

A Randomized Clinical Trial Showing Persisting Reductions in Depressive Symptoms in HIV-Infected Rural Adults Following Brief Telephone-Administered Interpersonal Psychotherapy

Timothy G. Heckman, PhD¹ • John C. Markowitz, MD² • Bernadette D. Heckman, PhD¹ • Henok Woldu, BS¹ • Timothy Anderson, PhD³ • Travis I. Lovejoy, PhD⁴ • Ye Shen, PhD¹ • Mark Sutton, BA² • William Yarber, HSD⁵

Published online 25 January 2018

© Society of Behavioral Medicine 2018. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

Abstract

Background Rural areas account for 5% to 7% of all HIV infections in the USA, and rural people living with HIV (PLHIV) are 1.3 times more likely to receive a depression diagnosis than their urban counterparts. A previous analysis from our randomized clinical trial found that nine weekly sessions of telephone-administered interpersonal psychotherapy (tele-IPT) reduced depressive symptoms and interpersonal problems in rural PLHIV from pre-intervention through postintervention significantly more than standard care but did not increase perceived social support compared to standard care.

Purpose To assess tele-IPT's enduring effects at 4- and 8-month follow-up in this cohort.

Methods Tele-IPT's long-term depression treatment efficacy was assessed through Beck Depression Inventory self-administrations at 4 and 8 months. Using intention-to-treat and completer-only approaches, mixed models

repeated measures, and Cohen's *d* assessed maintenance of acute treatment gains.

Results Intention-to-treat analyses found fewer depressive symptoms in tele-IPT patients than standard care controls at 4 ($d = .41$; $p < .06$) and 8-month follow-up ($d = .47$; $p < .05$). Completer-only analyses found similar patterns, with larger effect sizes. Tele-IPT patients used crisis hotlines less frequently than standard care controls at postintervention and 4-month follow-up ($p_s < .05$).

Conclusions Tele-IPT provides longer term depression relief in depressed rural PLHIV. This is also the first controlled trial to find that IPT administered over the telephone provides long-term depressive symptom relief to any clinical population.

Trial Registration: ClinicalTrials.gov Identifier: NCT02299453.

Keywords HIV • Tele-IPT • Depression • Tele-therapy • Rural

Introduction

Rural people living with HIV (PLHIV) urgently need easily accessible and cost-effective distance-delivered psychotherapies. More than 52,000 persons were living with HIV in the rural USA as of 2014 (1). Compared to urban PLHIV, rural PLHIV are 1.3 times more likely to receive a depression diagnosis than their metropolitan counterparts (2), less likely to have seen a mental health provider over the past year (3), and make fewer visits to mental health professionals (3).

Timothy G. Heckman
heckman@uga.edu

¹ Department of Health Promotion and Behavior, College of Public Health, University of Georgia, Athens, GA

² Columbia University College of Physicians & Surgeons, New York, NY

³ Department of Psychology, Ohio University, Athens, OH, USA

⁴ Oregon Health and Science University, Portland, OR, USA

⁵ Department of Applied Health and Science, Indiana University, Bloomington, IN USA

Meta-analyses and systematic reviews conclude that many psychological interventions, such as stress management, supportive interventions, and meditation—almost all of which have been evaluated using in-person formats—reduce depression in PLHIV, with cognitive-behavioral treatments being particularly beneficial (4–6). A small, but increasing, number of studies also shows that telephone-administered psychotherapies reduce depression in PLHIV (7–9), although null findings have also been reported (10). One study of PLHIV found that telephone-administered cognitive-behavioral therapy and face-to-face supportive therapy had comparable levels of therapeutic alliance and depression treatment efficacy but that ART adherence was greater in tele-cognitive behavioral therapy patients at follow-up than patients receiving in-person supportive therapy (11). Telephone-based depression treatments may be particularly helpful for PLHIV given low-attrition rates found in studies of telephone-based depression treatments for persons living with chronic health conditions (mean attrition rate = 7%) (12).

IPT is a particularly apt time-limited psychotherapy for rural PLHIV because it focuses on one's interpersonal context, enhancing interpersonal skills, and increasing social supports (13). IPT treats depressive symptoms by resolving a current interpersonal crisis related to the problem areas of role transition, interpersonal role dispute, grief, or interpersonal deficits. IPT has efficacy in treating Major Depressive Disorder (MDD) (14,15) and other mental health disorders, such as posttraumatic stress disorder (16) and eating disorders (17) and is an indicated treatment in mood disorder treatment guidelines. IPT's main treatment goals are to encourage the individual to master current social roles and ameliorate devolving interpersonal situations, thereby relieving depression. Although IPT has repeatedly been shown to provide long-term depressive symptom relief when administered to patients in-person (18–20), little is known about the *longer term* depression treatment efficacy of IPT administered via telephone.

We previously reported a randomized clinical trial showing that tele-IPT acutely reduced depressive symptoms and interpersonal problems in rural PLHIV significantly more than standard care (21). No research, however, has examined the enduring benefits of tele-IPT for depression in rural PLHIV with comorbid depression diagnoses—or indeed any treatment population for that matter. This paper reports on tele-IPT's ability to produce long-term persisting reductions in depression in a sample of 147 rural PLHIV. Administering depression assessments at 4- and 8-month follow-up to patients who previously completed preintervention and postintervention assessments (21), we hypothesized that acute reductions in depressive symptoms and interpersonal

problems would be maintained at longer term follow-up. Although our randomized clinical trial found no acute increases in social support between tele-IPT patients and standard care controls (21), we tested the possibility that increases in social support in tele-IPT patients might emerge over longer term follow-up as patients had additional time and opportunities to improve their social support resources and reduce interpersonal problems through skills acquired in tele-IPT, a pattern observed in previous IPT research (22).

