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Effects of Depression Alleviation on ART Adherence and HIV Clinic Attendance in Uganda, and the Mediating Roles of Self-Efficacy and Motivation

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Abstract

With depression known to impede HIV care adherence and retention, we examined whether depression alleviation improves these disease management behaviors. A sample of 1028 depressed HIV clients in Uganda enrolled in a cluster randomized controlled trial of two depression care models, and were surveyed over 12 months. Serial regression analyses examined whether depression alleviation was associated with self-reported antiretroviral therapy (ART) adherence and clinic attendance at month 12, and whether these relationships were mediated by self-efficacy and motivation. Among those with major depression, depression alleviation was associated with better ART adherence and clinic attendance at month 12; these relationships were fully mediated by self-efficacy at month 12, while adherence motivation partially mediated the relationship between depression alleviation and ART adherence. When both mediators were entered simultaneously, only self-efficacy was a significant predictor and still fully mediated the relationship between depression alleviation and adherence. These findings suggest that depression alleviation benefits both ART adherence and clinic attendance, in large part through improved confidence and motivation to engage in these disease management behaviors.

Keywords

HIV; depression; self-efficacy; motivation; adherence; clinic attendance; Uganda

INTRODUCTION

Depression is common in people living with HIV/AIDS (PLHA) in sub-Saharan Africa (SSA), with rates of clinical depression ranging from 10–20% (1–3), and an additional 20–40% having elevated depressive symptoms (1,2,4). Depression has ramifications for HIV disease management as it has been associated with lower immune function or CD4 count (5), higher HIV viral load (6), greater likelihood of mortality (7,8), and worse immunologic

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and virologic response to antiretroviral therapy (ART) (9,10). This negative impact of depression is thought to be largely a product of its deleterious effects on adherence to antiretroviral therapy (ART) (11–13), and engagement in HIV care (12).

Drawing on Social Cognitive Theory (14) and the Information, Motivation and Behavioral skills (IMB) model of health behavior (15), depression may influence HIV care adherence through its effects on self-efficacy and motivation to adhere well and attend clinic visits. Common symptoms of depression such as loss of interest, hopelessness, poor concentration, and fatigue may diminish self-efficacy and motivation to engage in healthy behaviors including taking medication every day and travelling to attend clinic visits. Use of depression treatment by PLHA has been associated not only with improved mental health (16), but also ART utilization and adherence (17,18). However, little research has examined whether and how depression alleviation or remission of depression leads to ART adherence and HIV care retention, especially in low-income countries where mental health knowledge is limited and services are largely nonexistent. Depression alleviation, via improvements in motivation and self-efficacy, may translate into increased self-care behaviors including taking medication as directed and attending clinic visits. An understanding of the mechanism by which (or how) depression impacts ART adherence and HIV care retention can help improve the cultural validity and effectiveness of depression care for PHLA in SSA. For example, depression alleviation has been associated with improvements in motivation and self-efficacy, which have been found to be critical factors in promoting self-care behaviors among those that have chronic illnesses in western countries (19); however, we are not aware of any study that has examined whether these pathways also apply to adherence in HIV care for PLHA in non-western low-income countries.

We report findings from a cluster randomized controlled trial of two approaches to integrating depression care into HIV clinics, in which depressed HIV clients were followed prospectively for 12 months with some receiving antidepressant therapy. Prior analyses from this study revealed that 76% of the whole sample achieved full remission of depressive symptoms or depression alleviation by the end of the study (20). In this paper we examine whether depression alleviation is associated with improvements in HIV care adherence and clinic attendance, whether these relationships are mediated by self-efficacy and motivation, and if they differ between those with major and minor depression. Study findings will inform policy regarding the importance of depression treatment for optimizing HIV disease management.

