Published in final edited form as:

Ann Behav Med. 2012 April ; 43(2): 189–197. doi:10.1007/s12160-011-9322-9.

Benefits of psychotropic medications on depressive symptoms and HIV medication adherence among HIV-positive men and women

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Abstract

Context—Psychiatric symptoms including depression are common among people living with HIV/AIDS (PLWHA), and antidepressant medications have been shown to reduce depressive symptoms and also enhance antiretroviral (ARV) adherence in this population.

Objective—Because these benefits have not been studied among PLWHA using other psychotropic (PSY) medications in addition to antidepressants, we examined the impact of adherence to a diverse range of PSY medications (including antidepressants, mood stabilizers, and anti-psychotic medications) on depressive symptoms and ARV adherence in PLWA.

Design—Participants for this cohort study were recruited through physician outpatient clinics. Depressive symptoms were assessed monthly using a 10-item version of the Center for Epidemiological Studies – Depression (CES-D) scale; PSY and ARV medication adherence were assessed using monthly unannounced telephone pill count assessments across a three-month period.

Setting—A general community-based, healthcare setting was utilized for the study.

Participants—Of the 353 PLWHA we identified on stable ARV medications, we were able to maintain contact with 324 (92%) across a 3-month period (227 men; 97 women). Mean age of this convenience sample was 45 years and 90% were African-American.

Intervention—None.

Main Outcome Measure—Mean ARV adherence across a 3-month study period.

Results—The results showed that greater depressive symptoms were associated with lower ARV adherence among our sample of PLWHA. Greater adherence to PSY medications regardless of medication class was positively related to higher ARV adherence. We also found that greater adherence to PSY medications significantly reduced the negative association between depressive symptoms and ARV medication adherence among PLWHA.

Conclusions—The results of this study point to the need for screening and treatment of depressive symptoms and also further study of the impact of multiple PSY medications regimens on health outcomes among PLWHA.

INTRODUCTION

Antiretroviral (ARV) therapy is an effective strategy to reduce viral burden and improve morbidity and mortality among people living with HIV/AIDS (PLWHA) (1–6). These medications have revolutionized the treatment of HIV disease such that it is now viewed as a chronic condition. ARV medication adherence is vital for optimal outcomes. Resistance and other clinical complications may result if patients are not close to 95% adherence with their ARV medications (7). Understanding the factors that influence ARV adherence is a key aspect in managing HIV disease.

Multiple factors influence medication adherence rates among PLWHA. Depression is one of the strongest independent psychosocial predictors of ARV adherence (8–11). Sub-clinical depressive symptoms can also reduce motivation and influence adherence behavior. A recent cohort study followed 225 PLWHA on ARV medications and found that those patients developing depressive symptoms had higher rates of suboptimal adherence at follow-up (45.1% vs. 25.9%) versus those not developing significant depressive symptoms (12). Among the patients with optimal baseline adherence, those with incident depression were nearly 2 times more likely to develop suboptimal adherence at follow-up. Thus, assessing and monitoring changes in depressive symptoms may help identify those at risk for poor ARV adherence.

Psychiatric disorders are quite prevalent among PLWHA. A nationally representative probability survey of 2,864 adults receiving care for HIV found that nearly half of the sample screened positive for a psychiatric disorder (13). Depression is one of the most prevalent psychiatric conditions observed among PLWA and subclinical depressive symptoms are also quite common (14–18). Thus, the need for mental health services, including medication management of depressive symptoms, is great among PLWHA.

Psychotropic drugs, including antidepressant medications, are often prescribed and help many PLWHA deal with the emotional aspects of managing their chronic medical illness. In a follow-up study to the survey noted earlier, it was estimated that 61.4% utilized mental health services and 29.6% took psychotropic medications (19). A meta-analysis showed that antidepressant medications are efficacious in treating depression among clinically depressed PLWHA (20). Depressed PLWHA on antidepressant medications are also more likely to

receive optimal care and treatment services (21). Drug therapy that reduces depressive symptoms may also have an impact of HIV medication adherence.

