate tertiles with 9–10 equals high, 11–16 equals moderate, and 17–36 equals low adherence.

In addition to the total score, two subscores were calculated based on a prior factor analysis (Holzemer et al., 2006): Pill-Taking Problems (5 items: *side effects, felt sick, too many pills to take, felt depressed/overwhelmed, and could not take pills at specified times*) and

Forgetfulness (4 items: *too busy, away from home, simply forgot, and slept through dose time*). In the current sample, the Cronbach's alpha coefficients for the two subscales were .80 and .83, respectively.

While this adherence scale does not estimate number of medications missed or the proportion of medications taken as directed, the total score is a proxy measure based on the assumption that respondents who report more and frequent reasons for missing medication are less adherent than those who report fewer and less frequent reasons. The measure is also not specific to ART, but rather it measures non-adherence to any part of participants' daily medication regimen.

Participants also completed a 3-day log of adherence to daily medication regimens. Each evening before going to bed, participants recorded whether they missed any of their medications that day. The number of days with missed medications ranged from 0 to 3.

Symptom experience—The Memorial Symptom Assessment Scale (MSAS) was used to assess symptom prevalence and intensity. The MSAS is a reliable and valid self-report measure that has been used in a variety of clinical populations (Sawicki, Sellers, & Robinson, 2008), including patients with HIV (Harding, Molloy, Easterbrook, Frame, & Higginson, 2006). The MSAS evaluates symptom prevalence in the previous week (*yes/no*), as well as symptom frequency, severity, and distress using 4- or 5-point Likert scales. Individual symptom scores were computed for each symptom as the average score on the frequency, severity, and distress scales. If the respondent did not report the symptom, the individual symptom score was 0. The symptom scores served as a measure of symptom experience, with an intense symptom experience being that which was frequent, severe, and/or distressing. The total number of symptoms reported served as a global measure of symptom prevalence and the average of the 32 individual symptom scores yielded the MSAS total score, a global measure of symptom experience. Three previously validated subscales were also computed: (a) PSYCH, the average of six psychological symptom scores, (b) PHYS, the average of 12 of the most common physical symptoms, and (c) the Global Distress Index (GDI), a measure of overall symptom distress calculated as the average frequency for four psychological symptoms and the average distress scores for six physical symptoms. The scores for each individual symptom and for each subscale range from 0 to 4, with higher scores indicative of greater symptom burden.

Analysis

All analyses were conducted using SPSS version 14.0 (SPSS, Inc, Chicago IL, USA). Descriptive statistics (means, standard deviations, and frequencies) were calculated to summarize demographic and clinical characteristics and describe the sample's symptom experience. Square root transformations were used to normalize the skewed distributions of symptom scores, and a logarithmic transformation was used to normalize viral load values. Medication adherence scores were split into tertiles and then compared on demographic, clinical, and symptom variables using chi-square tests for categorical variables and analysis of variance for continuous variables. Significant omnibus results were followed by post-hoc analysis using Bonferroni-adjusted *p*-values. All analyses based on non-normally distributed variables were confirmed with Kruskal Wallis or Mann-Whitney U tests. To compare the magnitude of group differences in individual symptom scores across adherence tertile, effect sizes were estimated using eta squared. Analysis of variance effect sizes of .01 were classified as small, .06 as medium, and .14 as large. Spearman correlations were used to estimate associations between adherence subscores and symptom subscores; *p*-values less than .05 were considered significant.

Results

Sample Characteristics

Of the 350 participants enrolled in the larger study, 32 were excluded due to positive or incomplete urine toxicology screening, 9 were excluded because they were not currently taking any medications, and 7 were excluded due to missing adherence data. The demographic and clinical characteristics of the final sample of 302 adults are presented in Table 2. The sample was predominantly male and ethnically diverse, reflecting the local population living with HIV. Most had been living with HIV for many years and just over half had been previously diagnosed with AIDS. Most were taking ART (74%), as well as a variety of medications for managing pain, cardiovascular disease, psychiatric illness, and other co-morbidities. Those not taking ART were retained in the sample to evaluate symptom experience and adherence to other medications in this sub-group of HIV-infected adults.

