OPEN

Long-Term Effect of Group Support Psychotherapy on Depression and HIV Treatment Outcomes: Secondary Analysis of a Cluster Randomized Trial in Uganda

Etheldreda Nakimuli-Mpungu, PhD, Colin M. Smith, MD, Kizito Wamala, MSc, James Okello, PhD, Josephine Birungi, MPH, Micheal Etukoit, MPH, Ramin Mojtabai, PhD, Jean B. Nachega, PhD, Ofir Harari, PhD, Seggane Musisi, FRCP (C), and Edward J. Mills, PhD

ABSTRACT

Objective: We aimed to determine the effect of group support psychotherapy (GSP) compared with group HIV education (GHE) on depression and HIV treatment outcomes 24 months after treatment. We further aimed to investigate the mediating role of depression and antiretroviral therapy (ART) adherence in the relationship between GSP and viral load suppression.

Methods: Thirty HIV clinics across three districts were randomly assigned to deliver either GSP or GHE for depression. Depression and optimal (≥95%) ART adherence was assessed at baseline and 6, 12, 18, and 24 months after treatment. Viral load was drawn from the medical charts at baseline and 12 and 24 months after treatment. Multilevel mixed-effects regression models and generalized structural equation modeling were used to estimate 24-month outcomes and mediation effects.

Results: Participants ($N = 1140$) were enrolled from HIV clinics offering either GSP ($n = 578$ [51%]) or GHE ($n = 562$ [49%]). Fewer GSP than GHE participants met the criteria for depression at 24 months after treatment (1% versus 25%; adjusted odds ratio [aOR] = 0.002, 95% confidence interval [CI] = 0.0002–0.018). More GSP than GHE participants reported optimal (≥95%) ART adherence (96% versus 88%; aOR = 20.88, 95% CI = 5.78–75.33) and improved viral suppression (96% versus 88%; aOR = 3.38, 95% CI = 1.02–11.02). The indirect effects of GSP through sequential reduction in depression and improvement in ART adherence at 12 months may partially explain the higher viral suppression rates at 24 months in GSP than GHE groups.

Conclusion: In settings where the HIV epidemic persists, depression treatment with GSP may be critical for optimal HIV treatment outcomes.

Trial Registration: The Pan African Clinical Trials Registry, number PACTR201608001738234.

Key words: depression, group support psychotherapy, HIV/AIDS, antiretroviral therapy adherence, viral suppression, Uganda.

INTRODUCTION

In sub-Saharan Africa, the prevalence of depression among persons living with HIV (PLWH) ranges from 9% to 32% (1,2). In areas such as postconflict northern Uganda, with estimated rates of depression as high as 70%, PLWH remain particularly vulnerable to developing depression (3). Insufficient attention to identifying and addressing mental health needs of PLWH has been recognized as a barrier to meeting World Health Organization guidelines for universal antiretroviral therapy (ART) in this population (4,5).

Previous research has shown that untreated depression among PLWH is associated with adverse HIV treatment outcomes, including suboptimal medication adherence, viral nonsuppression,

AE = adverse events, **ANS** = autonomic nervous system, **ART** = antiretroviral therapy, **GSEM** = generalized multilevel structural equation modeling, **GHE** = group HIV education, **GSP** = group support psychotherapy, **HIV** = human immunodeficiency virus, **LHW** = lay health worker, **PLWH** = people living with HIV

SDC Supplemental Digital Content

From the Department of Psychiatry, College of Health Sciences (Nakimuli-Mpungu, Seggane), Makerere University, Kampala, Uganda; Departments of Medicine (Smith) and Psychiatry and Behavioral Sciences (Smith), Duke University Medical Center, Durham, North Carolina; Department of Psychology (Wamala), Center for Victims of Torture; Department of Mental Health, Faculty of Medicine (Okello), Gulu University, Gulu; The AIDS Support Organization (TASO) (Birungi, Etukoit), Kampala, Uganda; Department of Mental Health, Bloomberg's School of Public Health (Mojtabai), Johns Hopkins University, Baltimore, Maryland; Department of Epidemiology, Pittsburgh Graduate School of Public Health (Nachega), University of Pittsburgh, Pittsburgh, Pennsylvania; Stellenbosch Center for Infectious Disease, Department of Medicine (Nachega), Stellenbosch University, Stellenbosch, South Africa; Department of International Health, Bloomberg's School of Public Health (Nachega), Johns Hopkins University, Baltimore, Maryland; MTEK Sciences Inc (Harari), Vancouver, British Columbia; and Department of Clinical Epidemiology and Biostatistics (Mills), McMaster University, Hamilton, Ontario, Canada.

Address correspondence to Etheldreda Nakimuli-Mpungu, MMED (Psych), PhD, Department of Psychiatry, College of Health Sciences, Makerere University, Mulago Hospital Complex, PO Box 7072, Mulago Hill Road, Kampala, Uganda. E-mail: etheldreda.nakimuli@mak.ac.ug

Received for publication August 31, 2021; revision received May 29, 2022.

DOI: 10.1097/PSY.0000000000001128

and increased mortality (6–9). These challenges are more prominent in postconflict settings where extreme poverty, food insecurity, and poor access to psychological care are common (10). Research is emerging in sub-Saharan Africa and other low- and middle-income countries on the development and evaluation of mental health interventions for PLWH (11–16). A recent systematic review of mental health interventions for PLWH in low- and middle-income countries indicated strong evidence that the common mental health problems that PLWH face—including depression, anxiety, and posttraumatic stress disorder—are responsive to first-line psychological treatments (17).

There remains a need to understand the underlying mechanisms through which mental health interventions impact HIV treatment outcomes. The outcome of prior research on this subject has been variable, with some studies reporting improved depression and HIV treatment outcomes (18), whereas others report only improved depression outcomes (19). More recent meta-analyses indicate that depression treatment improves ART adherence and viral suppression (20,21).

In Uganda, we developed culturally sensitive group support psychotherapy (GSP) as a first-line treatment of depression in rural primary care settings. A prior feasibility study (22) and pilot randomized clinical trial (23) of this intervention served to test procedures, recruitment, retention, and outcomes. Evaluation of process outcomes (24) indicated that acquisition of knowledge and skills enhanced social connections, support, and positive coping strategies, which led to a reduction in depression symptoms. However, the sustainability and impact of these interventions on HIV treatment outcomes were not studied.

Subsequently, we used a cluster randomized controlled trial to examine the intent-to-treat GSP effects through 24 months by comparing GSP with an active comparison, group HIV education (GHE) (25). At 12 months, GSP was more effective in treating mild to moderate depression in PLWH than GHE. Improvements in HIV treatment outcomes were greater among GSP than GHE participants; however, this difference was not statistically significant.

The current analysis aimed to document intent-to-treat GSP effects on HIV treatment outcomes for 24 months. GSP effects were compared with GHE on depression, ART adherence, and viral load suppression 24 months after treatment. We also investigated the mediating role of sequential changes in depression and ART adherence at 12 months in the relationship between GSP and viral load suppression at 24 months. We hypothesized that GSP may lead to a sustained greater reduction in depression when compared with GHE, which would lead to improved ART adherence and viral suppression.