Several studies have reported greater medication adherence among depressed HIV/AIDS patients on antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) (22–25). Less is known about how adherence to these psychotropic (PSY) medications influences ARV adherence and physical health status. A recent study of 3,359 PLWHA on HAART found that 42% had a depression diagnosis and 15% used SSRIs during HAART, and depression without SSRI use was associated with significantly decreased odds of achieving optimal adherence (>90%) to HAART (26). Depressed patients compliant with SSRI medications (>80%) had HAART adherence and viral control statistically similar to non-depressed HIV-infected patients taking HAART.

Each of the aforementioned studies only examined clinically depressed patients using antidepressant medications, particularly SSRIs (22–26). No study, to date, has evaluated a wider range of patients (including those with sub-threshold depressive symptoms) using other classes of PSY medications in addition to antidepressants. Several studies have found that more ARV medications can lead to “pill burden” effects and lower adherence rates (27–29), but this has not been fully studied with PSY medication in the context of HIV disease. Only one of the studies noted above examined adherence to the PSY medications, and it was solely based on pharmacy prescription pick-up records (25). No study, to date, has sought to utilize more advanced measures of medication adherence to better evaluate not only whether or not patients were prescribed PSY medications but if they were adherent to them.

The purpose of the current study was to examine the impact of using a diverse range of PSY medications (including antidepressants, mood stabilizers, and anti-psychotic medications) on depressive symptoms and ARV adherence among PLWHA across a three-month period. We utilized a community HIV-positive sample of men and women with varying levels of depressive symptoms, as many of the aforementioned PSY medications are not only prescribed for people who suffer from clinical levels of depression but also for those with sub-clinical depressive symptoms, especially within the context of HIV/AIDS. We also utilized unscheduled telephone pill counts, a valid and reliable adherence assessment in order to objectively quantify both ARV and PSY medication adherence.

We hypothesized that greater depressive symptoms will be associated with lower ARV adherence among PLWHA regardless of whether or not they are also prescribed PSY medications. We further hypothesized that ARV adherence rates will be significantly greater among those PLWHA who are prescribed PSY medications in addition to their ARV regimen than among those PLWHA who are prescribed only ARV medications. We also hypothesized that adherence to PSY medications regardless of medication class will be positively related to ARV adherence among PLWHA. Finally, we hypothesized that adherence to PSY medications would significantly reduce the negative impact of depressive symptoms on ARV medication adherence among our sample of PLWHA.

METHODS

Participants

Participants were HIV-positive men and women recruited from the Atlanta, GA metropolitan area. Our research team recruited participants by notifying AIDS service providers and infectious disease clinics about the study, and they subsequently placed recruitment brochures in provider's lobbies and waiting areas. Interested persons were instructed to contact our research site by phone to schedule an intake appointment. The study commenced March 2005 and enrollment ended in October 2008.

The study entry criteria were: (a) age 18 or older, (b) name-matching proof of positive HIV status and photo ID, and (c) currently prescribed ARV medication regimen. Participants were not screened for our main dependant variable (ARV adherence) to yield a full range of adherence behaviors and assure ecological validity of the study.

Procedure

The current study was part of a clinical trial examining the use of an integrated behavior intervention on sexual risk reduction and ARV adherence among PLWHA. The trial included a multiple baseline assessment that occurred prior to active intervention protocol; data collected as part of this pre-intervention portion of the trial was utilized for the current study. All participants were initially screened in person at our research offices. Demographic, health and behavioral assessments were administered using audio-computer-assisted structured interviews (ACASI) (30). Participants were asked their age, ethnicity, education level, income, HIV symptoms, employment and disability status, as well as a number of other psychosocial and behavioral characteristics.