There were demographic differences between the men, women, and transgender adults in this sample, consistent with local geographical trends. The men were more likely to be White/Caucasian ($\chi^2(1) = 22.1, p < .001$), while the women and transgender adults were more likely to be Black/African American ($\chi^2(1) = 33.5, p < .001$). Women were less likely than men and transgender adults to have completed high school ($\chi^2(1) = 28.1, p < .001$) and were more likely to be in a relationship ($\chi^2(1) = 6.8, p = .009$) and to have children ($\chi^2(1) = 84.1, p < .001$). There was no gender difference with respect to age, employment status, or income. Clinical characteristics were similar across genders, except that transgender adults (38%) were less likely than men (66%) to have achieved viral suppression (viral load < 400 copies/mL, $\chi^2(1) = 6.2, p = .013$); rate of viral suppression for women (57%) was not significantly different from men or transgender adults.

Adherence Measures

During the 3-day monitoring period, 12% of the sample reported missing medication in their adherence logs with no gender differences detected. As shown in Table 2, reports of missed medications were strongly associated with scores on the ACTG adherence scale. On the ACTG scale, 75% of the sample endorsed at least one reason for missing medication in the previous month. The reasons for non-adherence are listed in Table 1, along with the proportion of men, women, and transgender adults endorsing each reason. "Forgetting" was the most common reason for missing medications, with more than half endorsing this reason regardless of gender. Approximately one in four participants reported missing medications to avoid side effects. Having too many pills to take was the least common reason for non-adherence by males and females.

Total scores on the ACTG adherence scale were similar for men and women, but were significantly higher for transgender adults, indicating poorer adherence in this subgroup (see Table 1). Due to their higher total scores, transgender adults were 3 times more likely than males and females to score at or above the cut-off score of 21 ($OR = 3.27, 95\% CI: 1.25, 8.57$). Although the sample of transgender adults was small, they were significantly more likely than both males and females to report non-adherence due to feeling ill and having too many pills to take, resulting in higher scores on the Pill-Taking subscale.

Demographic and Clinical Characteristics Related to Adherence

Comparisons of the high, moderate, and low adherence groups on demographic and clinical variables are summarized in Table 2. There were no differences between the adherence groups with respect to age, gender, employment, income, time since HIV diagnosis, presumed route of infection, AIDS diagnosis, hepatitis C infection, CD4+ T cell count,

number of medications, or ART. There were racial/ethnic and education differences, with Hispanic adults ($\chi^2(1) = 8.9, p = .003$) and those who did not complete high school ($\chi^2(1) = 10.3, p = .001$) being over represented among the low adherers. Compared to more adherent groups, the low adherence group was less likely to have an undetectable viral load ($\chi^2(1) = 5.8, p = .016$) and more likely to have a viral load of 10,000 or higher ($\chi^2(1) = 11.1, p = .001$). Furthermore, low adherers were least likely to have achieved viral suppression ($\chi^2(1) = 8.4, p = .004$). The adherence groups also differed with respect to the number of days they reported missing medications, with those reporting more frequent reasons for non-adherence also more likely to report missing medication on at least 1 of the 3 monitoring days.

Adherence and Overall Symptom Burden

The level of adherence during the previous month was significantly related to global symptom prevalence, as measured by the total number of symptoms reported in the previous week. As shown in Table 3, the number of reported symptoms increased as adherence levels decreased. Similarly, the level of adherence was significantly related to the mean symptom score on the MSAS, an average of symptom prevalence, frequency, severity, and distress ratings. In addition, the three adherence groups differed with respect to each of the three MSAS subscales. The low adherence group reported significantly more physical symptoms, while the high adherence group scored substantially lower on the Global Distress Index and reported fewer psychological symptoms compared to the other adherence groups. Both the Forgetfulness and Pill-Taking problem subscales were associated with overall symptom burden and with each of the symptom subscales (PSYCH, PHYS, and GDI); Spearman correlations (ρ) ranged between .26 and .33.