METHODS

Study Design

We report the 2-year outcomes of a pragmatic two-arm cluster randomized trial where 30 HIV clinics across three districts (Gulu, Kitgum, Pader) in postconflict northern Uganda were randomly assigned to deliver either GSP or GHE. HIV clinics eligible for the trial nominated at least four lay health workers (LHWs) involved in HIV care who were able to read and write, and who resided within the villages served by the clinic.

Participants were PLWH on ART, 19 years and older with major depression, and antidepressant naive. Individuals with high suicide risk, severe medical disorder (e.g., pneumonia or active tuberculosis) psychotic symptoms, or hearing or visual impairment were excluded. Mild to moderate depression and adherence rates ≥95% were evaluated at baseline and 6, 12, 18, and 24 months after treatment. Viral load was obtained from medical charts at baseline and at 12 and 24 months after treatment.

Details of the recruitment have been published elsewhere (26). The study protocol is published (27) and registered in the Pan African Clinical Trials Registry PACTR201608001738234. The study was approved by both the Makerere University College of Health Sciences Research Ethics Committee and the Uganda National Council of Science and Technology. At the end of the treatment, all participants received 8000UGX (US $2.16) to defray transportation costs. The group facilitators received 80,000 UGX ($21.62) for compensation. Figure 1 summarizes the trial profile.

Randomization and Masking

Health center managers were invited to a stakeholders' meeting at the district's local government offices where our study purpose and procedures were explained to facilitate district leadership understanding of the trial. We randomized at the level of health centers by urn randomization (health center managers separately picked a paper containing the intervention allocation from a basket; ratio 1:1). By design, both experimental and control interventions were identifiable to participants and outcome assessors, but masked to the Data and Safety Monitoring Board, and data analysts up to 12 months after treatment.

Procedures

Primary care health workers delivered a health talk on depression to clients in the waiting area. Clients who felt that they had experienced symptoms of depression were invited for further evaluation. Clients diagnosed with major depression were approached by research assistants who explained study procedures, determined eligibility, and then obtained informed consent. Each client who gave informed consent received baseline assessments with a standardized questionnaire. Recruited participants from the same village were assigned to a trained LHW residing in or near their village to receive either GSP or GHE.

The contents of the GSP and GHE interventions were described in previous publications (23,24). GSP was delivered in eight weekly sessions, each lasting 2 to 3 hours. Participants were divided into sex-specific groups of 10 to 12 participants. Trained lay health workers delivering the intervention were of the same sex as the participants, and delivered the intervention material following a scripted manual. The target community was involved in the development of this intervention, thus making it culturally sensitive intervention. Cultural sensitivity is defined as being aware that cultural differences and similarities between people exist and affect values, learning, and behavior (28,29).

In developing GSP, a qualitative study of perceptions of depression and its local treatment strategies among the target population was completed (30). The most commonly used coping skills were similar to those previously reported in other African studies (31), such as faith/religion, social support, communal activities, distraction, acceptance, and cognitive reframing or meaning making. We designed GSP sessions to begin and end with rituals, such as a cultural song, dance, or prayer chosen by participants. Homework assignments were designed to enhance participation in communal activities and enhance social connections.

The first session addressed issues related to the group process, expectations, ground rules, and commitment after which participants were paired and each pair asked to interact in the week and provide feedback on their activity. The second session addressed triggers, symptoms, treatment options for depression, and the relationship between depression and HIV. Thereafter, participants were asked to communicate with community members and share newly learned knowledge. In our previous research, the target community attributed the cause of depression to ancestral spirits and witchcraft (30); hence, there is a need for a session on psychoeducation, which has been shown to increase treatment engagement and reduce attrition (32).

In sessions 3 and 4, group participants shared their most painful experiences. Thereafter, participants were encouraged to share other problems

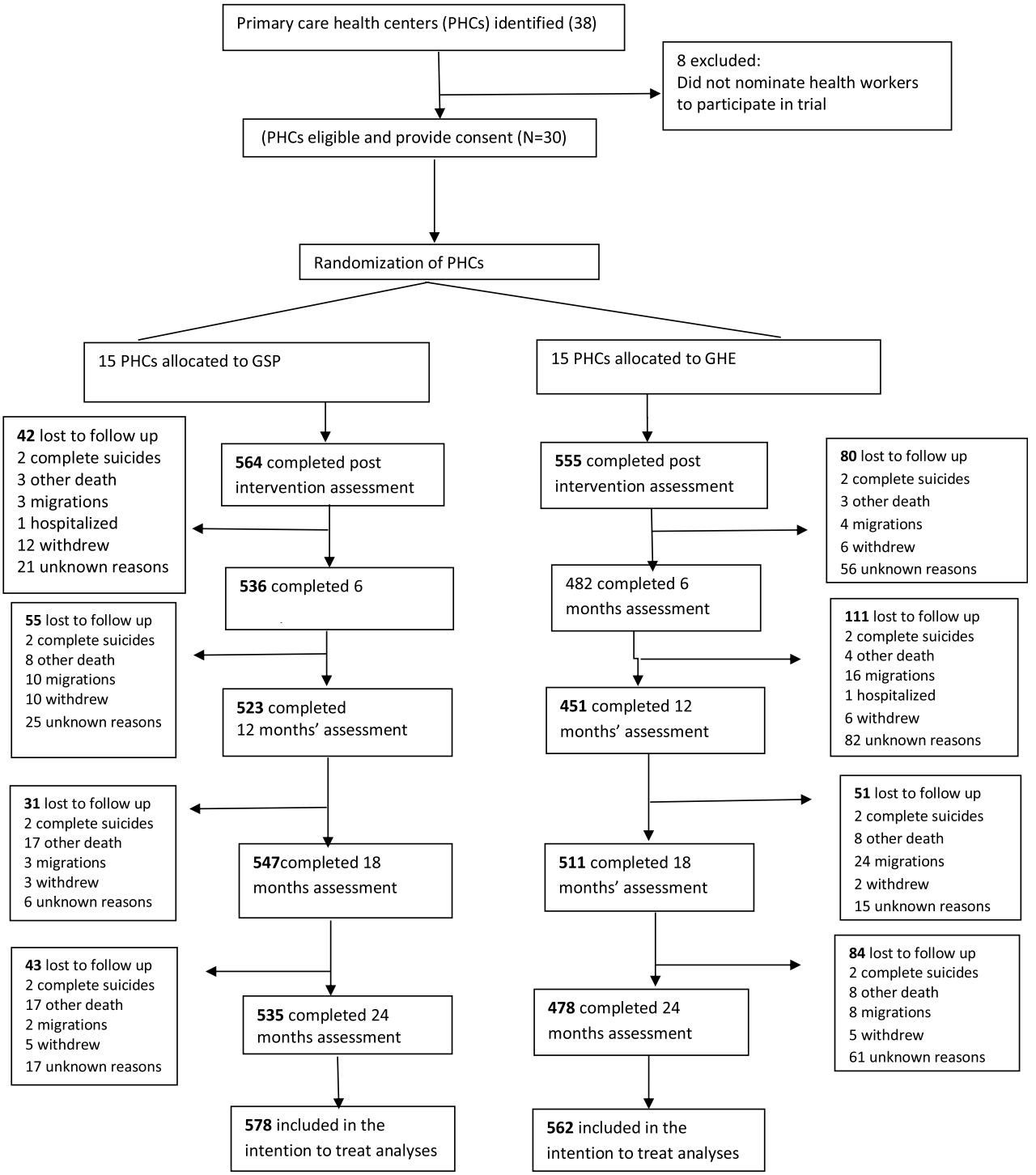

FIGURE 1. Flow diagram of trial health centers and participants. GHE = group HIV education; GSP = group support psychotherapy.

with a trusted elder in their household or community. Previous research has shown that catharsis is followed by decreased tension, increased mental clarity and feelings of well-being, and emotional stability (33,34). In sessions 5 and 6, GSP participants shared ways in which they cope with depression, whereas the group facilitator provided guidance on the use of positive and negative coping skills. In previous research (30), unhelpful coping strategies have been associated with depression in PLWH (35).