Materials and Methods

Patients and Procedures

Having previously reported acute study outcomes (21), we describe only key clinical trial procedures here. Between August 2010 and December 2015, AIDS service organizations (ASOs) in 28 states and the Rural Center for AIDS Prevention (RCAP) distributed recruitment brochures to their rural clients living with HIV through various media. Patients enrolled into the clinical trial were from the states of Alabama, Arkansas, California, Colorado, Florida, Georgia, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Minnesota, Mississippi, Missouri, Montana, New Hampshire, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Vermont, and Virginia. The Institutional Review Boards of all participating institutions approved the project's protocol. Written informed consent was obtained from each individual study patient. No patients reported adverse events during the trial.

When potential study enrollees contacted the research office via a toll-free telephone number or project-specific e-mail address listed in recruitment materials, research staff provided information about the study, described the informed consent process, and gathered preliminary screening demographic data. County of residence was used to determine the individual's US Department of Agriculture's Urban-Rural Continuum Code (23). Telephone-based eligibility interviews administered the Primary Care Evaluation of Mental Disorders (PRIME-MD) (24) and the Modified Mini Mental State Examination (3MS) (25).

All patients were: (i) ≥ 18 years old; (ii) living with HIV/AIDS; (iii) residing in a county with a US Department of Agriculture Rural-Urban Continuum Code of "4" (nonmetropolitan county; population of 20,000 or more, adjacent to a metro area) through "9" (nonmetropolitan county; completely rural or less than 2,500 urban population, not adjacent to a metro area); (iv) diagnosed with DSM-IV MDD, MDD in Partial Remission, or Dysthymic Disorder based on the Mood Module of the PRIME-MD; and (v) intending to stay in their

current residence for ≥ 1 year. The only two exclusion criteria were: (i) neurocognitive impairment based on the telephone-administered Modified Mini Mental State Examination (scores < 70); and (ii) persons whose only depressive symptoms were attributable to an adjustment disorder (e.g., feeling sad, stressed, or hopeless after experiencing a specific stressful life event).

While mild-to-moderate neurocognitive disorders are common in PLHIV, persons with modified mini mental state examination scores of 70 or below would likely be experiencing levels of neurocognitive impairment that precluded them from participating fully in telephone-administered therapy. Alcohol or substance use disorders, active bipolar disorder, psychotic symptoms, or current receipt of psychotherapy or pharmacotherapy were not exclusion criteria. Although enrolling patients currently receiving psychotherapy and/or on pharmacotherapy complicated efforts to quantify tele-IPT's depression treatment efficacy, enrolling these individuals was deemed ethically necessary. Relatedly, because some patients were involved in ongoing therapy and/or pharmacotherapy, this clinical trial technically assessed the adjunctive benefits of tele-IPT above-and-beyond patients' ongoing treatments.

Assessment Methodology

Patients provided data on depressive symptoms, interpersonal problems, and social support at preintervention, postintervention, and 4-, and 8-month follow-up through self-administered surveys. Standard care controls completed postintervention and follow-up assessments coincident with their time-matched tele-IPT counterparts. All Cronbach alphas and test–retest reliability coefficients (r_{tt}) derive from current study data. Test–retest coefficients were calculated using preintervention and postintervention data from standard care controls who were expected to report few, if any, changes on these measures.

Beck Depression Inventory

The study's primary outcome measure, the 21-item Beck Depression Inventory-II (BDI-II), assessed cognitive, affective, and somatic symptoms of clinical depression during the past week (26). Self-report responses made along four severity levels ("0" to "3") yielded a total score from 0 to 63, with higher scores indicating greater depressive symptom severity. The scale demonstrated good internal consistency ($\alpha = .86$) and test–retest reliability, $r_{tt}(61) = .82, p < .001$.

Inventory of Interpersonal Problems

The 64-item, self-administered Inventory of Interpersonal Problems (IIPs) assessed severity levels of

interpersonal problems (27). Its 5-point scale (0 = "Not at all" to 4 "Extremely") describes experiences with a range of interpersonal problems. Total inventory scores summate the 64 items, with higher scores indicating more severe interpersonal problems. The scale showed good internal consistency ($\alpha = .93$) and test–retest reliability, $r_{tt}(61) = .81, p < .001$.

Provision of Social Relations Scale

The 15-item Provision of Social Relations Scale (PSRS) assessed perceived social support from family members and friends, with each item using a 5-point Likert scale (28). Higher scores indicated greater perceived social support. The scale demonstrated good internal consistency ($\alpha = .86$) and test–retest reliability, $r_{tt}(62) = .77, p < .001$.

Mental Health and Substance Use Services Utilization

Patients indicated whether, over the past month, they participated (yes/no) in self-help groups for problems related to mental health or alcohol/drug use (e.g., AIDS-specific support groups or 12-step programs). Patients also specified if they sought help from any of the following practitioners in the past year for problems related to mental health or alcohol/drug use (yes/no); psychiatrist; psychologist; social worker; counselor; minister/priest/rabbi; or psychiatric nurse. Patients reported whether they used a crisis hotline (yes/no) for problems related to mental health or alcohol/drug use in the past month. In preintervention assessments only, patients indicated if they had current prescriptions for antidepressant or anxiolytic medications (yes/no for each).

Intervention Conditions

After completing preintervention surveys, patients were assigned to one of two conditions using a computerized randomization module.

Standard Care Control

Standard care controls received no active study treatment but had access to community-based support services for PLHIV (e.g., AIDS-related support groups, 12-step programs, individual therapy, antidepressant medications). The study imposed no limitations on patients' use of outside psychosocial services but did assess use of these services.