Adherence and Specific Symptoms

The relationship between medication adherence in the previous month and each of the 32 specific symptoms in the previous week was also evaluated. The mean score and prevalence of each symptom by adherence group is listed in Table 4. Adherence group was associated with 20 of the 32 symptoms. In most cases, symptom scores and prevalence increased as level of adherence decreased. For 11 symptoms, the low adherence group had significantly worse symptom experience than the moderate and high adherence groups, which did not differ. For eight other symptoms, only the high and low adherence groups differed, with neither group differing from the moderate group. Both the moderate and low adherence group had significantly more difficulty concentrating than the high adherence group.

Despite significant differences between adherence groups, most effect sizes were small. Of the five symptoms with medium effect sizes, difficulty sleeping and difficulty concentrating were the most commonly reported; in the low and moderate adherence groups, prevalence of these symptoms exceeded 50%. The other three symptoms with medium effect sizes (vomiting, change in food tastes, and hair loss) were uncommon in the high and moderate adherence groups (3–6% prevalence) and were reported at rates below 20% even among low adherers.

No clear pattern emerged with respect to the type of symptom most associated with level of adherence. There were differences in most, but not all, of the psychological symptoms across the three adherence groups. Feelings of sadness, irritability, and worry differed across adherence groups, but feelings of nervousness did not. Similarly, most of the gastrointestinal symptoms differed by adherence group, but some did not. Feelings of pain and numbness/tingling in hands or feet were worse and more prevalent in the less adherent groups, but again, the effect sizes were small.

Discussion

The relationship between symptom burden and medication adherence documented in this study confirms previous findings (Cooper et al., 2009; Holzemer et al., 1999; Ickovics et al., 2002; Sherr et al., 2008). In general, patients with lower levels of adherence reported more and worse symptoms compared to those with higher adherence. High adherers reported fewer psychological symptoms, and low adherers reported more physical symptoms.

Hispanic adults in this study were more likely than non-Hispanic adults to report low adherence. Previous studies have yielded inconsistent findings related to racial/ethnic differences in adherence, and the varied results have been attributed to the diversity of customs, health beliefs, and attitudes about treatment across different study groups (Ammassari et al., 2002). Furthermore, those who did not complete high school were more likely than those with more education to report low adherence. This finding contradicts past studies that have generally found education level to be unrelated to adherence (Ammassari et al., 2002). Clinicians and researchers should consider how cultural and educational factors might be influencing adherence.

While the sample of transgender adults in this study was small, the low rate of adherence in this subgroup is concerning. Nearly a quarter of the transgender adults reported missing medication during the 3-day assessment. Their reasons for non-adherence also differed compared to men and women, with significantly more transgender adults reporting missed medication because they felt sick or had too many pills to take. Additional research is needed to explore the unique adherence issues faced by this at-risk population.

Of the 32 individual psychological and physical symptoms studied, most were significantly related to level of adherence, although effect sizes were small. Consistent with other studies (Campos, Guimarães, & Remien, 2010; Kumar & Encinosa, 2009; Protopopescu et al., 2009), symptoms of depression and anxiety were associated with non-adherence in the current sample. Trouble sleeping was one of the symptoms most strongly associated with non-adherence. Sleep disturbance was reported by nearly 75% of low adherers, whereas only 45% of high adherers reported this common symptom. Given that sleep disturbance and depression often co-occur and that Phillips and colleagues (2005) also found that sleep disturbance and depression were associated with poor adherence, future research should further explore the relationship of these symptoms to non-adherence.

Sleep disturbance and fatigue were documented in our previous study as prevalent symptoms among adults with HIV (Lee et al., 2009) and sleep problems often result in daytime sleepiness, fatigue, and difficulty concentrating. Since “forgetting” was the most common reason given for non-adherence and more than one third of the current sample reported “sleeping through dose time,” further examination of the relationship between sleep and adherence is warranted. Effective management of these common symptoms could result in better adherence as well as improved clinical outcomes and quality of life.