METHODS

Study Design

INDEPTH-Uganda (INtegration of DEPression Treatment into HIV care in Uganda) is a cluster, randomized controlled trial that compared two models for integrating antidepressant treatment into HIV care, conducted within 10 health care facilities in Uganda. Five clinics were randomly assigned to implement a structured protocol for administering depression care, and five others relied on the clinical acumen of trained providers. Both models started with routine depression screening for all adult patients at each clinic visit using two items from the Patient Health Questionnaire (PHQ-2; 21), which was administered at the triage

station by trained expert clients. In the structured protocol model, patients who screened positive for potential depression (PHQ-2 ≥ 3) and were medically stable, were to be than seen by the depression care nurse for a depression diagnostic evaluation using the full 9-item PHQ (PHQ-9; 21) and Mini International Neuropsychiatric Interview (MINI; 22). In contrast, in the clinical acumen model data from the PHQ-2 screen were relayed to the primary care provider, but it was up to the judgment of the provider as to whether further evaluation was undertaken rather than being dictated by protocol. In both models, providers were trained to prescribe antidepressants (fluoxetine or imipramine) to patients diagnosed with depression and no treatment contraindications. Neither model included any form of counseling. Psychoeducation about depression and depression treatment was provided by expert clients and nurses to the larger clientele (via talked given in the waiting room) as well as diagnosed patients (during individual consults) in both models. Implementation of the models began after a one-day training workshop for clinic staff, followed by weekly on-site mentorship and supervision from the study psychiatrist for the first two months, and than monthly supervision throughout the two-year implementation (starting in January 2013).

To evaluate the models, data were collected from a cohort of adult clients who screened positive for potential depression and were followed for 12 months with assessments at baseline and months 6 and 12. A more detailed description of the study protocol and the depression care models has been published elsewhere (23). The trial is registered with the National Institutes of Health sponsored clinical trials registry (NCT02056106). The study protocol was approved by RAND's Human Subjects Protection Committee and the Makerere University School of Medicine Ethical Research Committee.

Setting

The study was conducted in collaboration with Mildmay Uganda, a non-government organization that provides holistic outpatient HIV care at its own clinics, as well as technical assistance in HIV care to healthcare facilities across Uganda. Of the 10 healthcare facilities that participated in the study, eight were run by the Ministry of Health and two were private, faith-based, not-for-profit healthcare facilities; the clinics were located in the districts of Mpigi, Mityana, Luweero, and Wakiso. Each facility operates an HIV clinic, in which the depression care was integrated; these clinics operate on one to three days per week, have a clientele of 350–3000, and a staff of one to two clinical or medical officers and two to five nurses.

Participants

Between January and December of 2013, clients who screened positive for potential depression on the 2-item Patient Health Questionnaire (21) (PHQ-2 ≥ 3) at the triage station were eligible for enrollment into the cohort if they were at least 18 years of age, medically stable (not about to start [or recently started] ART or treatment for an acute opportunistic infection), and the research coordinator confirmed their depression status after re-administering the PHQ-2. All clients who screened positive for potential depression on the days of recruitment (one day per week at each site) were informed of the study and asked to provide written informed consent. Records on refusals were not kept, but research coordinators indicate that the vast majority (> 95%) of eligible clients agreed to participate.

Measures

All measures were translated into Luganda using standard translation and back-translation methods, and were interviewer-administered by trained study coordinators. Participants were paid 10,000 Uganda Shillings ($3 USD) after each assessment to cover costs of transportation.

Demographic and background characteristics included age, gender, and education level (classified as primary school or less vs. at least some secondary education). CD4 count and ART status were abstracted from the client's medical chart.

Depression. The 9-item Patient Health Questionnaire (PHQ-9) was used to measure the presence of depressive symptoms over the past 2 weeks (21). The 9 items correspond to the symptoms used to diagnose depression according to the Diagnostic and Statistics Manual (24); responses to each item range from 0 'not at all' to 3 'nearly every day'. Item scores are summed and a score of 10 or greater has been found to correspond highly to major depression (21); scores of 5–9 reflect minor depression. The PHQ-9 has established validity and reliability when used with PLHA in sub-Saharan Africa (25).

A PHQ-9 total score less than 5 at Month 12 (Month 6, if Month 12 data is missing) was used to determine depression alleviation, a definition that has been used in other antidepressant research (26).