Tele-Interpersonal Psychotherapy (tele-IPT) + Standard Care

Tele-IPT patients received nine weekly, 1-hour telephone IPT treatments (adapted from the "Manual for Interpersonal Therapy with Depressed HIV-Seropositive

Patients”) (29). All tele-IPT therapists were PhD-level clinical psychologists, licensed in one or more states, and experienced in administering treatments via telephone (including IPT, motivational interviewing, supportive-expressive therapy, coping effectiveness training) to individuals and/or groups living with HIV as part of other clinical trials. Sessions 1 and 2 began with patient-therapist introductions and an overview of therapy protocol. Tele-therapists and patients also explored patients’ depressive symptoms, defined the depressive disorder, reviewed current interpersonal relationships, and identified a problem relationship or circumstance that served as the treatment’s therapeutic focus. Tele-therapists framed each patient’s primary interpersonal concern in one of four focal areas: interpersonal role dispute (e.g., conflict with partner); role transition (e.g., loss of employment, moving from an urban to a rural environment); grief (e.g., death of loved one); or interpersonal sensitivities (e.g., chronic difficulties forming or maintaining close relationships). Sessions 3 through 9 addressed the interpersonal focus identified in Sessions 1 and 2. Sessions 8 and 9 addressed therapy termination and maintenance of treatment gains. Copies of the “Tele-IPT Intervention Manual” are available upon request.

Tele-IPT patients used the following protocol during therapy to optimize privacy and reduce the likelihood of technical complications: (i) the use of a private, television- and computer-free location for therapy; (ii) weekly therapy sessions were scheduled at times when no interruptions were anticipated; (iii) avoidance of call waiting, except in possible emergency situations; (iv) avoiding tele-therapy via cellphone while driving; (v) when possible, using traditional landline telephones to reduce the likelihood of “dropped” calls; (vi) avoiding use of the speakerphone feature; and (vii) if using a cell phone, ensuring a fully charged battery. Activities related to tele-therapist training and supervision are reported elsewhere (21).

During tele-IPT sessions, if a patient reported acute distress (e.g., threats to one’s self or others), tele-therapists followed written protocol to assess the patient’s emotional state, prescribed medications, access to local mental health services, and other contextual information to determine whether immediate assistance or intervention was required. Based on this information, the tele-therapist could: (i) conclude that the individual was not at elevated risk for self-harm or harm to others and implement a standard “behavioral contract” with the patient; (ii) refer the patient to a medical or mental health care professional in his/her immediate geographic area for additional assistance (all tele-therapists were provided by research staff with patients’ local emergency crisis and mental health treatment resources), or (iii) make a 911 emergency call to the appropriate authorities in the patient’s locale to arrange crisis intervention.

Situations requiring option “3” did not occur during this clinical trial.

Patient Flow

Fig. 1 shows that of 719 individuals who inquired into the study, 552 were excluded for not satisfying the rurality criterion ($n = 340$), having subclinical depressive symptoms that did not meet diagnostic criteria for major depressive disorder, current or in partial remission, or dysthymic disorder ($n = 138$), could not be contacted ($n = 62$), or were study eligible but declined to participate ($n = 12$). Ultimately, 167 rural PLHIV satisfied inclusion and exclusion criteria, completed preintervention measures, and were randomly assigned to condition.

Although all patients were diagnosed with a PRIME-MD–based depressive disorder in eligibility screenings, 20 patients had preintervention BDI values <14 , the threshold for mild depressive disorder (26). Because assessing the efficacy of tele-IPT for subclinical depression has questionable utility, these patients were excluded from outcome analyses, yielding 147 intent-to-treat and 133 therapy completer patients (i.e., patients who completed all nine tele-therapy sessions). The exclusion of these 20 patients from long-term intervention-outcome analyses was based on an a priori decision and is consistent with the data analytic approach used in our acute intervention-outcome paper (21). Eighty-three percent of patients completed postintervention assessments, 78% completed 4-month follow-up, and 77% completed 8-month follow-up assessments.

Data Analysis Plan

For the BDI (primary outcome) and the IIPs and PSRS (secondary outcomes), intervention-outcome analyses were conducted twice. An intention-to-treat analysis used data from patients with preintervention BDI values ≥ 14 regardless of the number of tele-therapy sessions they attended ($N = 147$). The second approach, completers-only, used data from patients who reported preintervention BDI values ≥ 14 and attended all nine weekly tele-IPT sessions ($N = 133$).

The long-term efficacy of tele-IPT relative to standard care was evaluated using mixed-model repeated measures with multiple imputation for each outcome variable. The maintenance of previously reported acute reductions in depression and interpersonal problems (21) was assessed through pairwise comparisons that focused on data provided at 4- and 8-month follow-up. The effect size for between-group differences on study measures at 4- and 8-month follow-up was assessed using Cohen’s d and its traditional cutoff effect size values of large = 0.8, medium = 0.5, and small = 0.2 were used for data interpretation. Mixed models repeated measures analyses