The results of this cross-sectional examination of baseline measures did not indicate whether a causal relationship existed between symptom experience and adherence, and if so, whether symptom experience was primarily the cause or result of non-adherence. In all likelihood, the nature of the relationship depends on the symptom. Symptoms such as difficulty concentrating or swallowing likely interfere with adherence, while pain and cardiopulmonary symptoms may be the result of poor adherence. As specified in the UCSF Symptom Management Model, most symptoms are likely both the cause and result of poor adherence, reflecting a dynamic interaction between symptom experience, management, and outcome. For example, feeling depressed or fatigued may make it difficult to take medications, but missing medication may also exacerbate these symptoms. Future

longitudinal work is needed to help determine the direction of effects between treatment adherence and symptoms common among adults with HIV.

At least a portion of the association between poor adherence and symptom experience may not be causal at all, but rather due to other factors such as lifestyle. Substance abuse, mental illness, homelessness, and social isolation have been identified as predictors of poor adherence (Leaver, Bargh, Dunn, & Hwang, 2007; Mellins et al., 2009) and likely lead to diminished quality of life. While those testing positive for illicit drugs and those reporting a severe mental health diagnosis were excluded from this sample, many of the participants were nonetheless struggling with drug addiction and mental health issues. The independent negative effects these factors have on both adherence and symptom experience may partially account for their association. If such is the case, it will be essential to address these underlying issues in order to improve medication adherence.

Avoiding side effects was one of the less common reasons given for non-adherence; nonetheless, it was reported by 24% of the sample. Symptoms such as nausea, vomiting, dry mouth, constipation, and a change in the way food tastes may be medication side effects, and adherence could potentially exacerbate these symptoms. While it was beyond the scope of this study to examine whether participants perceived their symptoms as disease-related or treatment-related, such attributions are clearly relevant to adherence behaviors (Johnson, Stallworth, & Neilands, 2003) and would strengthen future research in this area.

Like all self-report adherence measures, those used in this study (the modified ACTG scale and the daily log of missed medications) likely overestimated the level of adherence. In fact, the proportion (14%) falling in the non-adherent category (scores 21–36) was substantially smaller than the 75% reported in Holzemer's study (2006). While this difference may be due, at least in part, to the exclusion of those testing positive for illicit drugs or reporting a severe mental health diagnosis from the current sample, actual adherence levels are likely lower than reported in this study. Despite this limitation, the overestimated adherence level during the prior month was able to distinguish levels of disease burden, as well as symptom prevalence and experience in the previous week. Furthermore, the number and frequency of reasons reported for non-adherence during the previous month was strongly associated with prospective reports of missing medication during a 3-day monitoring period, thereby providing convergent validation for the retrospective measure.

Another limitation of this study was the lack of information as to which medications were missed or how much. Patients are likely to be selective about medications they miss, and clinical effects of non-adherence may vary by medication as well as by quantity of medication involved. Future research in this area should include these important adherence parameters. While this study did not find that the adherence groups differed with respect to the number of medications they took, future research should also evaluate pill burden or the number of pills included in the patient's medication regimen. Finally, this study was not specific to adults on ART, and it was interesting to note that those currently taking ART were no more or less adherent than those not taking ART. Adherence to non-ART medications should be considered in future studies, particularly given the probable consequences for effective symptom management.

In light of the importance of medication adherence to achieving optimal clinical outcomes, numerous interventions have been developed to support patients in adhering to their medical regimens (Holzemer et al., 2006; Safren et al., 2009). Most focus on one or more correlates of adherence, such as medication beliefs or social support, but few have been effective (Simoni, Pearson, Pantalone, Marks, & Crepaz, 2006). Given the strength of the relationship between symptom experience and adherence, interventions that effectively manage

symptoms may also help to enhance adherence, clinical outcomes, and quality of life in those living with HIV.