Medication adherence and other relevant medical, psychosocial and behavioral factors were then monitored using unannounced pill counts over the following three months. Eligible participants were provided with a free cell phone that restricted service for project contacts and emergency use (e.g., 911) and were then contacted monthly by phone for 3 months post-screen and prior to the start of the intervention. Following an office-based training in the pill counting procedure, participants were called at undisclosed times by a trained phone assessor. During these telephone assessments, we assessed ARV medication adherence and also PSY medication adherence and depressive symptoms.

Measures

The primary outcome measure was adherence to ARV medications. HIV treatment adherence was monitored using monthly unannounced telephone-based pill counts as noted above. Unannounced pill counts are reliable and valid in assessing HIV treatment adherence when conducted in participants' homes or on the telephone (31–32). Pill counts occurred over 21 to 35 day intervals and were conducted for each of the ARV medications participants were taking. Pharmacy information from pill bottles was also collected to verify the number of pills dispensed between calls. Adherence was calculated as the ratio of pills counted relative to pills prescribed taking into account the number of pills dispensed. Two consecutive pill counts were necessary for computing adherence. Adherence data represents

the percentage of pills taken as prescribed following the initial office-based assessment averaged across antiretroviral medications.

We also utilized a similar method to quantify adherence to PSY medications. Our phone assessors recorded the names of each of the PSY medications that the participants were prescribed in addition to their ARV medications. As part of the monthly phone assessment participants also reported their most recent CD4 cell counts and HIV viral load (detectable versus non-detectable) if known.

We also assessed depressive symptoms using the brief 10-item version of Center for Epidemiological Studies – Depression (CES-D) scale (CESD-10) (33). The abbreviated form did not include cognitive and somatic items that overlap with physical symptoms of HIV disease to avoid confounding depression with disease progression. The CESD-10 has shown good predictive accuracy and test-retest reliability when compared to the full-length 20-item version of the CES-D (34).

Statistical analyses

We utilized multiple regression analyses to test the associations hypothesized in the study. Analyses of variance (ANOVA) were used to examine mean differences in depression scores and adherence between groups. Our main outcome measure in the study was ARV medication adherence assessed at three monthly telephone assessments; we utilized mean ARV adherence across the three months as our primary dependent measure. Our main predictor variables were PSY medication adherence and depressive symptoms also assessed at the three monthly telephone assessments; we also utilized mean PSY adherence and mean CESD-10 scores across the three months as our primary independent measures. In a final regression path analysis, we examined the unique contribution of both depressive symptoms and PSY medication adherence in association with ARV medication adherence. All variable distributions were examined for outliers to assure normality. Effect sizes for multiple regression analyses are the reported beta weights. Demographic and medical covariates were included in the regression analyses if they were related to the primary dependent measure (ARV medication adherence) at $p < .05$. Beta weights from the regression analyses are reported unadjusted and adjusted for covariates.

RESULTS

Participants

We screened 490 HIV-positive individuals, of which 353 were currently on a stable ARV medication regimen. The 137 people not currently on a stable ARV medication regimen were excluded from the current analyses. The 353 on ARV medications and the 137 not on ARV medications did not differ significantly on any major demographic variables (p 's $> .10$). Of the 353 individuals on ARV medications, we were able to maintain contact with 324 (92%) across a 3-month period through phone call interviews. Those that dropped out of the study ($n=29$) and those that remained in the study ($n=324$) did not differ significantly on any major demographic or HIV disease variable (p 's $> .10$).

Participant characteristics

Demographic and medical characteristics of the 324 HIV-positive individuals examined in this study are presented in Table 1. The average age was 44.64 ($SD = 6.72$) years. Approximately 70% of the sample were men ($n=227$) and 30% were women ($n=97$). The vast majority of the sample (90%) was African-American. Roughly 76% reported completing twelve or more years of school. Most of the participants (67%) reported an income level in the range of \$0–\$10,000 per year. The majority of participants (90%) reported their employment status as either unemployed (31%) or on disability (58%).