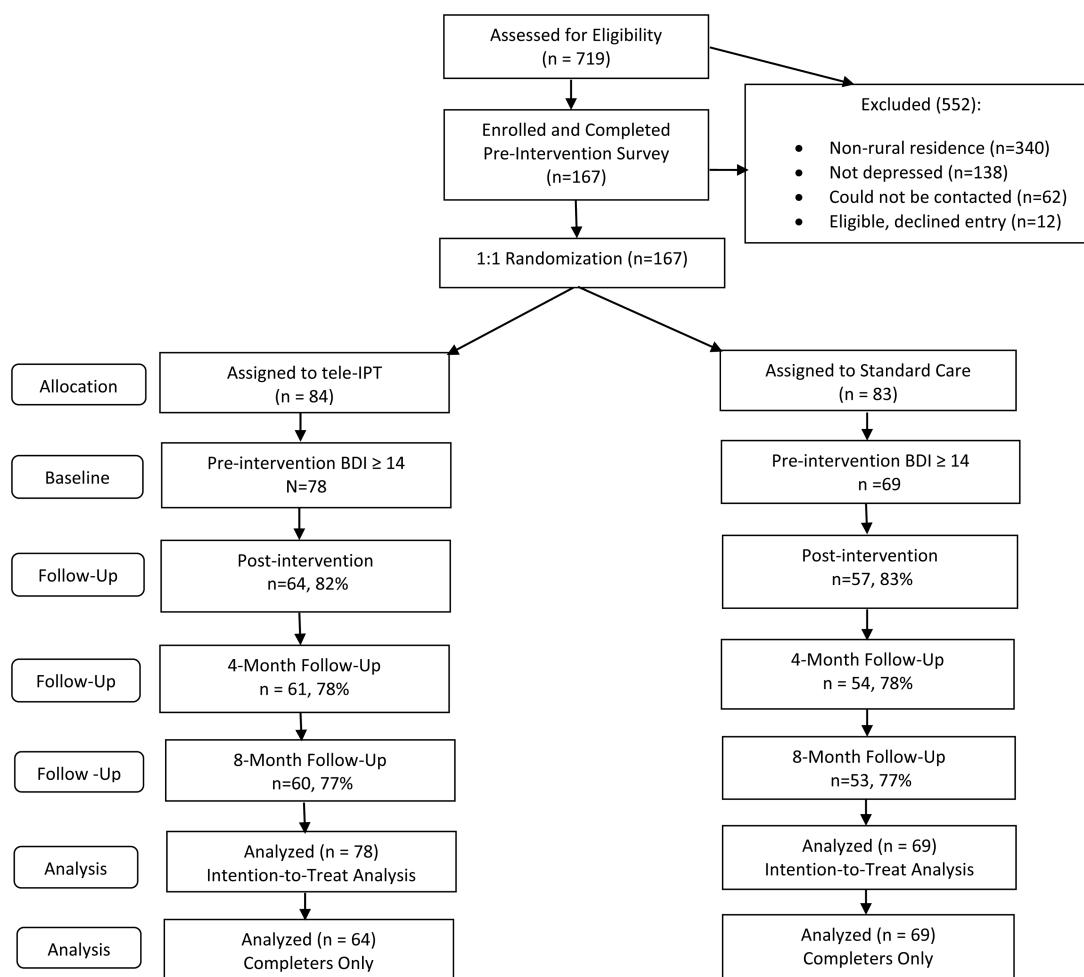


Fig. 1. Patient flow chart following consolidated standards of reporting trials guidelines.

with multiple imputation were conducted using SAS 9.4 (30). All statistical comparisons used two-tailed tests and a significance level of $\alpha = .05$.

This report contains 15 more preintervention patients ($N = 147$) than the sample size in our acute intervention-outcome paper ($N = 132$) (21). The reason for the greater preintervention sample size in the current report is that it was determined that 15 patients were missing one ($n = 12$) or two ($n = 3$) items on the BDI at pre-intervention. To retain these 15 patients in long-term intervention-outcome analyses, the missing BDI item for patients was imputed using the item's modal response (in every case, either "0" or "1").

Results

Patient Population

The first patient enrolled in August 2010 and the final 8-month follow-up was received in December 2015. Patients ($N = 147$) were, on average, 52.0 years of age (range = 20–73), Caucasian (73.5%), and diagnosed

with AIDS (55.8%); half self-identified as gay/bisexual (50.3%). On average, patients had been living with HIV for 17.8 years ($SD = 7.8$). The modal patient (36.1%) lived in a county with a population of 2,500 to 19,999 that was adjacent to a metropolitan area. The mean preintervention BDI value was 26.9 ($SD = 9.7$; range = 14–60). No difference by treatment condition was found on any pre-intervention variable (all $p_s > .05$).

Tele-therapy Participation and Postintervention Assessment Completion

On average, tele-IPT patients participated in 7.8 tele-therapy sessions ($SD = 2.8$); 82.1% attended all nine sessions (median = 9, mode = 9, range = 0–9). Of the 147 patients, 18 (12.2%) completed no postintervention or follow-up assessments and were considered lost to follow-up (i.e., discontinued). Discontinued patients ($n = 18$) did not differ significantly from those who completed at least one post or follow-up BDI ($n = 129$) on any preintervention demographic, clinical, or psychiatric outcome variable (all $p_s > .05$).

Table 1 Proportions of patients who used standard care services by treatment condition during the randomized clinical trial. Proportions with differing superscripts within a row differ at $p < .05$. Denominators vary due to patient attrition and missing data.

Standard care service	Tele-IPT				SC controls			
	Pre	Post	4 Mo	8 Mo	Pre	Post	4 Mo	8 Mo
Taking antidepressants at preintervention ^a	64.9, 50/77				62.3, 43/69			
Taking anxiolytic at preintervention ^a	47.3, 35/74				38.5, 25/65			
Sought assistance for health care professional	39.7, 31/78	32.8, 21/64	28.1 ^A , 18/64	31.7, 20/63	43.5, 30/69	40.3, 25/62	43.5 ^B , 27/62	25.8, 16/62
Used self-help groups (e.g., AA, NA)	23.1, 18/78	20.3, 13/64	23.4, 15/64	15.9, 10/63	14.5, 10/69	17.5, 11/63	15.0, 9/60	8.2, 5/61
Used crisis hotlines for alcohol, drugs, emotions	9.0, 7/78	0.0 ^A , 0/65	1.6 ^A , 1/64	1.6, 1/63	4.3, 3/69	7.9 ^B , 5/63	11.3 ^B , 7/62	1.6, 1/62

^aAssessed at preintervention only.

Patient Utilization of Standard Care During the Clinical Trial

Table 1 shows two significant and one marginally significant association between treatment condition and use of standard care services during the clinical trial. Treatment condition and seeking assistance from a health care professional were marginally associated at 4 month follow-up, with slightly fewer tele-IPT patients (28.1%) seeing a health care professional in the past month compared to standard care controls (43.5%), $X^2(1) = 3.26$, $p = .071$. Treatment condition was also associated with use of crisis hotlines at two assessment periods. Specifically, at postintervention, significantly more standard care controls (7.9%) used hotlines than tele-IPT patients (0.0%), $X^2(1) = 5.39$, $p = .021$. Additionally, at 4-month follow-up, significantly more standard care controls (11.3%) used hotlines compared to tele-IPT patients (1.6%), $X^2(1) = 5.01$, $p = .025$.