ART adherence was assessed by asking respondents to report the number of missed doses in the past 7 days (from which a binary variable was created to indicate whether any missed doses were reported), and to estimate the percentage of prescribed doses taken over the past month on a scale of 0 'no doses taken' to 100 'every dose taken' (from which a binary variable was created to represent 100 versus any score less than 100).

Clinic attendance was assessed by asking respondents to report the numbed of scheduled clinic visits that they missed in the past 6 months (from which a binary variable was created to indicate whether any appointments had been missed).

HIV care management self-efficacy. Two items were used to assess self-efficacy with regard to ART adherence and clinic attendance as respondents were asked to rate their level of confidence in being able to "take all of my medication exactly as directed by my doctor" and "return to the clinic for my regular appointments with my doctor as scheduled" using a scale of 0 'cannot do at all' to 10 'certain I can do'.

Adherence motivation was assessed with a single item, "One of the most important things of my day is to make sure I take all of my HIV medication when I should"; response options ranged from 1 'strongly disagree' to 4 'strongly agree'.

Data Analysis

Participants with either major or minor depression (based on the PHQ-9 score) at baseline were included in the analysis. Month 12 values of depression alleviation, the three outcomes of interest (binary and continuous ART adherence; binary clinic attendance), and self-

efficacy and motivation were used in all analyses. When month 12 data were missing, month 6 values were used. Responses to the adherence motivation item were very skewed, so a binary variable was derived ('strongly disagree' or 'somewhat disagree' vs. 'strongly agree' or 'somewhat agree') and used in all analyses. Bivariate statistics (two-tailed, independent t-tests and chi square tests) were used to examine the associations between depression alleviation and the month 12 assessments of the three outcome measures, with separate analyses conducted for those with major depression or minor depression at baseline.

We used a hierarchical regression analysis to examine depression alleviation as a predictor of each of the three outcome measures, and whether self-efficacy and motivation mediated these associations. A set of three regression models was computed with each outcome at month 12 as the dependent variable, with the sample stratified by participant's major or minor depression status at baseline. The first model consisted of depression alleviation as the only independent variable. If depression alleviation was significantly associated with the outcome in the first model, and depression alleviation was significantly associated with self-efficacy (related to ART adherence or clinic attendance, corresponding to the dependent variable) and adherence motivation (for the two ART adherence outcomes only), than self-efficacy or motivation was added to depression alleviation as independent variables in the second model. The third model also added in the following covariates: age, sex, secondary education, CD4, antidepressant status, depression treatment arm, and baseline measure of the dependent variable. For the two ART adherence outcome variables, we ran two additional models. In the fourth model we included both adherence self-efficacy and motivation, in addition to depression alleviation as independent variables to determine which of these two potential mediators was most influential. The fifth model replicated the fourth model and included the covariates. We evaluated the significance of the direct and indirect effects associated with a mediation hypothesis using a bootstrap estimation approach with 1000 samples (27,28).

To include all cases missing a follow up assessment, we included attrition weights in all regression models. Attrition weights were calculated using a logistic regression model of retention status with baseline measures of demographics (age, gender, education, relationship status), HIV disease management (CD4 count, ART status, clinic attendance), depression, and variables associated with attrition (internalized HIV stigma, cognitive functioning, general self-efficacy) as predictors of retention. These weights were calculated separately for those with major and minor depression.

RESULTS

Sample Characteristics

A sample of 1252 clients enrolled in the study, including 640 and 612 clients from sites in the protocolized and clinical acumen arms, respectively. The sample's mean PHQ-9 at study entry was 8.2 (SD = 4.3), with 17.7% (n=221) having no/minimal depression symptoms (PHQ-9 < 5), 52.8% (n=659) having minor depression (PHQ-9: 5–9) and 29.5% (n=369) having major depression (PHQ-9 > 9) (3 cases were missing PHQ-9 data). The analysis for this paper used data only from those with minor or major depression (n = 1028) at baseline, given its focus on examining effects of depression alleviation. In this sample of 1028, mean

PHQ-9 at baseline was 9.2 (SD=8.0), 78.2% were female, mean age was 39.8 years (SD=11.2), 17.9% had at least some secondary education, and 38.5% were in a relationship; average time since HIV diagnosis was 43.8 months (SD=39.7), mean CD4 count was 426 cells/mm^3, and 74.0% were on ART.