Of the 324 participants, 308 knew their most recent CD4 cell counts and reported an average of 439.30 ($SD = 305.65$) cells/mm³ across the three-month study period. Of the 324 participants, 312 knew the results of their most recent viral load test and 122 (39%) reported at least one detectable viral load and 190 (61%) reported no detectable viral load across the study period.

Medication adherence

Mean ARV medication adherence of the 324 participants across the 3-month study period was 84.09% ($SD = 19.26\%$). Of the demographic and HIV disease variables, age, CD4 cell counts, and viral load status were related to mean ARV adherence (p 's $< .10$) and were controlled for in subsequent regression analyses. Mean CESD-10 score for the 324 participants across the 3-months was 6.46 ($SD = 5.64$). Of the 324 participants, 106 individuals (33%) were also prescribed at least one PSY medication during the 3-month study period. Psychotropic drugs varied across the sample, with 61% on antidepressants exclusively ($n=65$), 18% on antidepressants along with a mood stabilizer and/or antipsychotic medication ($n=19$), and 21% on mood stabilizers and/or antipsychotics without antidepressant medications ($n=22$). We were able to capture pill count adherence on 102 of the 106 people prescribed PSY medications. Mean PSY medication adherence was 79.86% ($SD = 20.88\%$) across the 3-month study period.

Association between depressive symptoms and medication adherence

Higher mean depression score was significantly associated with lower ARV medication adherence across the 3-month study period ($\beta = -.21$, $p < .001$). These results held even after controlling for age, mean CD4 cell counts, and viral load status across the study period ($\beta = -.22$, $p < .001$). Depression scores were significantly greater among those individuals prescribed at least one PSY medication versus those on ARV medications alone ($t(318) = 3.32$, $p = .001$). Depression scores did not differ across the three main classes of PSY medications (antidepressants alone, antidepressants with mood stabilizers and/or antipsychotic medications, and mood stabilizers and/or antipsychotic medications without antidepressants) examined in this study ($F(2,101) = .12$, $p = .890$). Depressive symptoms were marginally associated with PSY medication adherence ($\beta = -.19$, $p < .060$).

Association between PSY medication and ARV medication adherence

For individuals on at least one psychotropic medication, greater mean PSY medication adherence was significantly associated with greater ARV medication adherence ($\beta = .26$, $p = .009$). These results held even after controlling for age, mean CD4 cell counts, and viral

load across the study period ($\beta = .23$, $p = .019$). ARV adherence was significantly greater (87.40% vs. 82.43%) among those individuals prescribed at least one psychotropic medication versus those on ARV medications alone ($t(318) = 2.15$, $p = .032$). ARV medication adherence did not significantly differ across the three main classes of PSY medications (antidepressants alone, antidepressants with mood stabilizers and/or antipsychotic medications, and mood stabilizers and/or antipsychotic medications without antidepressants) examined in this study ($F(2,101) = .71$, $p = .495$). PSY medication adherence also did not significantly differ across the three main classes of PSY medications (antidepressants alone, antidepressants with mood stabilizers and/or antipsychotic medications, and mood stabilizers and/or antipsychotic medications without antidepressants) examined in this study ($F(2,101) = 1.26$, $p = .289$).

Final path analysis

In a final regression path analysis (see Table 2), we examined the effect of both depressive symptoms and PSY medication adherence simultaneously on ARV medication adherence. Greater mean PSY medication adherence was significantly associated with greater mean ARV medication adherence even after adjusting for level of depressive symptoms ($\beta = .26$, $p = .011$). These results held even after controlling for age, mean CD4 cell counts, and viral load across the study period ($\beta = .23$, $p = .022$). When adjusting for PSY medication adherence, depression was no longer significantly related to ARV medication adherence when either controlling or not controlling for age, mean CD4 cell counts, and viral load across the study period (p 's $> .10$).