Between-Group Differences in Depressive Symptoms at 4- and 8-Month Follow-Up

Intention-to-Treat Approach

Preintervention and acute postintervention BDI means for tele-IPT patients were 26.7 and 21.4, respectively, while pre-and post-intervention means for standard care controls were 27.1 and 25.5, respectively. Table 2 shows estimated BDI means by condition at 4- and 8-Month follow-up from intention-to-treat analyses. In intention-to-treat analyses, the between-group difference was marginally significant at 4-month follow-up (tele-IPT = 21.71, controls = 25.08, Cohen's $d = .41$, $p = .058$) and statistically significant at 8-month follow-up (tele-IPT = 20.55, controls = 24.43, Cohen's $d = .47$, $p = .029$). Intention-to-treat BDI means tested in acute intervention-outcome analyses (21) and 4- and 8-month comparisons in this report are shown in Fig. 2.

Completer-Only Approach

Preintervention and postintervention BDI means for tele-IPT patients in completer-only analyses were 26.5 and 20.7, respectively, while preintervention and postintervention means for standard care controls were 27.1 and 25.5, respectively. Table 2 shows estimated means by condition and assessment period in completers-only analyses. Between-group differences were statistically significant at 4-month (tele-IPT = 21.28, controls = 25.08, Cohen's $d = .46$; $p = .035$) and 8-month follow-up (tele-IPT = 20.12, controls = 24.43, Cohen's $d = .52$; $p = .017$).

Between-Group Differences in Interpersonal Problems at 4- and 8-Month Follow-Up

Intention-to-Treat Approach

Preintervention and postintervention IIPs scale means for tele-IPT patients were 108.1 and 88.3, respectively, while pre-and post-intervention means for standard care controls were 97.0 and 98.1, respectively. Table 2 shows estimated IIP means by condition and assessment period. The mean between-group differences were not significant at 4-month (tele-IPT = 87.18, controls = 94.42, Cohen's $d = .26$, $p = .302$) or 8-month follow-up (tele-IPT = 86.91, controls = 88.79, Cohen's $d = .07$, $p = .780$).

Completer-Only Approach

Preintervention and postintervention IIPs means for tele-IPT patients were 108.2 and 88.0, respectively, while pre-and post-intervention means for standard care controls were 97.0 and 98.1, respectively. In completer-only analyses, between-group differences were not statistically significant at 4-month (tele-IPT = 86.96, controls = 94.42, Cohen's $d = .264$, $p = .298$) or 8-month follow-up (tele-IPT = 86.84, controls = 88.79, Cohen's $d = .07$, $p = .779$).

Table 2 BDI means and standard errors by condition and follow-up assessment period

Variable	No.	4-month follow-up	8-month follow-up
BDI			
Intent-to-treat			
IPT	78	21.71 ± 1.14	20.55 ± 1.13
Standard care	69	25.08 ± 1.36	24.43 ± 1.35
Cohen's <i>d</i>		.41	.47 [#]
Completer-only			
IPT	64	21.28 ± 1.18	20.12 ± 1.17
Standard care	69	25.08 ± 1.36	24.43 ± 1.35
Cohen's <i>d</i>		.46 [#]	.52 [#]
IIP-64			
Intent-to-treat			
IPT	78	87.18 ± 4.79	86.91 ± 4.74
Standard care	69	94.42 ± 5.11	88.79 ± 4.83
Cohen's <i>d</i>		.26	.07
Completer-only			
IPT	64	86.96 ± 4.98	86.84 ± 4.93
Standard care	69	94.42 ± 5.13	88.79 ± 4.84
Cohen's <i>d</i>		.26	.07
PSRS			
Intent-to-treat			
IPT	78	49.80 ± 1.32	50.34 ± 1.31
Standard care	69	48.51 ± 1.48	49.71 ± 1.48
Cohen's <i>d</i>		.13	.06
Completer-only			
IPT	64	50.07 ± 1.39	50.69 ± 1.39
Standard care	69	48.51 ± 1.48	49.71 ± 1.47
Cohen's <i>d</i>		.16	.10

[#]Pairwise difference significant at $p < .05$.

Between-Group Differences in Social Support at 4- and 8-Month Follow-Up

Intention-to-Treat Approach

Preintervention and postintervention PSRS means for tele-IPT patients were 46.9 and 49.0, respectively, while

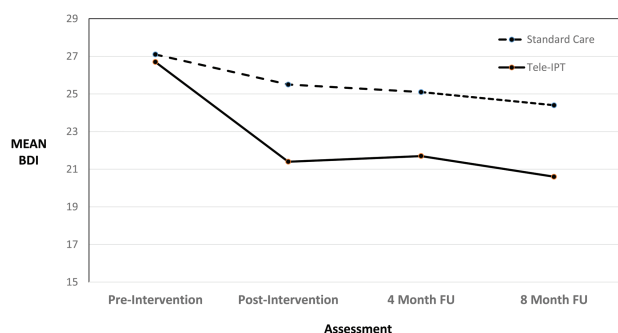


Fig. 2. Beck Depression Inventory means by treatment condition and assessment period.

pre-and post-intervention means for standard care controls were 47.4 and 48.6, respectively. Table 2 shows estimated scale means by condition and assessment period. Between-group differences were not statistically significant at 4-month (tele-IPT = 49.80, controls = 48.51, Cohen's $d = .133$, $p = .520$) or 8-month follow-up (tele-IPT = 50.34, controls = 49.71, Cohen's $d = .064$, $p = .755$).

Completer-Only Approach

Preintervention and postintervention scale means for tele-IPT patients were 47.2 and 49.4, respectively, while pre-and post-intervention means for standard care controls were 47.4 and 48.6, respectively. Between-group differences were not statistically significant at 4-month (tele-IPT = 50.07, controls = 48.51, Cohen's $d = .016$, $p = .446$) or 8-month follow-up (tele-IPT = 50.69, controls = 49.71, Cohen's $d = .100$, $p = .634$).