Alleviation of Depression

Of the 1028 participants in the study who had either major or minor depression at baseline, 383 received antidepressants (234 of the 369 with major depression, and 149 of the 659 with minor depression) during their participation in the study; 92% of those treated started antidepressants after entry into the study, including 82% at or within three months following study baseline and 10% between 3–6 months after baseline. At month 12, the sample's mean PHQ-9 was 2.8 (SD=3.9), with 80.3% (n=760/946) having no/minimal depressive symptoms or complete depression alleviation, including 75.4% (258/342) of those with major depression at baseline and 83.1% (n=502/604) of those with minor depression. For those without month 12 data, month 6 data were used in determining this classification, while the 82 participants (8.0%) with only baseline data were excluded from this analysis. Participants who had follow-up data (at month 6 and/or month 12) were more likely to have at least some secondary education (18.6% vs. 9.8%; chi square = 4.0, df=1, p=.045), to be on ART (75.4% vs. 58.5%; chi square = 11.1, df=1, p=.001), and have been diagnosed with HIV for a longer period of time (44.7 months vs. 33.1; t = 3.4, df=973, p=.001) compared to those with only baseline data.

Relationship Between Depression Alleviation and ART Adherence

At baseline, 727 (70.7%) were on ART, of whom 679 had follow-up data and 666 remained on ART at their final follow-up assessment. At month 12, mean ART adherence over the past month was 93.4% (SD=10.7), and 81.5% reported no missed doses in the prior week. Mean ART adherence was positively correlated with adherence self-efficacy (r= .60, p=.000) and motivation (r= .29, p=.000), and those who reported no missed doses had higher adherence self-efficacy (mean = 9.5 vs. 8.4; t=7.6, df= 805, p=.000) and were more likely to agree with the importance of medication adherence (96.4% vs. 83.2%; chi square = 36.7, df=1, p=.000) compared to those who had missed doses. Of the 666 participants on ART, 232 had major depression at baseline, and 434 had minor depression.

Analysis of subgroup with major depression—Among those with major depression, 16.5% of the 176 who achieved depression alleviation at month 12 reported missed ART doses in the prior week and a mean adherence of 94.2% (SD=10.9) over the past month at this time point. These statistics reflect significant improvements compared to 33.9% (chi square = 7.9, df=1, p=.005) reporting missed doses and 86.9% (SD=16.6; t=3.1, df=70.6, p=.003) mean adherence among the 56 who remained depressed. We then fit a series of regression models with separate analyses for the binary (see Table 1) and continuous (see Table 2) adherence measures at month 12 as dependent variables. Achievement of depression alleviation was significantly associated with better adherence as assessed by both adherence measures when it was the sole independent variable in the model. When the month 12 measure of adherence self-efficacy was added to the models, results for both adherence measures revealed that depression alleviation was no longer related to adherence,

while higher self-efficacy was a significant predictor of higher adherence. These results remained unchanged when the covariates were added in the third and fully adjusted model. Adherence self-efficacy fully mediated the association of depression alleviation, with significant indirect effects for both the binary [b = −1.46, 95% CI = (−2.54, −.52)] and continuous [b = 7.27, 95% CI = (3.87, 10.88)] measures of ART adherence.

When adherence motivation was added to a model with only depression alleviation as the independent variable, the results for both adherence outcomes showed that higher motivation was a significant predictor of better adherence. While depression alleviation was marginally associated with the binary adherence measure, it was not associated with the continuous adherence measure, after controlling for adherence motivation. When all covariates were added to the model, adherence motivation remained significantly associated with both adherence measures, and fully mediated the relationship between depression alleviation and the binary measure of ART adherence with a significant indirect effect [b = −0.41, 95% CI = (−1.07, −0.02)]; the direct effect of depression alleviation was not significant. The indirect effect of adherence motivation on the continuous adherence outcome was also significant [b = 2.91, 95% CI = (1.03, 6.20)]; however, adherence motivation only partially mediated the relationship between depression alleviation and the continuous adherence measure, because the direct effect of depression alleviation on adherence was significant [b = 4.36, 95% CI = (0.35, 8.36)].