The last two sessions were dedicated to income-generating skills. Our previous research revealed a need for an intervention that focused on treatment of depression symptoms and skills development to improve participant livelihood (30). Poor mental health interacts with poverty in a negative cycle, and researchers have called for development of interventions that could break this cycle (36).

The first GHE session focused on rationale for HIV education and orientation, and the second session focused on the progression of HIV. The

third and fourth sessions covered transmission and prevention of HIV infection, and the fifth and sixth sessions covered mother-to-child transmission. The last two sessions focused on basic facts about ART. Group members were allowed to ask questions at the end of every session (for details of the training of the lay health workers, see Supplemental Digital Content 1, Boxes 1 and 2, http://links.lww.com/PSYMED/A866).

Strategies to ensure fidelity in both arms included the use of standardized intervention materials, structured health worker training, and ongoing supervision. LHWs delivered the interventions following a manual translated into the local language and were supervised by trained health center workers who had participated in the earlier pilot trial (23).

Outcomes

We assessed depression using the major depressive episode module of the Mini-International Neuropsychiatric Interview (6.0; based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*) (37). Functioning was evaluated using a five-item locally developed function assessment measure (38). Items were derived from qualitative interviews with individuals and their caregivers in the target population about participant expectations regarding function outcomes (38). The five categories of tasks assessed included household (e.g., washing clothes), field (e.g., grazing animals), social (e.g., attending social events) and job-related or school-related tasks (e.g., participating in income-generating activities), and tasks related to personal hygiene (e.g., bathing). Participants were asked to rate their ability to do a given task on a 3-point scale, with responses ranging from 0 ("No, I am not able"), and 1 ("Yes, but not like before"), to 2 ("Yes, I am able to"). Summary scores ranged from 0 to 10. The measure attained a Cronbach α reliability coefficient of .86 in this study population.

The SAD PERSONS scale was used to assess suicide risk (39) at each assessment point. Also, the total number of suicide attempts before each time point was recorded. The study cohort was monitored closely for suicide attempts and other adverse events (AEs). All trained lay health workers in both intervention arms made weekly home visits to remind caregivers to closely monitor and report any AEs. When a suicide attempt occurred, it was reported to LHWs and the study team, who took steps to confirm the incident. Once confirmed, the incident was reported to the principal investigator, the institutional review board, and the data safety and monitoring board (for details on AEs, see Supplemental Digital Content 1, http://links.lww.com/PSYMED/A866).

Adherence to ART was measured by one question: "during the past week, on how many days have you missed taking all your medication doses?" Using the responses, we computed a binary variable with <95% adherence coded 0 and those with ≥95% adherence rates coded 1. Viral load was assessed every 12 months and at variable times for each PLWH (standard in Uganda). Visits to assess viral loads preceded the study visits for the 6-month interval assessments, and we did not assess the difference in timing. Measures of viral load were obtained from the medical charts of study participants, but the actual assay used to measure viral load in the laboratory was not recorded. We computed a binary variable where individuals with <1000 viral copies per milliliters were categorized as being suppressed (coded 1), whereas those with ≥1000 as nonsuppressed (coded 0).

Statistical Analyses

Data were analyzed using STATA version 16. First, we conducted bivariate analyses using cluster adjusted χ^2 tests and *t* tests to compare baseline variables between GSP and GHE participants. We also conducted bivariate analyses to compare these variables between those who completed all follow-up assessments (completers) and those who had not (noncompleters). Given the clustered nature of our data and the need to adjust for covariates in our analyses, missing values were multiply imputed 20 times assuming a joint multivariate normal distribution (Supplementary File 1, http://links.lww.com/PSYMED/A866). We used the postestimation STATA program *how_many_imputations* to determine the number of imputations needed (40). A multivariate normal regression model allows interdependencies within clusters and enables all clusters to be imputed simultaneously. Furthermore, simulation studies have shown that assuming an MVN distribution leads to reliable estimates given a large sample size even when the normality assumption is violated (41–43).

Specifically, the STATA command *mi set* was used for these imputations. We then used the STATA command *mi impute mvn* to specify the imputation model and to create 20 imputed datasets. Sex, age, education, marital status, employment, and intervention arm were used for these imputations. We did not include transformed variables in the imputation model.

All regression models used to evaluate the effect of GSP on depression and HIV treatment outcomes were estimated using multiply imputed data. Four separate models were analyzed in which the dependent variables were depression, function scores, ART adherence, and viral suppression. In each model, the independent variables included intervention arm, time (ordinal variable in 6-month units capturing the effect of time), and the interaction of study arm by time (capturing the effect of each additional unit of time among GSP participants relative to GHE participants). See detail in Supplemental Digital Content 2, http://links.lww.com/PSYMED/A867.

Given that randomization was performed at the cluster (health center) level, some baseline variables were not comparable between the study arms at baseline. Therefore, multiple imputation was used given the adjustment of covariates in the multilevel mixed regression models. All multilevel regression models were adjusted for covariates (employment status, marital status, function scores) repeated measures nested within person and person nested within health worker (44). Therefore, the models contained random intercepts at the health worker and person levels (three-level models). In the mediation analyses using generalized multilevel structural equation modeling (GSEM), only a random intercept term for health worker was introduced (two-level models).

In the mediation model (Figure 2), viral suppression is the dependent variable, therapy group is the independent variable, and depression and ART adherence are the two mediators. We used GSEM to estimate coefficients for depression on therapy group (β_1), ART adherence on therapy group (β_5), and ART adherence on depression (β_2), as well as coefficients for viral suppression on depression (β_6), viral suppression on ART adherence (β_3), and viral suppression on therapy group (β_4), while considering the nesting of the data into therapy groups (45). All models included time and therapy group and its interaction. For binary outcomes, the Stata command *gsem* was used with a binomial family distribution and a logit link.

We conducted cross-sectional mediation analyses using the *nlcom* (nonlinear combination) STATA command to compute the indirect effect coefficients and their standard errors at each time point as shown in Table 1 (46). Next, we used sequential mediation analysis to examine if the effects of therapy group on viral load at 24 months were mediated by sequential changes in depression and ART adherence at 12 months (47). We again used *nlcom* command to compute the indirect effect coefficients and their standard errors for depression and ART adherence at 12 months separately and thereafter obtained indirect effects for sequential changes in depression and adherence. We then computed the total indirect effect by summing up the indirect effects through depression and ART adherence at 12 months in the relationship between therapy group and viral suppression at 24 months with the indirect effects through depression in the relationship between therapy group and ART adherence. Lastly, we ran *nlcom* to compute the total effects by combining direct effect of therapy group on viral suppression at 24 months and the total indirect effects. Bootstrap standard errors and bootstrap bias-corrected confidence intervals were computed for all effects (48).