Discussion

Many rural PLHIV experience comorbid depression, yet there are very few evidenced-based depression treatments for this group capable of circumventing barriers to care in rural areas, such as vast geographic distance between patients and practitioners, the lack of public and private transportation, and confidentiality concerns (31–34). However, because almost all rural PLHIV own landline, cellular, or smart phones, telephone-administered psychotherapy can reach many members of this isolated group.

This study found that significant acute reductions in depressive symptoms in rural PLHIV following nine weekly sessions of telephone-administered IPT (21) were maintained through 4- and 8-month follow-up, with treatment effect sizes typically in, or approaching, the “medium” range. The effect sizes associated with tele-IPT's depression treatment efficacy in this study are noteworthy in light of a recent meta-analysis (4) which found that the effect sizes of psychosocial interventions to reduce psychological distress in PLHIV are generally “small” (i.e., Hedge's $g = .19$). Moreover, both intention-to-treat and completer-only intervention-outcome analyses found evidence of longer term depression treatment efficacy of tele-IPT. The same pattern of findings across the two approaches is predictable given that 82% of tele-IPT patients in intention-to-treat analyses had completed all nine tele-therapy sessions.

The finding that only nine sessions of tele-IPT reduces depression in this group is noteworthy because, in addition to living with HIV and depression, many patients reported actively utilizing treatment services at the time of study enrollment for alcohol and drug use dependence, other comorbid medical conditions (e.g., hypertension, diabetes, migraine disorders), financial and employment difficulties, and childcare and caregiving

responsibilities, suggesting that many patients in this study confronted difficult medical and psychosocial complexities. Along with persistent reductions in depressive symptoms, tele-IPT patients reported less frequent use of crisis hotlines and fewer interactions with health care professionals following treatment to address problems associated with emotions and alcohol/substance use. Given their weekly access to tele-therapists, tele-IPT patients may have found the need for crisis hotlines and interactions with health care providers to be less necessary. Conversely, it could be that standard care controls who established relationships with helping professionals were encouraged to use hotlines more frequently.

Study findings are important for several reasons. First, the positive intervention-outcome findings provide rural-based practitioners with a time-limited, manualized treatment easily translatable for use with their rural patients. Second, from a more general psychotherapeutic perspective, this clinical trial found that brief telephone-administered IPT produced significant acute reductions in depressive symptoms in rural PLHIV (21) and that these reductions were maintained over longer term follow-up. This is also the first controlled study to show that tele-IPT provides long-term depressive symptom relief to *any treatment population*. While brief tele-IPT has provided acute reductions in depressive symptoms in women with breast cancer (35), women who experience miscarriages (36), and women with histories of recurrent depression (37), these formative studies typically relied on small convenience samples and included only acute posttreatment assessments. This clinical trial thus provides the first evidence of brief tele-IPT's ability to provide depressive symptom relief over an extended time period in a clinical sample.

While tele-IPT patients maintained their acute improvements in depressive symptoms at longer term follow-up, we found no differences in interpersonal problems or perceptions of social support between the two conditions at longer term follow-up. Anecdotally, study tele-therapists reported that their patients had physical access to very few social support resources and/or had confidentiality concerns that precluded them from accessing these resources. Given the lack of in-person social supports in rural areas, interventions that connect rural PLHIV with virtual sources of support, such as internet- or cellphone-based chat rooms, message boards, or webcams to improve perceptions of social support and reduce loneliness may be helpful (38, 39). Although tele-IPT patients reported reductions in interpersonal problems from preintervention to postintervention compared to controls, patients in both groups reported comparable interpersonal problems across longer term follow-up. The inability of tele-IPT to decrease interpersonal problems and increase perceptions of social support suggests

that the mechanism(s) underlying tele-IPT's depression treatment efficacy for this group lies elsewhere. Earlier data analyses from this clinical trial (40) suggest that patients' depressive symptom relief may be related to concomitant reductions in social avoidance, although the cross-sectional nature of these analyses prohibits any definitive conclusions. Future research assessing the depression treatment efficacy of tele-IPT should use longitudinal designs to more precisely identify the mechanism(s) through which tele-IPT reduces depression in PLHIV or other clinical populations.

This clinical trial has several limitations. A more rigorous study design would have included an attention-equivalent control group, although the study's use of a standard care comparator provided a reasonable and ethically tolerable control condition. Approximately 10% to 20% of patients were attending self-help groups and 20% to 40% were receiving services during the study from health care professionals. Some reductions in depressive symptoms may have been associated with standard care services unrelated to tele-IPT. While the study collected data on patients' use of antidepressants and anxiolytics at preintervention, no data on pharmacological treatments were collected at any follow-up assessment. This is a major limitation because tele-IPT may have prompted more patients to start taking antidepressant medication and contributed to their depressive symptom relief. The limited study sample size provided inadequate statistical power to identify potential moderator variables of tele-IPT, such as type of depression diagnosis, current use of alcohol or illicit substances, or demographic variables, such as number of years living with HIV, gender, and race. We did not collect data on patients' lifetime histories of depressive episodes or length of the depressive episode at study enrollment, thereby precluding our determining whether patients' depressive disorders occurred before or after their HIV diagnosis. Patients' use of alcohol and illicit substances was not assessed rigorously during the clinical trial. These data may have helped to more accurately characterize the mental health needs of rural PLHIV and the impact of alcohol and substance use on tele-IPT's depression treatment efficacy. This clinical trial purposely employed very few exclusion criteria in order to increase external validity. The use of additional or different exclusion criteria might have altered intervention-outcome findings. Finally, all data were collected through self-report methodologies; no data were collected through chart reviews or electronic medical records. Future research to identify logistically and financially feasible ways to collect current and reliable physiologic data from rural PLHIV would make important contributions to the literature.