DISCUSSION

Utilizing a community sample of PLWHA, we examined the impact of using a diverse range of PSY medications on ARV medication adherence and well as the potential role these PSY medications played in the relationship between depressive symptoms and ARV adherence. In addition, we were able to capture depressive symptoms, adherence to PSY medications, and adherence to ARV medications across a three-month period using a standardized and objective telephone-based pill count assessment.

We found that mean ARV medication adherence of the 324 participants across the 3-month study period was 84%, placing participants at risk for developing resistant variants of HIV (7). The mean ARV adherence rate in our sample was higher than rates reported in other studies examining the impact of depressive symptoms on ART adherence (23, 25–26), but this is likely due to these studies relying on either self-report or pharmacy records to quantify HIV adherence. Roughly one-third of our sample was also prescribed at least one psychotropic medication during the 3-months, with the majority prescribed antidepressant medication alone. This percentage of antidepressant use in our study is lower than in other studies examining the impact of depressive symptoms on ART adherence (24–26), but this is likely due to sampling differences and the fact that depression was more severe in these other studies. In our sample, there were also a sizeable number on mood stabilizers and/or antipsychotics without antidepressant medications which was not reported in the studies noted above (22–26). We found that overall mean PSY medication adherence was

approximately 80% across the 3-month study period. This is comparable to other studies (25–26) examining PSY medication adherence in the context of HIV disease; however, these other studies only tracked antidepressants and relied on self-report or pharmacy records.

As predicted, higher mean depression scores were significantly associated with lower ARV medication adherence across the 3-month study period, even after controlling for age, mean CD4 cell counts, and viral load. Our data supports prior research noting the association between depression and ARV adherence (22–26), but our sample includes individuals with a broad range of depressive symptoms and not just those who meet diagnostic criteria for major depression. As expected, mean depression scores were significantly greater among those individuals prescribed at least one psychotropic medication versus those on ARV medication alone. However, mean depression scores were only marginally associated with PSY medication adherence. This might be due to the PSY medication being prescribed for conditions other than depressive symptoms.

Our results also showed that greater mean PSY medication adherence was significantly associated with greater mean ARV medication adherence, even after controlling for age, mean CD4 cell counts, and viral load across the study period. This supports prior research of clinically depressed PLWHA (25–26). However, our study is the first, to date, to document the adherence of non-antidepressant PSY medications and its effect on ARV adherence in this population. In fact, ARV adherence was significantly greater among those individuals prescribed at least one psychotropic medication regardless of class versus those on ARV medication alone. It is important to point out that ARV adherence did not significantly differ depending on whether participants were prescribed antidepressants alone, antidepressants with mood stabilizers and/or antipsychotics, and mood stabilizers and/or antipsychotics without antidepressants. Both PSY and ARV adherence were assessed using unannounced telephone pill counts, a valid, objective and reliable measure of medication adherence as opposed to either self-report or pharmacy records. These data provide initial evidence for the salutary effects of PSY adherence on ARV adherence when using multiple PSY medications and does not support a pill burden effect with these additional PSY medications as seen with ARV medications (27–29).

We also examined the simultaneous effects of both depressive symptoms and PSY medication adherence on ARV medication adherence. We found that when adjusting for PSY medication adherence, depression was no longer significantly related to ARV medication adherence. However, when adjusting for level of depressive symptoms, PSY medication adherence remained significantly associated with greater mean ARV medication adherence. These results held even after controlling for age, mean CD4 cell counts, and viral load across the study period. Ours is the first study, to date, to document this interaction between PSY medication adherence, depressive symptoms and ARV medication adherence, and point to the benefits of utilizing PSY medications in addition to ARV medications in this population.