RESULTS

Between September 13 and December 15, 2016, we assessed 1473 individuals, of whom 1140 were recruited from health centers offering GSP ($n = 578$) or GHE ($n = 562$). Figure 1 illustrates the trial profile. Regarding intervention attendance, 33 of 578 GSP (6%) and 15 of 562 GHE (3%) participants missed all sessions. Individuals who did not attend any group session were not excluded from

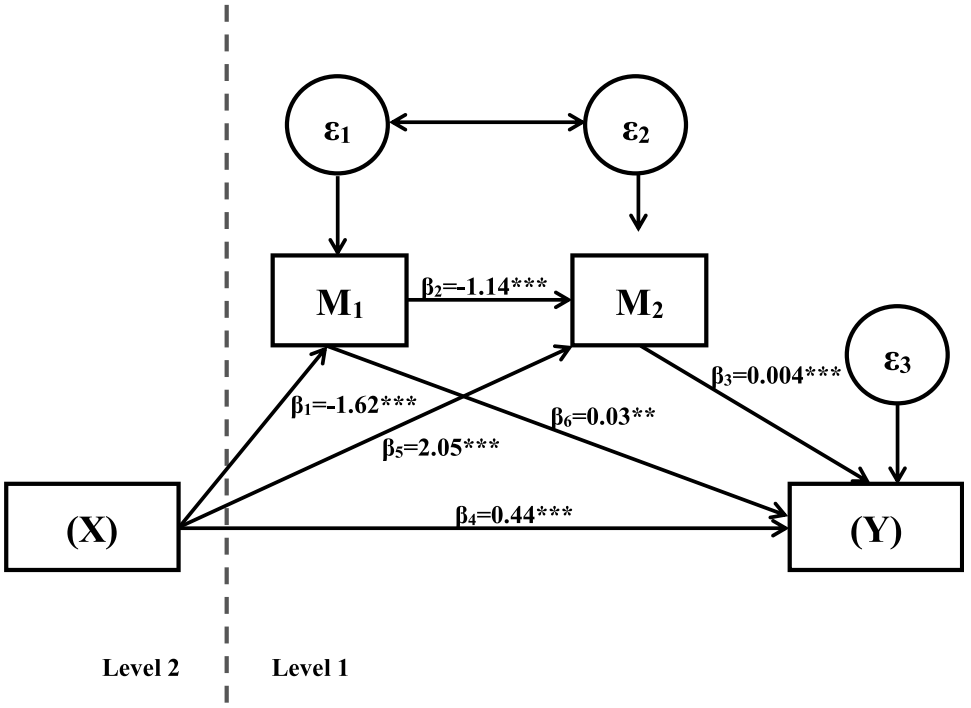

FIGURE 2. Generalized multilevel structural equation modeling to estimate coefficients for depression on therapy group (β_1), ART adherence on therapy group (β_5), and ART adherence on depression (β_2), as well as coefficient for viral suppression on depression (β_6), viral suppression on ART adherence (β_3), and viral suppression on therapy group (β_4), while taking into account the nesting of the data into therapy groups. All models included time and therapy group and its interaction. Arrows denote associations; ε in circles represents error terms for each of the outcome (Y) and mediators (M1, M2) regressions. X, therapy group (group support psychotherapy coded 1, group HIV education coded 0); M1, depression symptoms; M2, ART adherence; ART, antiretroviral therapy; Y, viral suppression.

TABLE 1. Cross-Sectional Direct, Indirect, and Total Effects of Group Support Psychotherapy Through Depression and ART Adherence on Viral Suppression

	β	SE	Bootstrapped 95% CI	*p*
Baseline				
Indirect effects through adherence	−0.010	0.005	−0.020 to 0.0001	.053
Indirect effects through depression	0.013	0.007	−0.001 to 0.027	.059
Indirect effects through depression and adherence	0.003	0.01	−0.014 to 0.02	.723
Total indirect effects	−0.470	0.214	−0.889 to −0.051	.028
Total effects	−1.052	0.359	−1.76 to −0.348	.003
12 mo after treatment				
Indirect effects through adherence	−0.0014	0.004	−0.01 to 0.006	.730
Indirect effects through depression	−0.038	.011381	−0.060 to −0.015	.001
Indirect effects through depression and adherence	−0.039	0.012	−0.063 to −0.015	.001
Total indirect effects	1.336	0.215	0.915 to 1.756	<.001
Total effects	1.184	0.358	0.48 to 1.89	.001
24 mo after treatment				
Indirect effects through adherence	0.007	0.005	−0.002 to 0.016	.124
Indirect effects through depression	−0.089	0.023	−0.135 to −0.043	<.001
Indirect effects through depression and adherence	−0.081	0.024	−0.128 to −0.035	.001
Total indirect effects	3.14	0.226	2.69 to 3.58	<.001
Total effects	3.421	0.372	2.69 to 4.15	<.001

ART = antiretroviral therapy; SE = standard error.

TABLE 2. Baseline Study Population Characteristics

Variable	GSP (n = 578), n (%)	GHE (n = 562), n (%)	Cluster-Adjusted χ^2 or t Test
Age, mean (SD), y	38.85 (10.44)	38.06 (11.50)	−0.58
Sex			
Female	317 (54.84)	295 (52.49)	0.41
Male	261 (45.16)	267 (47.51)	
Educational background			
Primary education or lower	503 (87.02)	480 (85.41)	0.27
Secondary education or higher	75 (12.98)	82 (14.59)	
Occupational status			
Not employed	221 (38.24)	184 (32.74)	
Employed	49 (8.48)	64 (11.39)	0.27
Peasant farmer	308 (53.29)	314 (55.87)	
Relationship status			
Never married	57 (9.86)	94 (16.73)	
Married or living with partner	422 (73.01)	394 (70.11)	3.52
Separated or divorced	44 (7.61)	43 (7.65)	
Widowed	55 (9.52)	31 (5.52)	
Function scores β, mean (SD)	4.35 (2.83)	5.56 (2.86)	1.58
Viral load			
Detectable (≥1000 viral copies/ml)	69 (11.94)	70 (12.46)	
Undetectable (<1000 viral copies/ml)	509 (88.06)	492 (87.54)	0.01
Adherence rate to ART			
<95%	155 (26.82)	105 (18.68)	1.57
≥95%	423 (73.18)	457 (81.32)	

GSP = group support psychotherapy; GHE = group HIV education; SD = standard deviation; ART = antiretroviral therapy.

follow-up assessments. Four hundred fifty of 578 GSP (78%) and 502 of 562 GHE (89%) participants attended all eight group sessions. Details of group session attendance by intervention group have been included in Supplemental Digital Content 1, http://links.lww.com/PSYMED/A866. Comparisons of baseline variables between the treatments arms are shown in Table 2. More detail is included in Supplemental Digital Content 3, Table 1, http://links.lww.com/PSYMED/A868. Attrition was greater in the GHE than GSP group at 24-month follow-up (84 [15%] versus 43 [7%]). In comparison to study completers, noncompleters were more likely to be male (56% versus 25%), had more viral nonsuppression (42% versus 30%), less suicide risk (72% versus 56%), and more hazardous alcohol consumption at baseline (40% versus 29%; Supplementary Digital Content 1, http://links.lww.com/PSYMED/A866).