IPT has relieved depression in many different demographic groups, including adolescents, the elderly, and

postpartum women as well as patients with mental health diagnoses other than depression (41). The present study provides robust evidence that acute reductions in depressive symptoms following receipt of brief tele-IPT persist through longer term follow-up. To counter the dearth of psychotherapies for rural PLHIV, rural-based practitioners now have access to a brief, time-limited manualized treatment they can deliver to their clients that leverages the privacy and convenience of the telephone. Future research should identify ways to best implement tele-IPT into systems of care that serve the geographically and psychologically isolated group of rural people living with HIV/AIDS.

Acknowledgements Research supported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R01MH087462. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Compliance With Ethical Standards All authors of this manuscript agree that: (i) the corresponding author has permission to submit and publish this version of the manuscript; (ii) they have provided legitimate contributions to the manuscript; (iii) the research reported in this manuscript is original and has not been published elsewhere nor is it currently “under review” elsewhere; (iv) the material in the manuscript has been obtained following modern ethical standards and approved by appropriate ethical committees; (v) the article does not contain material copied from anyone else without their written permission and that all material derived from previous work is properly cited; (vi) all material conflicts of interest have been declared; (vii) the manuscript will be maintained on the journal’s servers of the journal and identified by the journal only as long as all statements in these principles are true; and (viii) that if any of the above statements are no longer true that the study team is responsible for notifying the journal as soon as possible so that the manuscript can be withdrawn.

Conflict of Interest Authors Timothy Heckman, Bernadette Heckman, Henok Woldu, Timothy Anderson, Travis Lovejoy, Ye Shen, Mark Sutton, and William Yarber report no conflicts of interest. Author John Markowitz reports salary support from New York State Psychiatric Institute; grant support from NIMH, the Fund for Psychoanalytic Research, and the Mack Foundation; an editorial stipend from Elsevier Press as Editor-in-Chief of Comprehensive Psychiatry; and minor book royalties from American Psychiatric Press, Basic/Perseus Books, and Oxford University Press. (We will leave it to the discretion of the publishers if they want to report the COIs of Dr Markowitz. We thought we should err on the side of reporting them proactively).

Authors’ Contributions Timothy Heckman conceptualized the study, oversaw the conduct of the study, contributed to the interpretation of study results, and oversaw the preparation of the manuscript. John Markowitz assisted in the conceptualization of the study, assisted in the development of the teletherapy, trained tele-therapists in intervention delivery, assisted in the development of the study survey, interpreted study results, and contributed to the preparation of the manuscript. Bernadette Heckman assisted in the conceptualization of the study, provided teletherapy to participants, interpreted study results, and contributed to the

preparation of the manuscript. Henok Woldu analyzed study data and contributed to the preparation of the manuscript. Timothy Anderson assisted in the conceptualization of the study, assisted in developing the study survey, provided teletherapy to patients, interpreted study results, and assisted in the preparation of the manuscript. Travis Lovejoy provided teletherapy to participants, assisted in the interpretation of study results, and assisted in the preparation of the manuscript. Ye Shen analyzed study data and contributed to the preparation of the manuscript. Mark Sutton assisted in the conceptualization of the study, oversaw day-to-day participant recruitment and retention efforts, interpreted study results, and contributed to the preparation of the manuscript. William Yarber provided assistance in participant recruitment efforts, interpreted study results, and assisted in the preparation of the manuscript.

Informed Consent All participants provided written informed consent prior to study participation.

Ethical Approval The study was approved by all relevant Institutional Review Boards (IRB).

References

- Centers for Disease Control and Prevention. *HIV surveillance report. Diagnoses of HIV infection in the United States and dependent areas*, 2015 <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2015-vol-27.pdf>. Accessibility verified February 3, 2017.
- Sheth SH, Jensen PT, Lahey T. Living in rural New England amplifies the risk of depression in patients with HIV. *BMC Infect Dis*. 2009; 9: 25. <http://www.biomedcentral.com/1471-2334/9/25>. Accessibility verified June 10, 2017.
- Reif S, Whetten K, Ostermann J, Raper JL. Characteristics of HIV-infected adults in the Deep South and their utilization of mental health services: a rural vs. urban comparison. *AIDS Care*. 2006; 18 (suppl 1): S10–S17.
- van Luenen S, Garnefski N, Spinhoven P, Spaan P, Dusseldorp E, Kraaij V. The benefits of psychosocial interventions for mental health in people living with HIV: a systematic review and meta-analysis. *AIDS Behav*. 2017. doi: 10.1007/s10461-017-1757-y. Epub ahead of print.
- Sherr L, Clucas C, Harding R, Sibley E, Catalan J. HIV and depression—a systematic review of interventions. *Psychol Health Med*. 2011; 16(5): 493–527.
- Gentry S, van-Velthoven MHMMT, Tudor Car L, Car J. Telephone delivered interventions for reducing morbidity and mortality in people with HIV infection. *Cochrane Database Syst Rev* 2013; 5: CD009189.
- Ransom D, Heckman TG, Anderson T, Garske J, Holroyd K, Basta T. Telephone-delivered, interpersonal psychotherapy for HIV-infected rural persons diagnosed with depression: a pilot randomized clinical trial. *Psychiatric Services*. 2008; 59: 871–877.
- Heckman TG, Heckman BD, Anderson T, et al. Supportive-expressive and coping group teletherapies for HIV-infected older adults: a randomized clinical trial. *AIDS Behav*. 2013; 17(9): 3034–3044.
- Lovejoy TI. Telephone-delivered motivational interviewing targeting sexual risk behavior reduces depression, anxiety, and stress in HIV-positive older adults. *Ann Behav Med*. 2012; 44(3): 416–421.
- Stein MD, Herman DS, Bishop D, et al. A telephone-based intervention for depression in HIV patients: negative results