There are some limitations to this study that would inform future research. We did not conduct a psychiatric interview of our participants because this study by design utilized a community sample assessed primarily via telephone. Thus, we do not know which of our

participants meets diagnostic criteria for major depression or any other disorders. However, we were still able to discern associations between depression, PSY adherence, and ARV adherence in a sample that likely represents a broad range of depressive symptoms and perhaps is more generalizable. Future research might incorporate psychiatric screening tools to denote clinical levels of depression and other co-morbid conditions. Also, we do not know if our subjects were on any medications other than ARV and PSY medications. It is possible that some participants were on additional prescribed or over-the-counter medications that impacted the associations under investigation. Future research should also query participants on all medications used including those prescribed “prn” as well as complementary/alternate medications.

In summary, we found that depressive symptoms, even perhaps sub-clinical depressive symptoms, negatively impact ARV adherence among PLWHA. However, we also found that if PLWHA are prescribed PSY medications (and not just solely antidepressants), they are more likely to adhere to their ARV regimens. In fact, we found that PSY medication adherence seems to modify the association between depressive symptoms and ART adherence which may have an impact on morbidity and mortality in this population. Given that depression has such a strong impact on ARV adherence (8–12) and also has been shown to have deleterious effects on immune system parameters relevant to HIV disease progression (16, 35–38), it seems like a prominent target for intervention. Based on the results of this study and others (22–26), there are clearly significant benefits of assessing psychiatric symptoms (including depressive symptoms) and prescribing PSY medications, and randomized controlled clinical trials examining long-term health outcomes are warranted.

Acknowledgments

This work was supported by National Institute of Mental Health grant R01MH071164

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Table 1

Demographic and medical characteristics of the participants (N=324)

Participant Characteristic	Group	Value
Age: Mean (SD)		44.6 (6.7)
Gender: n (%)	Female	97 (29.9%)
	Male	227 (70.1%)
Ethnicity: n (%)	White	24 (7.4%)
	African American or Black	292 (90.1%)
	Hispanic or Latino	4 (1.2%)
	Asian or Pacific Islander	1 (0.3%)
	Other	3 (0.9%)
Education Level: n (%)	Grade 7–11	78 (24.1%)
	Grade 12	120 (37.0%)
	Grade 13+	126 (38.9%)
Income: n (%)	\$0–\$10,000	217 (67.0%)
	\$11,000–\$20,000	72 (22.2%)
	\$21,000–\$30,000	26 (8.0%)
	\$30,000+	7 (2.2%)
	Refused to answer	2 (0.6%)
Employment Status: n (%)	Unemployed	100 (30.9%)
	Working	27 (8.3%)
	On Disability	188 (58.0%)
	Student	3 (0.9%)
	Other	5 (1.5%)
	Refused to answer	1 (0.3%)
CD4 cell counts: Mean (SD)	308 of 324 (95.1%) responded	439.3 (305.7%)
Viral Load Status (n=312)	Detectable	122 (39.1%)
	Undetectable	190 (61.0%)
Medication Status	ART plus no PSY	218 (67.3)
	ART plus ADM	65 (20.1)
	ART plus ADM plus other PSY	19 (5.9)
	ART plus other PSY (no ADM)	22 (6.8)

Table 2

Unadjusted and adjusted regression models associating the independent variables (PSY adherence, CESD-10 scores) and the dependent variable, ARV adherence (N=324)

	Unadjusted			Adjusted*		
Individual Models	Beta	t	P-value	Beta	t	P-value
CESD-10 scores	-.21	-3.94	<.001	-.22	-3.99	<.001
ARV adherence						
PSY adherence	.26	2.65	.009	.23	2.39	.019
ARV adherence						
Final Models	Beta	t	P-value	Beta	t	P-value
CESD-10 scores	-.00	.01	.993	-.00	-.02	.983
ARV adherence						
PSY adherence	.26	2.59	.011	.23	2.32	.022
ARV adherence						

* All models are adjusted for age, mean CD4 cell counts, and viral load status across the study period. Final models are also adjusted for either PSY adherence or CESD scores respectively.