By the 24-month follow-up study visit, we had recorded 89 serious AEs in 49 participants. These included 25 suicide attempts, 35 hospital admissions, and 29 deaths. Four of the deaths were completed suicides (GSP, 2; GHE, 2), and 25 were medical related deaths (GSP, 17; GHE, 8). All the 25 study participants who attempted suicide were referred to the district hospital or health centers for management. However, of these, only 12 had the resources to access hospital care. The rest were kept under close observation by relatives, caregivers, and lay health workers who made weekly home visits. AEs reported by 24 months after the end of treatment are summarized in Supplemental Digital Content 1, http://links.lww.com/PSYMED/A866.

Depression Cases

Fewer GSP than GHE participants met the criteria for major depression at 6 months (2% versus 30%; adjusted odds ratio [aOR] = 0.013, 95% confidence interval [CI] = 0.004–0.035), 12 months (2% versus 41%; aOR = 0.011, 95% CI = 0.004–0.029), 18 months (1% versus 29%; aOR = 0.013, 95% CI = 0.004–0.036), and 24 months (1% versus 25%; aOR = 0.002, 95% CI = 0.0002–0.018). See detailed results in Supplemental Digital Content 3, Table 2, http://links.lww.com/PSYMED/A868. Figure 3 in Supplemental

TABLE 3. Indirect and Total Effects of Group Support Psychotherapy Through Depression and ART Adherence at 12 Months (T2) on Viral Suppression at 24 Months (T3)

	β	SE	Bootstrapped 95% CI	p
Intervention → depression (T2) → adherence (T3)				
Indirect effects through depression	1.38	0.022	0.943 to 1.807	<.001
Total effects	3.06	0.976	1.154 to 4.983	.002
Intervention →depression (T2) → viral suppression (T3)				
Indirect effects through depression	−0.038	0.0114	−0.060 to −0.015	.001
Total effects	0.240	0.252	−0.252 to 0.735	.339
Intervention →adherence (T2) → viral suppression (T3)				
Indirect effects through adherence	−0.0014	0.004	−0.01 to 0.006	.730
Total effects	0.277	0.250	−0.214 to 0.768	.269
Intervention→ depression (T2) → adherence (T2) → viral suppression (T3)				
Indirect effects through depression and adherence	−0.039	0.012	−0.063 to −0.015	.001
Total indirect effects	1.396	0.214	0.975 to 1.816	<.001
Total effects	1.674	0.366	0.955 to 2.393	<.001

ART = antiretroviral therapy; SE = standard error; CI = confidence interval.

Digital Content 4, http://links.lww.com/PSYMED/A869, illustrates the multilevel mixed-effects regression model of GSP effects on depression using raw data (complete cases) adjusted for baseline employment, marital status, function scores, and ART adherence.

Function Scores

GSP participants had higher function scores than those receiving GHE at 6 months (mean [standard deviation {SD}] = 9.87 [0.86] versus 6.83 [2.85]; β =4.10, 95% CI = 3.75–4.44), 12 months (mean [SD] = 9.85 [0.76] versus 5.94 [2.94]; β =5.07, 95% CI = 4.71–5.43), 18 months (mean [SD] = 9.88 [0.82] versus 6.18 [2.86]; β =4.82, 95% CI = 4.48–5.16), and 24 months (mean [SD] = 9.99 [0.47] versus 6.59 [3.24]; β =4.49, 95% CI = 4.13–4.86). See detailed results in Supplemental Digital Content 3, Table 3, http://links.lww.com/PSYMED/A868. Figure 4 in Supplemental Digital Content 4, http://links.lww.com/PSYMED/A869, illustrates the multilevel mixed-effects regression model of GSP effects on functioning using raw data (complete cases) adjusted for baseline employment, marital status, and ART adherence.

ART Adherence

More GSP than GHE participants reported ≥95% adherence rates at 12 months (94% versus 86%; aOR = 7.01, 95% CI = 3.10–18.81), 18 months (97% versus 84%; aOR = 58.14, 95% CI = 16.64–203.16), and 24 months (96% versus 88%; aOR = 20.88, 95% CI = 5.78–75.33). See detailed results in Supplemental Digital Content 3, Table 2, http://links.lww.com/PSYMED/A868. Figure 1 in Supplemental Digital Content 4, http://links.lww.com/PSYMED/A869, illustrates the multilevel mixed-effects regression model of GSP effects on ART adherence using raw data (complete cases) adjusted for baseline employment, marital status, and function scores.

Viral Suppression

The proportion of study participants with viral suppression was comparable between the two groups 12 months after treatment (89% versus 84%; aOR = 1.08, 95% CI = 0.57–2.02). However, 24 months after treatment, the GSP group had a significantly greater proportion of participants with viral suppression compared with the GHE group (96% versus 88. %; aOR = 3.38, 95% CI = 1.02–11.02) See detailed results in Supplemental Digital Content 3, Table 2, http://links.lww.com/PSYMED/A868. Figure 2 in Supplemental Digital Content 4, http://links.lww.com/PSYMED/A869, illustrates the multilevel mixed-effects regression model of GSP effects on viral suppression using raw data (complete cases) adjusted for baseline employment, marital status, function scores, and ART adherence.

The Relationship Between Therapy Groups and Viral Suppression at 24 Months Through Sequential Changes in Depression and ART Adherence at 12 Months

Sequential mediation analyses indicated the indirect effects through sequential changes in depression and ART adherence at 12 months in the relationship between GSP and viral suppression at 24 months were small but significant (β = −0.039, 95% CI = −0.063 to −0.015). On addition of the indirect effects through depression in the relationship between therapy group and ART adherence, the total indirect effects through depression and ART adherence at 12 months (β = 1.396, 95% CI = 0.975–1.816) became large and significant indicating that the improvement in ART adherence through reduction in depression contributes greatly to the mediation effects through which GSP leads to viral suppression. The total effect of GSP on participants' viral suppression at 24 months after treatment remained significant in this sequential model (β = 1.67, 95% CI = 0.69–2.35) although less than what we observed in the cross-sectional mediation model (β = 3.42, 95% CI = 2.69–4.15). Table 3 shows the detail of total and indirect effects of GSP through sequential changes in depression and ART adherence at 12 months on viral suppression at 24 months.

DISCUSSION

This study examined the long-term effect of culturally sensitive GSP delivered by lay health workers compared with an active comparison, GHE, on depression and HIV treatment outcomes. The intervention had significant short-term effects on depression and functioning, which were sustained in the long term. These results were generally consistent with our prior study of GSP delivered by diploma-level mental health workers, which showed similar improvements of depression and functioning overtime (23). Studies demonstrating positive long-term effects of psychological interventions for depression are limited (49,50). Indeed, the literature has generally shown diminishing effects of psychological treatments for depression with time (51). The striking sustained reductions in depression speak to the potential utility of GSP and require replication in other low-resource settings.

The beneficial effects of GSP may be attributed to its active ingredients (emotional and social support, positive coping skills, and income-generating skills), which are potent buffers against depression. GSP allows participants to interact with one another as they execute their livelihood projects (30). Although participants no longer receive guidance from a trained LHW after the completion of GSP, they continue to receive social support from one another, which may buffer group members from developing depression in the long term (30). Furthermore, the stress-buffering model asserts that social support mitigates the relation between stressful life events and depression (52,53). It is plausible that increased social support, connections, and networks may mitigate the impact of various stressors and reduce depression (54).