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Table 1
Reasons for Missing Medications and ACTG Adherence Scores ($M \pm SD$) by Gender

	Overall (N = 302)	Male (n = 206)	Female (n = 74)	Transgender (n = 22)
1. Simply forgot	59%	60%	55%	67%
2. Too busy with other things	42%	43%	35%	64%
3. Away from home	38%	39%	36%	41%
4. Problems taking pills at specified times	38%	37%	38%	50%
5. Slept through dose time	37%	35%	41%	41%
6. Felt depressed or overwhelmed	33%	31%	34%	50%
7. Felt sick or ill	28%	27%	23%	59% ^{**}
8. Wanted to avoid side effects	24%	22%	23%	45%
9. Had too many pills to take	16%	12%	16%	50% ^{**}
Non-Adherence Total Score	14.2 $\pm$ 5.2	13.9 $\pm$ 5.0	14.4 $\pm$ 5.6	17.1 $\pm$ 5.7 [*]
Pill-taking problem score	7.4 $\pm$ 3.2	7.1 $\pm$ 2.9	7.6 $\pm$ 3.4	9.7 $\pm$ 4.0 ^{**}
Forgetfulness score	6.8 $\pm$ 2.9	6.7 $\pm$ 2.8	6.8 $\pm$ 3.1	7.4 $\pm$ 3.3
% Non-Adherent (Total score > 20)	14%	12%	14%	32% [*]

Note. M = mean; SD = standard deviation

* significantly higher than male adults ($p < .05$);

** significantly higher than both male and female adults ($p < .01$)

Table 2
Sample Demographic and Clinical Characteristics by Adherence Group ($N = 302$)

	TOTAL ($N = 302$)	High Adherence (scores 9–10) ($n = 100$)	Moderate Adherence (scores 11–16) ($n = 114$)	Low Adherence (scores > 16) ($n = 88$)	Statistic
DEMOGRAPHICS					
Age	45.3 ± 8.3	45.5 ± 8.1	45.4 ± 8.4	45.1 ± 8.4	ns
Gender					ns
Male	68%	34%	40%	26%	
Female	25%	34%	34%	32%	
Transgender	7%	18%	32%	50%	
Race/Ethnicity					$\chi^2(6) = 15.2, p = .019$
African American	39%	36%	32%	32%	
Caucasian	41%	35%	44%	21%	
Hispanic	9%	18%	29%	54% ^a	
Mixed/Other	11%	28%	44%	28%	
Education					$\chi^2(2) = 11.9, p = .003$
< High school	14%	31%	19%	50% ^a	
≥ High school	86%	33%	41%	26%	
Employment Status					ns
Employed	16%	16%	17%	14%	
Unemployed	9%	12%	5%	10%	
Medical Disability	75%	72%	78%	76%	
CLINICAL CHARACTERISTICS					
Presumed route of infection					ns
Sexual contact	62%	63%	68%	55%	
IVDU	11%	13%	7%	14%	
Either Sex or IVDU	21%	18%	19%	25%	
Other/Unknown	6%	6%	6%	7%	
Time since HIV diagnosis					
$M \pm SD$ (years)	12.2 ± 6.9	12.8 ± 6.5	12.0 ± 7.3	11.8 ± 6.8	ns
Range (years)	0.2–27	0.3–25	0.2–25	0.6–27	

	TOTAL (N = 302)	High Adherence (scores 9–10) (n = 100)	Moderate Adherence (scores 11–16) (n = 114)	Low Adherence (scores > 16) (n = 88)	Statistic
AIDS diagnosis	54%	50%	56%	59%	ns
Hepatitis C infection (n = 287/302)	34%	30%	34%	37%	
CD4+ T cell count (n = 288/302)					
Category:					ns
% < 200 cells/mm ³	18%	17%	13%	26%	
% = 200–499 cells/mm ³	44%	40%	49%	41%	
% ≥ 500 cells/mm ³	38%	43%	38%	34%	
M ± SD (cells/mm ³)	445 ± 264	473 ± 283	458 ± 253	395 ± 253	ns
Viral load (n = 281/302)					
Category					
% = Undetectable	52%	56%	57%	41% ^b	$\chi^2(4) = 11.9, p = .018$
% = 50–9,999 copies/mL	30%	31%	29%	29%	
% ≥ 10,000 copies/mL	18%	17%	14%	30% ^b	
Viral suppression (< 400 copies/mL)	62%	67%	67%	48% ^b	
Median detectable value (n = 135)	4197	1287	2533	10158	$\chi^2(2) = 8.4, p = .015$ $F(2,132) = 3.7, p = .027$
Medication regimen					
Total # of medications M ± SD	6.8 ± 4.2	6.6 ± 3.9	7.1 ± 4.4	6.4 ± 4.0	ns
Type of HIV therapy					ns
None	26%	25%	22%	33%	
NRTI-based	6%	6%	4%	7%	
NNRTI-based	21%	25%	25%	11%	
PI-based	43%	39%	45%	46%	
Other	4%	5%	4%	3%	
Adherence log (3 days)					
% missing medication on ≥ 1 day	12%	2%	11%	24%	$\chi^2(2) = 21.8, p < .001^c$