To assess which of the two cognitive variables was more influential, we estimated a model for each adherence measure in which the month 12 measures of both self-efficacy and motivation were both included as independent variables along with depression alleviation; self-efficacy was the sole significant predictor of both measures of adherence. This pattern of results persisted when the covariates including baseline ART adherence were added. These findings were confirmed by the direct and indirect effects observed in the dual mediation models. In the model with the binary adherence measure as the outcome, the specific indirect effect of self-efficacy was significant [b = −1.50, 95% CI = (−2.58, −0.53)]. In the model with continuous adherence as the outcome, the specific indirect effect of self-efficacy [b = 8.01, 95% CI = (4.26, 13.52)] was again significant. In both models, the specific indirect effect of motivation and the direct effect of depression alleviation were non-significant, suggesting that the effect of depression alleviation on adherence was fully mediated by self-efficacy when controlling for motivation.

Analysis of subgroup with minor depression—Among those with minor depression, 13.6% of the 359 who achieved depression alleviation at month 12 reported missed ART doses in the prior week and 94.7% (SD=9.7) mean adherence over the past month at this time point, compared to 32.0% (chi square = 14.9, df=1, p=.000) reporting missed doses and 90.5% (SD=11.2; t=3.0, df=98.4, p=.003) mean adherence among the 75 who remained depressed.

The series of regression models that were performed for adherence among those with major depression were replicated with the subgroup exhibiting minor depression (see Tables 1 and 2). Achievement of depression alleviation was a significant predictor of better adherence as assessed by both adherence measures when it was the only independent variable in the

model. When adherence self-efficacy was added to the model, self-efficacy was a significant predictor of better adherence as assessed by both adherence measures. Also, depression alleviation remained significantly associated with the binary adherence measure, but only marginally associated with the continuous measure. This pattern of results remained unchanged when covariates were added to the model. Therefore, adherence self-efficacy partially mediated the association of depression alleviation with the binary adherence measure as both the indirect effect [b = −0.30, 95% CI = (−0.60, −0.10)] and direct effect [b = −0.93, 95% CI = (−1.57, −0.28)] was significant. Adherence self-efficacy also fully mediated the association of depression alleviation with the continuous adherence measure with an indirect effect [b = 2.05, 95% CI = (0.72, 3.95)] that was significant (the direct effect of depression alleviation was non-significant).

In a model that included adherence motivation and depression alleviation as independent variables, higher motivation was a significant predictor of better adherence as assessed by the continuous adherence measure but was unrelated to the binary adherence measure. Depression alleviation remained significantly correlated with both adherence measures (though with a lower magnitude compared to the first model). When the covariates were added to the model with the continuous adherence measure as the dependent variable, adherence motivation remained a significant predictor, while depression alleviation was only marginally associated with adherence. We found that adherence motivation fully mediated the relationship between depression alleviation and the continuous adherence measure as the indirect effect was significant [b = 2.42, 95% CI = (.73, 3.95)], while the direct effect of depression alleviation was non-significant.

When self-efficacy and motivation were both included in a model with depression alleviation, the binary adherence measure was significantly correlated with depression alleviation and self-efficacy (but not motivation), while the continuous adherence measure was significantly correlated with self-efficacy and marginally correlated with motivation (but not depression alleviation); this pattern of results persisted when the covariates were included. In the model with the binary adherence measure as the outcome, the specific indirect effect of self-efficacy [b = −0.35, 95% CI = (−0.49, −0.22)] was significant. In the model with the continuous adherence measure as the outcome, the specific indirect effects of both self-efficacy [b = 4.27, 95% CI = (3.43, 5.68)] and motivation [b = 2.26, 95% CI = (1.22, 3.48)] were significant. In both these models, the direct effect of depression alleviation on the outcomes was non-significant, suggesting that its effect on adherence was fully mediated by the cognitive variables.