The improvement in depression and functioning observed in GHE groups could be explained by therapeutic factors common to both interventions, such as a supportive environment, and therapeutic alliance, which generate positive feelings. However, because GHE lacks the active elements of GSP, such as opportunity to express emotions, and acquisition and practice of positive coping skills and livelihood skills, positive feelings generated might not be sustained.

In keeping with findings from similar studies of psychological interventions for HIV-related depression (20), our study showed that a reduction in depression was accompanied by improved ART adherence in the long term. Two years after the end of interventions, the proportion of those with self-reported ≥95% ART adherence had increased by almost 22% in the GSP group compared with only 7% in the control group. Some prior studies of cognitive-behavioral therapy integrated with adherence counseling for depression treatment showed sustained improvements in ART adherence (17,55), whereas others did not (56). In these studies, the relationship between cognitive-behavioral therapy integrated with adherence counseling, depression, and ART adherence was not assessed using mediation analyses.

Intensive adherence counseling is part of routine HIV care in Uganda (57), which may explain the relatively high baseline adherence rate of our study population. Addition of depression treatment with GSP to routine HIV care in Ugandan HIV clinics may be necessary to achieve optimal HIV treatment outcomes.

Our mediation analyses indicate that decreased depression (over and above improving adherence) led to improved viral suppression even after adjusting for self-reported adherence. This finding is in keeping with findings from previous studies that have demonstrated strong links between stress and HIV viral replication (58–60). Cole et al. (58) showed that autonomic nervous system (ANS) neurotransmitter norepinephrine could accelerate HIV-1 replication and documented that the relationship between psychological risk factors, such as social inhibition and viral nonsuppression, was mediated by heightened ANS activity (60).

Taken together, these data suggest that it is plausible that the sustained reduction in depression we observed among GSP participants could have led to a reduction in ANS activity and enhanced viral load suppression. The impact of a first-line psychological intervention on biological indicators of immunopathogenesis in HIV-1 infection has been demonstrated in some (61–64) but not all analyses (65). Moreover, prior studies have identified greater rates of ART discontinuation in people with depression (66).GSP may also promote ART persistence over and above improving adherence, which could be tested in future studies.

Several limitations of this study need to be considered. First, outcome assessors were not blinded; therefore, detection bias could have affected the outcome measurement. Second, the diagnostic criteria of the depression module of the Mini-International Neuropsychiatric Interview could not rule out the presence of individuals with substance-related depression or bipolar depression. Third, the measure for ART adherence was not validated, even though such single-item self-report adherence measures have been found to be useful for assessing adherence in clinical care and are recommended in low resource settings where more complex instruments may be impractical (67).

Furthermore, the retrospective use of conservative viral load suppression threshold results from clinical files, which are only taken once a year, might not represent an accurate measure of viral loads for the assessment period. However, the study could not afford viral load measures, which cost up to$400 per person. As such, our mediators may be affected by measurement error and misclassification. These concerns, however, would be expected to bias the mediation effects toward the null. The mediation effects we observe may be even stronger in the absence of measurement error and misclassification.

Fourth, mediation analyses assumed sequential ignorability; that is, the absence of unobserved confounders of the (i) exposure-outcome and (ii) exposure-mediator relationships and (iii) the absence of unobserved (baseline or postexposure) confounders of the mediator-outcome relationship. Fifth, attrition at 24 months was significantly more common among GHE than GSP participants. Given that this attrition was associated with detectable viral load at baseline, the observed GSP effects on viral load maybe biased away from the null. Lastly, LHWs were instructed to conduct home visits to reengage participants who missed a group session and to mobilize them to return for their follow-up assessments, but we do not have a record of these home visit contacts. If home visits were more common among GSP than GHE participants, this could bias the treatment effects. Nonetheless, the present study adds to the literature a potentially useful first-line psychological treatment for depression, targeting rural and socially disadvantaged communities (68).

The limitations discussed are balanced by several strengths. First, it was a cluster randomized trial with a real-world sample that was representative of treatment-seeking rural PLWH in northern Uganda. Second, the study did not exclude individuals addicted to alcohol; such individuals are often screened out of randomized trials. Third, the study had a 2-year follow-up period and achieved high treatment adherence rates and retention numbers, which demonstrate acceptability and sustainability of intervention effects.

Fourth, this trial is the first in sub-Saharan Africa to compare a group psychotherapeutic intervention with an active comparison group intervention to control for the effects of common therapeutic factors. Previous researchers have recommended the use of active comparison groups when evaluating the effectiveness of newly developed therapies. The active comparison group omits the unique ingredients of the new therapy while possessing the common factors (e.g., therapeutic alliance) in equal measure (69). Other control conditions previously studied, such as sending a letter to the medical provider, emphasizing the need for depression treatment, a single session of adherence counseling, and waiting-list controls, might be biased because of resentment at not receiving an intervention, changes in disease state over time, or decreased engagement in care (70). Lastly, GSP is a highly cost-effective intervention. Prior estimates of cost-effectiveness to prevent 1-year lost to depression equates to $13 using GSP compared with $26 using group education sessions.

CONCLUSIONS

GSP improved viral suppression through the sequential reduction of depression and improvement in ART adherence. These results highlight the need to integrate GSP into existing HIV treatment platforms to reduce the burden of depression and improve HIV treatment outcomes.

Source of Funding and Conflicts of Interest: The SEEK-GSP study is funded by Grand Challenges Canada (grant no. 0770-05) and the MQ Mental Health Fellowship Award (grant no. MQ15FIP100024). All authors declare no competing interests.

Disclaimer: The views expressed are those of the authors and do not necessarily represent the views of the US government or any agency thereof.

Contributors: E.N.-M., K.W., J.O., S.M., S.N., R.M., J.B., E.J.M., and J.B.N. conceptualized the study, and E.N.-M. sought and obtained funding. E.J.M. and O.H. conducted statistical analyses. E.N.-M., C.M.S. and J.O. managed the literature searches. E. N.-M., C.M.S., E.J.M., and J.B.N. wrote the initial manuscript. S.M., R.M., C.M.S., M.E., N.E.M., and J.B.N. revised the manuscript critically for important intellectual content. All authors contributed to the final manuscript.

Open Access publication for this article, which is part of a special themed issue of Psychosomatic Medicine, was funded by the National Institute of Mental Health.

REFERENCES

1. Chibanda D, Benjamin L, Weiss HA, Abas M. Mental, neurological, and substance use disorders in people living with HIV/AIDS in low-and middle-income countries. J Acquir Immune Defic Syndr 2014;67:S54–67.