Note. Demographic percentages are tallied by row, clinical characteristics are tallied by column. NRTI = nucleoside reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; M = mean; SD = standard deviation; IVDU = intravenous drug use

^aHispanic adults and those who did not complete high school were more likely to report low adherence.

^bThose in the low adherence group were more likely to have a viral load $\geq 10,000$ copies/mL and less likely to have an undetectable viral load or viral suppression.

^cAll three adherence groups differed significantly based on Bonferroni-adjusted post-hoc tests.

Table 3

Global Symptom Scores by Adherence Group ($N = 302$)

Symptom Measures	High Adherence (scores 9–10) ($n = 100$) ($M \pm SD$)	Moderate Adherence (scores 11–16) ($n = 114$) ($M \pm SD$)	Low Adherence (scores > 16) ($n = 88$) ($M \pm SD$)	Statistic
Number of symptoms reported	7.2 $\pm$ 4.9	9.3 $\pm$ 5.3	11.8 $\pm$ 6.8	$F(2,299) = 14.7, p < .001^a$
Total symptom score	0.50 $\pm$ 0.40	0.62 $\pm$ 0.40	0.90 $\pm$ 0.59	$F(2,299) = 17.8, p < .001^a$
Symptom subscales				
Global distress index	0.79 $\pm$ 0.66	1.02 $\pm$ 0.70	1.26 $\pm$ 0.79	$F(2,299) = 10.0, p < .001^b$
Physical symptoms	0.51 $\pm$ 0.44	0.62 $\pm$ 0.44	0.89 $\pm$ 0.62	$F(2,299) = 12.8, p < .001^c$
Psychological symptoms	0.81 $\pm$ 0.80	1.08 $\pm$ 0.83	1.39 $\pm$ 0.95	$F(2,299) = 10.6, p < .001^b$

Note. M = mean; SD = standard deviation

^a All three adherence groups were significantly different

^b High adherence group differed from the Moderate and Low adherence groups

^c Low adherence group differed from the High and Moderate groups

Table 4
Individual Symptom Scores and Prevalence Rates by Adherence Group in Order of Effect Size ($N = 302$)