Relationship Between Depression Alleviation and Clinic Attendance

At month 12, 18.7% reported any missed clinic appointment in the prior 6 months, and those who had attended all scheduled appointments had higher clinic attendance self-efficacy compared to those who had missed appointments (mean = 9.5 vs. 8.7, df=943, p<.0001).

Analysis of subgroup with major depression—At baseline, 25.5% of the 368 (1 case had missing data) with major depression at baseline reported having missed at least one clinic appointment in the past 6 months. Among those with a follow-up assessment, 15.6%

of the 257 who achieved depression alleviation at month 12 reported missing a clinic appointment in the past 6 months, compared to 28.6% of the 84 who remained depressed (chi square = 7.0, df=1, p=.008). In regression analyses, achievement of depression alleviation was significantly associated with not missing clinic appointments when it was the sole independent variable in the model (see Table 3). When clinic attendance self-efficacy was added to the model, depression alleviation was no longer a significant predictor, while higher self-efficacy was significantly correlated with better clinic attendance; this pattern of results remained when the covariates were added. Self-efficacy fully mediated the relationship between depression alleviation and clinic attendance as the indirect effect was significant [b = −1.06, 95% CI = (−1.85, −.50)], while the direct effect was not.

Analysis of subgroup with minor depression—At baseline, 24.7% of the 656 (3 cases had missing data) with minor depression at baseline reported having missed at least one clinic appointment in the past 6 months. Among those with a follow-up assessment, 17.3% of the 502 who achieved depression alleviation at month 12 reported missing a clinic appointment in the past 6 months, compared to 25.5% of the 102 who remained depressed (chi square = 3.7, df=1, p=.054). In regression analyses (see Table 3), achievement of depression alleviation was not associated with clinic attendance when it was the sole independent variable in the model, so no further regression analyses were performed.

DISCUSSION

The findings from this analysis show that alleviation of major depression is associated with better self-reported ART adherence and HIV clinic attendance among PLHA in Uganda. Self-efficacy, and to a lesser extent motivation, are mediators of these relationships, suggesting that depression (and alleviated or treated depression) influences these HIV care management behaviors through influence on confidence and motivation to engage in such behaviors. Some of these findings held true for alleviation of minor depression as well.

Depression has been consistently associated with HIV care adherence (11–13) and retention (12), but few studies have examined how HIV care management is associated with whether or not depression is alleviated. Our study shows that when depression is alleviated, whether as a result of antidepressant treatment or not, ART adherence and clinic attendance improves significantly in bivariate regression models. This was true for those experiencing major depression as well as those with minor depression at baseline, except for clinic attendance, which was not associated with alleviation of minor depression in our regression analysis. Some studies have observed no effects of antidepressant therapy on ART adherence (29,30), and Safren et al. (31) have shown that cognitive-behavioral therapy that addresses both depression and adherence results in much improved ART adherence—all of which could suggest that depression treatment needs to include a counseling component in order to impact ART adherence. However, our findings, as well as that of other studies (17,18) suggest that antidepressant therapy alone can benefit treatment adherence.

Consistent with theories of health behavior such as IMB and Social Cognitive Theory, our data revealed that both self-efficacy and motivation serve to mediate the influence of depression alleviation on HIV care adherence and retention. Among those with major

depression, self-efficacy fully mediated the relationship between depression alleviation and both measures of ART adherence, as well as clinic attendance. Among those with major depression, adherence motivation was only associated with the continuous adherence measure and partially mediated the relationship between it and depression alleviation. However, when both self-efficacy and motivation were in the regression model and controlled for, only self-efficacy continued to be a significant mediator of the relationship between depression alleviation and both ART adherence measures, suggesting that self-efficacy has a greater influence on adherence. Among those with minor depression, adherence self-efficacy and motivation each only partially mediated the relationship between depression alleviation and ART adherence when they were the sole mediators in the model, but when both were in the model they served to fully mediate the relationship between depression alleviation and adherence. Overall, these findings suggest that depression alleviation serves to improve ART adherence and clinic attendance primarily through improved cognitive processes such as confidence and motivation to engage in these disease management behaviors. To the extent that these cognitive processes only partially mediate the relationship between depression alleviation and HIV care adherence and retention suggests that reduced somatic and cognitive/affective depression symptoms also influence adherence and clinic attendance.