2. Bernard C, Dabis F, de Rekeneire N. Prevalence and factors associated with depression in people living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. PloS One 2017;12:e0181960.
3. Roberts B, Ocaka KF, Browne J, Oyok T, Sondorp E. Factors associated with posttraumatic stress disorder and depression amongst internally displaced persons in northern Uganda. BMC Psychiatry 2008;8:38.
4. World Health Organization. Policy brief: consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: what's new. Published November 2015. Available at: https://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf. Accessed June 18, 2020.
5. Parcesepe AM, Bernard C, Agler R, Ross J, Yotebieng M, Bass J, et al. Mental health and HIV: research priorities related to the implementation and scale up of 'treat all'in sub-Saharan Africa. J Virus Erad 2018;4(Suppl 2):16–25.
6. Cook JA, Grey D, Burke J, Cohen MH, Gurtman AC, Richardson JL, et al. Depressive symptoms and AIDS-related mortality among a multisite cohort of HIV-positive women. Am J Public Health 2004;94:1133–40.
7. Patel R, Kassaye S, Gore-Felton C, Wyshak G, Kadzirange G, Woelk G, et al. Quality of life, psychosocial health, and antiretroviral therapy among HIV-positive women in Zimbabwe. AIDS Care 2009;21:1517–27.
8. Pence BW, Mills JC, Bengtson AM, Gaynes BN, Breger TL, Cook RL, et al. Association of increased chronicity of depression with HIV appointment attendance, treatment failure, and mortality among HIV-infected adults in the United States. JAMA Psychiat 2018;75:379–85.
9. Cristea IA, Karyotaki E, Hollon SD, Cuijpers P, Gentili C. Biological markers evaluated in randomized trials of psychological treatments for depression: a systematic review and meta-analysis. Neurosci Biobehav Rev 2019;101:32–44.
10. Patel S, Schechter MT, Sewankambo NK, Atim S, Kiwanuka N, Spittal PM. Lost in transition: HIV prevalence and correlates of infection among young people living in post-emergency phase transit camps in Gulu District, Northern Uganda. PloS One 2014;9:e89786.
11. Wagner GJ, McBain RK, Akena D, Ngo V, Nakigudde J, Nakku J, et al. Maternal Depression Treatment in HIV (M-DEPTH): study protocol for a cluster randomized controlled trial. Medicine (Baltimore) 2019;98:e16329.
12. Joska JA, Andersen LS, Smith-Alvarez R, Magidson J, Lee JS, O'Cleirigh C, et al. Nurse-delivered cognitive behavioral therapy for adherence and depression among people living with HIV (the Ziphamandla study): protocol for a randomized controlled trial. JMIR Res Protoc 2020;9:e14200.
13. Andersen LS, Magidson JF, O'Cleirigh C, Remmert JE, Kagee A, Leaver M, et al. A pilot study of a nurse-delivered cognitive behavioral therapy intervention (Ziphamandla) for adherence and depression in HIV in South Africa. J Health Psychol 2018;23:776–87.
14. Petersen I, Hanass Hancock J, Bhana A, Govender K. A group-based counselling intervention for depression comorbid with HIV/AIDS using a task shifting approach in South Africa: a randomized controlled pilot study. J Affect Disord 2014;158:78–84.
15. Stockton MA, Udedi M, Kulisewa K, Hosseinipour MC, Gaynes BN, Mphonda SM, et al. The impact of an integrated depression and HIV treatment program on mental health and HIV care outcomes among people newly initiating antiretroviral therapy in Malawi. PLoS One 2020;15:e0231872.
16. Safren SA, O'Cleirigh C, Andersen LS, Magidson JF, Lee JS, Bainter SA, et al. Treating depression and improving adherence in HIV care with task-shared cognitive behavioural therapy in Khayelitsha, South Africa: a randomized controlled trial. J Int AIDS Soc 2021;24:e25823.
17. Nakimuli-Mpungu E, Musisi S, Smith CM, Von Isenburg M, Akimana B, Shakarishvili A, et al. Mental health interventions for persons living with HIV in low-and middle-income countries: a systematic review. J Int AIDS Soc 2021;24:e25722.
18. Safren SA, O'cleirigh C, Tan JY, Raminani SR, Reilly LC, Otto MW, et al. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. Health Psychol 2009;28:1–10.
19. Simoni JM, Wiebe JS, Sauceda JA, Huh D, Sanchez G, Longoria V, et al. A preliminary RCT of CBT-AD for adherence and depression among HIV-positive Latinos on the U.S.-Mexico border: the Nuevo Dia study. AIDS Behav 2013;17:2816–29.
20. Sin NL, DiMatteo MR. Depression treatment enhances adherence to antiretroviral therapy: a meta-analysis. Ann Behav Med 2014;47:259–69.
21. Passchier RV, Abas MA, Ebuenyi ID, Pariante CM. Effectiveness of depression interventions for people living with HIV in sub-Saharan Africa: a systematic review & meta-analysis of psychological & immunological outcomes. Brain Behav Immun 2018;73:261–73.
22. Nakimuli-Mpungu E, Wamala K, Okello J, Alderman S, Odokonyero R, Musisi S, et al. Outcomes, feasibility and acceptability of a group support psychotherapeutic intervention for depressed HIV affected Ugandan adults: a pilot study. J Affect Disord 2014;166:144–50.
23. Nakimuli-Mpungu E, Wamala K, Okello J, Alderman S, Odokonyero R, Mojtabai R, et al. Group support psychotherapy for depression treatment in people with HIV/AIDS in northern Uganda: a single-centre randomised controlled trial. Lancet HIV 2015;2:e190–9.
24. Nakimuli-Mpungu E, Wamala K, Okello J, Ndyanabangi S, Kanters S, Mojtabai R, et al. Process evaluation of a randomized controlled trial of group support psychotherapy for depression treatment among people with HIV/AIDS in Northern Uganda. Community Ment Health J 2017;53:991–1004.
25. Nakimuli-Mpungu E, Musisi S, Wamala K, Okello J, Ndyanabangi S, Birungi J, et al. Effectiveness and cost-effectiveness of group support psychotherapy delivered by trained lay health workers for depression treatment among people with HIV in Uganda: a cluster-randomised trial. Lancet Glob Health 2020;8:e387–98.
26. Nakimuli-Mpungu E, Musisi S, Wamala K, Okello J, Ndyanabangi S, Birungi J, et al. Recruitment and baseline characteristics of participants in the social, emotional, and economic empowerment through knowledge of group support psychotherapy study (SEEK-GSP): cluster randomized controlled trial. JMIR Res Protoc 2019;8:e11560.
27. Nakimuli-Mpungu E, Musisi S, Wamala K, Okello J, Ndyanabangi S, Mojtabai R, et al. The effect of group support psychotherapy delivered by trained lay health workers for depression treatment among people with HIV in Uganda: protocol of a pragmatic, cluster randomized trial. JMIR Res Protoc 2017;6:e250.
28. Kleinman A, Eisenberg L, Good B. Culture, illness, and care: clinical lessons from anthropologic and cross-cultural research. Ann Intern Med 1978;88:251–8.
29. Ayonrinde O. Importance of cultural sensitivity in therapeutic transactions. Dis Manag Health Outcomes 2003;11:233–48.
30. Nakimuli-Mpungu E, Wamala K, Okello J, Alderman S, Odokonyero R, Musisi S, et al. Developing a culturally sensitive group support intervention for depression among HIV infected and non-infected Ugandan adults: a qualitative study. J Affect Disord 2014;163:10–7.
31. Gladden J. The coping skills of east African refugees: a literature review. Refugee Surv Q 2012;31:177–96.
32. Delgadillo J, Groom M. Using psychoeducation and role induction to improve completion rates in cognitive behavioural therapy. Behav Cogn Psychother 2017;45:170–84.
33. Vinogradov S, Yalom ID. Concise Guide to Group Psychotherapy. Washington, DC: American Psychiatric Pub; 1989.
34. Brandler S, Roman CP. Group Work: Skills and Strategies for Effective Interventions. London, United Kingdom: Routledge; 2012.
35. Carrico AW, Antoni MH, Durán RE, Ironson G, Penedo F, Fletcher MA, et al. Reductions in depressed mood and denial coping during cognitive behavioral stress management with HIV-positive gay men treated with HAART. Ann Behav Med 2006;31:155–64.
36. Lund C, De Silva M, Plagerson S, Cooper S, Chisholm D, Das J, et al. Poverty and mental disorders: breaking the cycle in low-income and middle-income countries. Lancet 2011;378:1502–14.
37. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59:22–33.
38. Nakimuli-Mpungu E, Alderman S, Kinyanda E, Allden K, Betancourt TS, Alderman JS, et al. Implementation and scale-up of psycho-trauma centers in a post-conflict area: a case study of a private-public partnership in northern Uganda. PLoS Med 2013;10:e1001427.
39. Patterson WM, Dohn HH, Bird J, Patterson GA. Evaluation of suicidal patients: the SAD PERSONS scale. Psychosomatics 1983;24:343–5, 348.
40. Von Hippel PT. How many imputations do you need? A two-stage calculation using a quadratic rule. Sociol Methods Res 2020;49:699–718.
41. Demirtas H, Freels SA, Yucel RM. Plausibility of multivariate normality assumption when multiply imputing non-Gaussian continuous outcomes: a simulation assessment. J Stat Comput Simul 2008;78:69–84.
42. Lee KJ, Carlin JB. Multiple imputations for missing data: fully conditional specification versus multivariate normal imputation. Am J Epidemiol 2010;171:624–32.
43. Enders CK. Applied Missing Data Analysis. New York: Guilford Press; 2010.
44. Hayes RJ, Moulton LH. *Cluster randomised trials*. *Chapman and Hall/CRC*. Boca Raton, FL: CRC Press Online; 2017:1–398.
45. Rabe-Hesketh S, Skrondal A, Zheng X. Multilevel structural equation modeling. In: Handbook of Latent Variable and Related Models. Amsterdam, the Netherlands, North-Holland; 2007:209–27.
46. Hayes AF. Beyond Baron and Kenny: statistical mediation analysis in the new millennium. Commun Monogr 2009;76:408–20.
47. Mitchell MA, Maxwell SE. A comparison of the cross-sectional and sequential designs when assessing longitudinal mediation. Multivar Behav Res 2013;48:301–39.
48. Hayes AF, Scharkow M. The relative trustworthiness of inferential tests of the indirect effect in statistical mediation analysis: does method really matter? Psychol Sci 2013;24:1918–27.
49. Sherr L, Clucas C, Harding R, Sibley E, Catalan J. HIV and depression—a systematic review of interventions. Psychol Health Med 2011;16:493–527.
50. Spies G, Asmal L, Seedat S. Cognitive-behavioural interventions for mood and anxiety disorders in HIV: a systematic review. J Affect Disord 2013;150:171–80.
51. Karyotaki E, Smit Y, Beurs DP, Henningsen KH, Robays J, Huibers MJH, et al. The long-term efficacy of acute-phase psychotherapy for depression:a meta-analysis of randomized trials. Depress Anxiety 2016;33:370–83.
52. Cohen S, Wills TA. Stress, social support, and the buffering hypothesis. Psychol Bull 1985;98:310–57.
53. Stein ER, Smith BW. Social support attenuates the harmful effects of stress in healthy adult women. Soc Sci Med 2015;146:129–36.