- from a randomized clinical trial. *AIDS Behav.* 2007; 11(1): 15–23.
11. Himelhoch S, Medoff D, Maxfield J, et al. Telephone based cognitive behavioral therapy targeting major depression among urban dwelling, low income people living with HIV/AIDS: results of a randomized controlled trial. *AIDS Behav.* 2013; 17(8): 2756–2764.
 12. Mohr DC, Vella L, Hart S, Heckman T, Simon G. The effect of telephone-administered psychotherapy on symptoms of depression and attrition: a meta-analysis. *Clin Psychol (New York)*. 2008; 15(3): 243–253.
 13. Weissman MM, Markowitz JC, Klerman GL. *Comprehensive guide to interpersonal psychotherapy*. New York, NY: Basic Books; 2000.
 14. Frank E, Kupfer DJ, Perel JM, et al. Three-year outcomes for maintenance therapies in recurrent depression. *Arch Gen Psychiatry.* 1990; 47(12): 1093–1099.
 15. Cuijpers P, Geraedts AS, van Oppen P, Andersson G, Markowitz JC, van Straten A. Interpersonal psychotherapy for depression: a meta-analysis. *Am J Psychiatry.* 2011; 168(6): 581–592.
 16. Krupnick JL, Melnikoff E, Reinhard M. A pilot study of interpersonal psychotherapy for PTSD in women veterans. *Psychiatry.* 2016; 79(1): 56–69.
 17. Wilfey DE. Treatment of binge eating disorder: research findings and clinical applications. In: BT Walsh (Chair), Integrating Research and Clinical Practice. Plenary session presented at the meeting of the 4th International Conference on Eating Disorders, London. 1999.
 18. Swartz HA, Frank E, Zuckoff A, et al. Brief interpersonal psychotherapy for depressed mothers whose children are receiving psychiatric treatment. *Am J Psychiatry.* 2008; 165(9): 1155–1162.
 19. Saloheimo HP, Markowitz J, Saloheimo TH, et al. Psychotherapy effectiveness for major depression: a randomized trial in a Finnish community. *BMC Psychiatry.* 2016; 16: 131.
 20. Mulcahy R, Reay RE, Wilkinson RB, Owen C. A randomized controlled trial for the effectiveness of group Interpersonal Psychotherapy for postnatal women. *Arch Womens Ment Health.* 2010; 13(2): 125–139.
 21. Heckman TG, Heckman BD, Anderson T, et al. Tele-interpersonal psychotherapy acutely reduces depressive symptoms in depressed HIV-infected rural persons: a randomized clinical trial. *Behavioral Medicine.* 2017; 43(4): 285–295.
 22. Weissman MM, Klerman GL, Prusoff BA, Sholomskas D, Padian N. Depressed outpatients. Results one year after treatment with drugs and/or interpersonal psychotherapy. *Arch Gen Psychiatry.* 1981; 38(1): 51–55.
 23. United States Department of Agriculture. Rural-Urban Continuum Codes. 2013. <http://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx> Accessibility verified February 7, 2017.
 24. Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. *JAMA.* 1994; 272(22): 1749–1756.
 25. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. *J Clin Psychiatry.* 1987; 48(8): 314–318.
 26. Beck AT, Steer RA, Brown GK. *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation; 1996.
 27. Alden LE, Wiggins JS, Pincus AL. Construction of circumplex scales for the Inventory of Interpersonal Problems. *J Pers Assess.* 1990; 55(3–4): 521–536.
 28. Turner RJ, Frankel BG, Levin DH. Social support: conceptualization, measurement, and implications for mental health. In: Greenley JR, Simmons RG, eds. *Research in community and mental health* Greenwich, CT: JAI Press; 1983: 67–111.
 29. Markowitz JC, Klerman G, Clougherty K, Josephs L. *Manual for interpersonal therapy with depressed HIV-seropositive patients*. 1993. Unpublished.
 30. SAS Institute. *Base SAS 9.4 Procedures Guide*. Cary, NC: SAS Institute; 2014.
 31. Heckman TG, Somlai AM, Peters J, et al. Barriers to care among persons living with HIV/AIDS in urban and rural areas. *AIDS Care.* 1998; 10(3): 365–375.
 32. Reif S, Golin CE, Smith SR. Barriers to accessing HIV/AIDS care in North Carolina: rural and urban differences. *AIDS Care.* 2005; 17(5): 558–565.
 33. Wood SA. Health care services for HIV-positive substance abusers in a rural setting: an innovative program. *Soc Work Health Care.* 2008; 47(2): 108–121.
 34. McKinney MM. Variations in rural AIDS epidemiology and service delivery models in the United States. *J Rural Health.* 2002; 18(3): 455–466.
 35. Donnelly JM, Kornblith AB, Fleishman S, et al. A pilot study of interpersonal psychotherapy by telephone with cancer patients and their partners. *Psychooncology.* 2000; 9(1): 44–56.
 36. Neugebauer R, Kline J, Bleiberg K, et al. Preliminary open trial of interpersonal counseling for subsyndromal depression following miscarriage. *Depress Anxiety.* 2007; 24(3): 219–222.
 37. Miller L, Weissman M. Interpersonal psychotherapy delivered over the telephone to recurrent depressives. A pilot study. *Depress Anxiety.* 2002; 16(3): 114–117.
 38. Kingod N, Cleal B, Wahlberg A, Husted GR. Online peer-to-peer communities in the daily lives of people with chronic illness: a qualitative systematic review. *Qual Health Res.* 2017; 27(1): 89–99.
 39. Allen C, Vassilev I, Kennedy A, Rogers A. Long-term condition self-management support in online communities: a meta-synthesis of qualitative papers. *J Med Internet Res.* 2016; 18(3): e61.
 40. Anderson T, McClintock AS, McCarrick SS, et al. Working alliance, interpersonal problems, and depressive symptoms in tele-interpersonal psychotherapy for HIV-infected rural persons: evidence for indirect effects. *J Clin Psychol.* 2017, [Epub ahead of print] doi: 10.1002/jclp.22502.
 41. Markowitz JC, Weissman MM. Interpersonal psychotherapy: past, present and future. *Clin Psychol Psychother.* 2012; 19(2): 99–105.