We observed high rates of depression alleviation, even with a minority of the participants receiving antidepressant therapy. Nearly two-thirds of participants with major depression received antidepressant treatment, as the depression care models focused on treatment of major depression, but less than one quarter of those with minor depression received treatment. Nonetheless, the vast majority of those with either major or minor depression experienced depression alleviation. One possible explanation is the added attention and appreciation of clinic staff to depression and mental health as a result of implementing the treatment models—this included psychoeducation talks about depression in the waiting room to all clients, and the depression evaluations and depression monitoring that many untreated participants received. These services may have led patients to feel that their mental health needs were being attended to and that the staff cared for them, even if they did not receive treatment. We have observed in our other research that ART and HIV care has mental health benefits and is associated with reduced depression for patients who have just started receiving care (32), but it is not clear how applicable such effects are in this study given that the vast majority of participants were not new to HIV care or ART, and rates of ART use were equivalent between those with and without depression alleviation.

Our analyses were limited by a number of measurement limitations. ART adherence and clinic attendance were both measured by self-report, which have been shown to overestimate actual behavior (33); a more objective measure of adherence, such as microelectronic monitoring, or HIV viral load assays to assess virologic suppression would have yielded a more valid measure of adherence. Similarly, our data regarding depression diagnoses were limited by our reliance on the PHQ9, rather than a more rigorous diagnostic interview, although the PHQ-9 has been found to have high correspondence with diagnostic interviews (21).

In summary, our findings highlight the benefits of depression care for PLHA and their HIV care adherence and clinic attendance, and provide insight into the cognitive mechanisms by which depression alleviation serves to improve these HIV disease management behaviors. Furthermore, these data bolster the argument for the need for mental health and depression care to be fully integrated into HIV care services in Uganda and the larger region of SSA (2). In fact, other findings from our study have demonstrated the feasibility and effectiveness of task-shifted depression care in this setting (20), as have other studies with HIV patients in both high and low resource settings (26,34). Evidence of the individual and public health benefits of depression treatment, as demonstrated in this study, may be key to moving the policy debate and mobilizing funders and budget allocations to place greater priority on provision of mental health services for PLHA.

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Table 1

Hierarchical regression models of the relationship between depression alleviation and the binary measure of ART adherence, and the mediating roles of adherence self-efficacy and motivation

Model Specification	Depression Alleviation (DA)	DA + M1[a]	DA + M1[b]	DA + M2[a]	DA + M2[b]	DA + M1+ M2[a]	DA + M1+ M2[b]
Major Depression							
Depression Alleviation	0.372*** (0.19, 0.71)	0.776 (0.41, 1.48)	0.879 (0.51, 1.52)	0.543* (0.27, 1.09)	0.43*** (0.22, 0.86)	0.775 (0.43, 1.4)	0.811 (0.47, 1.39)
Adherence Self-Efficacy		0.378*** (0.2, 0.71)	0.233*** (0.12, 0.45)			0.378*** (0.2, 0.73)	0.225*** (0.12, 0.43)
Adherence Motivation				0.264*** (0.1, 0.69)	0.262** (0.07, 0.94)	1.008 (0.42, 2.4)	1.868 (0.4, 8.79)
Observations	292	292	234	292	234	292	234
Minor Depression							
Depression Alleviation	0.310*** (0.16, 0.61)	0.388*** (0.21, 0.7)	0.394** (0.18, 0.87)	0.399** (0.18, 0.89)	0.350** (0.14, 0.85)	0.433** (0.21, 0.88)	0.392** (0.17, 0.89)
Adherence Self-Efficacy		0.506*** (0.43, 0.59)	0.507*** (0.41, 0.62)			0.520*** (0.47, 0.58)	0.506*** (0.42, 0.61)
Adherence Motivation				0.341 (0.09, 1.29)	0.477 (0.09, 2.57)	0.586 (0.12, 2.78)	1.032 (0.12, 8.92)
Observations	512	512	434	512	434	512	434

DA = depression alleviation; M1 = adherence self-efficacy; M2 = adherence motivation;

[a] = model includes depression alleviation and mediator(s) only;

[b] = model includes depression alleviation, mediator(s) and the following baseline covariates: age, secondary education, sex, CD4 count, antidepressant treatment status, depression treatment arm, and baseline measure of ART non-adherence

*** p<0.01,

** p<0.05,

* p<0.1; Odds ratio with 95% confidence interval in parentheses.