54. Berkman LF, Glass T, Brissette I, Seeman TE. From social integration to health: Durkheim in the new millennium. Soc Sci Med 2000;51:843–57.
55. Safren SA, Bedoya CA, O'Cleirigh C, Biello KB, Pinkston MM, Stein MD, et al. Cognitive behavioural therapy for adherence and depression in patients with HIV: a three-arm randomised controlled trial. Lancet HIV 2016;3:e529–38.
56. Safren SA, O'Cleirigh CM, Bullis JR, Otto MW, Stein MD, Pollack MH. Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected injection drug users: a randomized controlled trial. J Consult Clin Psychol 2012;80:404–15.
57. Ministry of Health. 2020 Consolidated guidelines for prevention and treatment of HIV/AIDS. Available at: https://uac.go.ug/sites/default/files/Consolidated%20HIV%20Guidelines%202020.pdf. Accessed June 18, 2020.
58. Cole SW, Korin YD, Fahey JL, Zack JA. Norepinephrine accelerates HIV replication via protein kinase A–dependent effects on cytokine production. J Immunol 1998;161:610–6.
59. Cole SW, Naliboff BD, Kemeny ME, Griswold MP, Fahey JL, Zack JA. Impaired response to HAART in HIV-infected individuals with high autonomic nervous system activity. Proc Natl Acad Sci 2001;98:12695–700.
60. Cole SW, Kemeny ME, Fahey JL, Zack JA, Naliboff BD. Psychological risk factors for HIV pathogenesis: mediation by the autonomic nervous system. Biol Psychiatry 2003;54:1444–56.
61. Petrie KJ, Fontanilla I, Thomas MG, Booth RJ, Pennebaker JW. Effect of written emotional expression on immune function in patients with human immunodeficiency virus infection: a randomized trial. Psychosom Med 2004;66:272–5.
62. Antoni MH, Carrico AW, Durán RE, Spitzer S, Penedo F, Ironson G, et al. Randomized clinical trial of cognitive behavioral stress management on human immunodeficiency virus viral load in gay men treated with highly active antiretroviral therapy. Psychosom Med 2006;68:143–51.
63. Creswell JD, Myers HF, Cole SW, Irwin MR. Mindfulness meditation training effects on CD4+ T lymphocytes in HIV-1 infected adults: a small randomized controlled trial. Brain Behav Immun 2009;23:184–8.
64. Tsai AC, Weiser SD, Petersen ML, Ragland K, Kushel MB, Bangsberg DR. A marginal structural model to estimate the causal effect of antidepressant medication treatment on viral suppression among homeless and marginally housed persons with HIV. Arch Gen Psychiatry 2010;67:1282–90.
65. Tsai AC, Karasic DH, Hammer GP, Charlebois ED, Ragland K, Moss AR, et al. Directly observed antidepressant medication treatment and HIV outcomes among homeless and marginally housed HIV-positive adults: a randomized controlled trial. Am J Public Health 2013;103:308–15.
66. Carrico AW, Riley ED, Johnson MO, Charlebois ED, Neilands TB, Remien RH, et al. Psychiatric risk factors for HIV disease progression: the role of inconsistent patterns of anti-retroviral therapyutilization. J Acquir Immune Defic Syndr 2011;56:146–50.
67. Feldman BJ, Fredericksen RJ, Crane PK, Safren SA, Mugavero MJ, Willig JH, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav 2013;17:307–18.
68. World Health Organization. WHO mhGAP Guideline Update. Update of the Mental Health Gap Action Programme (mhGAP) Guideline for Mental, Neurological and Substance Use Disorders. Published May 2015. Available at: https://apps.who.int/iris/handle/10665/204132. Accessed June 18, 2020.
69. Safer DL, Hugo EM. Designing a control for a behavioral group therapy. Behav Ther 2006;37:120–30.
70. Mohr DC, Spring B, Freedland KE, Beckner V, Arean P, Hollon SD, et al. The selection and design of control conditions for randomized controlled trials of psychological interventions. Psychother Psychosom 2009;78:275–84.