Individual Symptom	High Adherence (scores 9–10)			Moderate Adherence (scores 11–16)		Low Adherence (scores > 16)		Statistic	Effect size (η^2 , eta squared)
	($n = 100$)	($M \pm SD$)	($n = 114$)	($M \pm SD$)	($n = 88$)	($M \pm SD$)	($n = 88$)		
Vomiting	0.05 ± 0.32 (4%)		0.07 ± 0.32 (6%)		0.40 ± 0.86 (19%)		$F(2,297) = 11.3, p < .001^a$		.076
Difficulty sleeping	1.12 ± 1.35 (45%)		1.17 ± 1.19 (54%)		1.94 ± 1.39 (73%)		$F(2,299) = 11.5, p < .001^a$		.072
Change in food tastes	0.05 ± 0.31 (3%)		0.09 ± 0.41 (5%)		0.42 ± 0.97 (17%)		$F(2,299) = 10.0, p < .001^a$		.063
Hair loss	0.12 ± 0.56 (5%)		0.06 ± 0.37 (4%)		0.50 ± 1.17 (17%)		$F(2,299) = 9.7, p < .001^a$		.061
Difficulty concentrating	0.72 ± 1.02 (39%)		1.13 ± 1.16 (54%)		1.41 ± 1.23 (62%)		$F(2,298) = 8.9, p < .001^b$		.056
Weight loss	0.04 ± 0.22 (3%)		0.15 ± 0.61 (7%)		0.41 ± 1.00 (17%)		$F(2,298) = 7.5, p = .001^a$		.048
Lack of appetite	0.48 ± 1.03 (21%)		0.67 ± 1.12 (30%)		1.10 ± 1.33 (47%)		$F(2,298) = 6.9, p = .001^a$		.044
Feeling sad	0.66 ± 1.06 (36%)		1.03 ± 1.15 (50%)		1.24 ± 1.29 (53%)		$F(2,297) = 5.9, p = .003^c$		.039
Difficulty swallowing	0.06 ± 0.47 (2%)		0.13 ± 0.47 (9%)		0.39 ± 1.04 (15%)		$F(2,294) = 5.8, p = .003^a$		.038
Swelling of arms or legs	0.07 ± 0.38 (4%)		0.09 ± 0.55 (4%)		0.35 ± 0.93 (15%)		$F(2,299) = 5.7, p = .004^a$		.037
Shortness of breath	0.37 ± 0.88 (17%)		0.37 ± 0.81 (20%)		0.78 ± 1.20 (34%)		$F(2,296) = 5.6, p = .004^a$		.037
Feeling irritable	0.81 ± 1.17 (39%)		1.03 ± 1.10 (53%)		1.38 ± 1.32 (59%)		$F(2,295) = 5.4, p = .005^c$		.036
Constipation	0.20 ± 0.67 (10%)		0.33 ± 0.82 (17%)		0.61 ± 1.11 (27%)		$F(2,299) = 5.4, p = .005^c$		.035
Don't look like oneself	0.25 ± 0.83 (10%)		0.26 ± 0.82 (11%)		0.66 ± 1.27 (24%)		$F(2,298) = 5.2, p = .006^a$		.034
Dizziness	0.11 ± 0.49 (6%)		0.34 ± 0.71 (21%)		0.46 ± 1.03 (20%)		$F(2,295) = 5.2, p = .006^c$		.034
Pain	1.09 ± 1.34 (44%)		1.41 ± 1.31 (59%)		1.72 ± 1.44 (64%)		$F(2,296) = 5.0, p = .007^c$		.033
Problems with urination	0.21 ± 0.69 (10%)		0.30 ± 0.84 (13%)		0.61 ± 1.19 (24%)		$F(2,298) = 5.0, p = .008^c$		.032
Lack of energy	1.40 ± 1.28 (62%)		1.37 ± 1.18 (63%)		1.86 ± 1.44 (75%)		$F(2,298) = 4.6, p = .011^a$		.030
Worrying	0.82 ± 1.21 (36%)		1.26 ± 1.25 (56%)		1.35 ± 1.51 (49%)		$F(2,297) = 4.5, p = .011^c$		.030
Numb/tingling hands/feet	0.92 ± 1.40 (34%)		1.06 ± 1.32 (43%)		1.46 ± 1.41 (57%)		$F(2,296) = 3.9, p = .022^c$		.025

Note. M = mean; SD = standard deviation; Symptom scores ($M \pm SD$) were computed as the mean of frequency, severity, and distress ratings; absent symptoms had a score of 0. Symptom prevalence rates (%) in each adherence group are also included (e.g., 73% of those with low adherence reported difficulty sleeping). Statistics and effect sizes are based on comparisons of the symptom scores.

The following 12 symptoms were unrelated to adherence: mouth sores, changes in skin, sweats, nausea, itching, cough, feeling drowsy, dry mouth, diarrhea, feeling nervous, sexual problems, and feeling bloated.

^a Low adherence group differed from the High and Moderate adherence groups
^b High adherence group differed from the Moderate and Low adherence groups
^c High adherence group differed from the Low adherence group