Table 2

Hierarchical regression models of the relationship between depression alleviation and the continuous measure of ART adherence, and the mediating roles of adherence self-efficacy and motivation

Model Specification	Depression Alleviation (DA)	DA + M1[a]	DA + M1[b]	DA + M2[a]	DA + M2[b]	DA + M1+ M2[a]	DA + M1+ M2[b]
Major Depression							
Depression Alleviation	7.885** (2.30,13.47)	2.339 (1.34,6.02)	−0.003 (−2.44,2.43)	3.967 (−1.24,9.18)	3.877 (−1.38, 9.13)	1.750 (−1.49, 4.99)	0.350 (−2.23, 2.93)
Adherence Self-Efficacy		6.040*** (2.90,9.18)	7.403*** (4.74,10.07)			5.882*** (2.52, 9.24)	7.517*** (4.97, 10.06)
Adherence Motivation				14.930*** (6.43, 0.69)	12.870** (2.82, 22.92)	2.801 (−3.10, 8.70)	−1.767 (−6.73,3.20)
Observations	512	512	434	512	434	512	434
Minor Depression							
Depression Alleviation	4.325** (1.55, 7.10)	2.271* (0.24, 4.30)	2.282* (−0.09,4.66)	2.599** (0.52, 4.68)	2.892* (0.16, 5.62)	1.620 (−0.21, 3.45)	1.732 (−0.42, 3.89)
Adherence Self-Efficacy		4.619*** (3.11, 6.13)	4.507*** (3.14, 5.88)			4.420*** (2.99, 5.85)	4.258*** (2.99, 5.53)
Adherence Motivation				8.002*** (4.69,11.31)	8.919*** (4.89, 12.95)	3.429* (0.16,6.7)	4.127* (0.05, 8.21)
Observations	512	512	434	512	434	512	434

DA = depression alleviation; M1 = adherence self-efficacy; M2 = adherence motivation;

[a]= model includes depression alleviation and mediator(s) only;

[b]= model includes depression alleviation, mediator(s) and the following baseline covariates: age, secondary education, sex, CD4 count, antidepressant treatment status, depression treatment arm, and baseline measure of ART non-adherence

*** p<0.01,

** p<0.05,

* p<0.1; Regression coefficient from OLS with 95% confidence intervals in parentheses.

Table 3

Hierarchical regression models of the relationship between depression alleviation and clinic attendance, and the mediating role of clinic attendance self-efficacy

Model Specification	Depression Alleviation (DA)	DA + Self-Efficacy[a]	DA + Self-Efficacy[b]
Major Depression			
Depression Alleviation	0.461*** (0.29, 0.74)	1.052 (0.53, 2.08)	1.071 (0.51, 2.25)
Self-Efficacy		0.266*** (0.18, 0.38)	0.258*** (0.17, 0.4)
Observations	341	341	340
Minor Depression			
Depression Alleviation	0.651 (0.35, 1.2)	0.846 (0.43, 1.67)	0.786 (0.41, 1.51)
Self-Efficacy		0.240*** (0.14, 0.41)	0.249*** (0.15, 0.41)
Observations	601	601	601

DA = depression alleviation;

[a] = model includes depression alleviation and mediator(s) only;

[b] = model includes depression alleviation, mediator and the following baseline covariates: age, secondary education, sex, CD4 count, antidepressant treatment status, depression treatment arm, and baseline measure of ART non-adherence

*** p<0.01,

** p<0.05,

* p<0.1; Odds ratio with 95% confidence interval in parentheses.