Title

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Publication Date

2019-05-01

DOI

10.1016/j.jsat.2019.02.003

Peer reviewed

Establishing the Feasibility, Acceptability and Preliminary Efficacy of a Multi-Component Behavioral Intervention to Reduce Pain and Substance Use and Improve Physical Performance in Older Persons Living with HIV

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Funding: This study was supported by the National Institutes of Health grant R21DA038163. Authors were also supported by K24AG053462 (AAM), K23AI110532 (JEL), P30AG028748 (AAM and AK), P30AG021684 (AAM), P30AG022845 (MCR), and K24AGO53462 (MCR)..

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Abstract

Older persons living with HIV (PLWH), often defined as age 50 years and older, are a rapidly growing population, with high rates of chronic pain, substance use, and decreased physical functioning. No interventions currently exist that address all three of these health outcomes simultaneously. An 8-week behavioral intervention combining cognitive-behavioral therapy and tai chi reinforced with text messaging (CBT/TC/TXT) was developed and pilot tested in a community-based AIDS service organization with substance using PLWH aged 50 years and older who experienced chronic pain. Fifty-five participants were enrolled in a three arm randomized controlled trial that compared the CBT/TC/TXT intervention (N=18) to routine Support Group (SG) (N=19) and Assessment Only (AO) (N=18) to assess the intervention's feasibility, acceptability and preliminary efficacy to reduce pain and substance use and improve physical performance. Participants were assessed at baseline, treatment-end (week 8) and week 12. Feasibility and acceptability indicators showed moderate levels of participant enrollment (62% of those eligible), excellent 12-week assessment completion (84%) and high attendance at CBT and tai chi sessions (> 60% attended at least 6 of 8 sessions). Efficacy indicators showed within-group improvements from baseline to week 12 in the CBT/TC/TXT group, including all four substance use outcomes, percent pain relief in the past 24 hours, and in two physical performance measures. Observed between-group changes included greater reductions in days of heavy drinking in the past 30 days for both CBT/TC/TXT (19%) and SG (13%) compared to the AO group. Percent pain relief in the past 24 hours improved

in the CBT/TC/TXT group relative to SG, and the CBT/TC/TXT's physical performance score improved relative to both the SG and AO groups. Findings demonstrate that the CBT/TC/TXT intervention is feasible to implement, acceptable and has preliminary efficacy for reducing substance use and pain and improving physical performance among a vulnerable population of older PLWH.

Keywords: randomized clinical trial; HIV; pain; older; physical performance, substance use

1. Introduction

Older persons living with HIV (PLWH), often defined as age ≥ 50 years, represent a rapidly growing population. More than 50% of PLWH in the U.S. are ≥ 50 years, (Sangarlangkarn & Appelabaum, 2016). Furthermore, older PWLH have high rates of multimorbidity (Sangarlangkarn & Appelabaum, 2016; Kim & Ritchie, 2016). Chronic pain and substance use occur commonly in this population and are associated with poor health outcomes (Jiao et al., 2016; Parsons, Starks, Millar, Boonrai, & Marcotte, 2014; Edelman, Tetrault, & Fiellin, 2014) and increased use of healthcare services (Jiao et al., 2016; DeLorenze, Tsai, Horberg, & Quesenberry, 2014). PLWH are also at risk for declining physical functioning and reduced physical performance (Brooks, Buchacz, Gebo, & Mermin, 2012; Greene et al, 2014).

Given the high prevalence of co-morbid pain, substance use, and reduced physical functioning in older PLWH, multi-component interventions targeting all three are needed. Cognitive behavioral therapy (CBT) is an evidence-based approach for managing both pain and substance use (Ilgen et al, 2016; Lunde, Inger, Nordhus, & Pallesen, 2009; Center for Substance Abuse Treatment, 2005). According to the Infectious Diseases Society of America guidelines, CBT is a recommended first line non-pharmacologic treatment for chronic pain management among PLWH (Bruce et al., 2017).

In addition, exercise therapies reduce pain, reverse muscle atrophy, and decrease fall risk among older adults with chronic pain (Hayden, van Tulder, & Tomlinson, 2004; American Geriatrics Society Panel on Exercise and Osteoarthritis, 2001). Tai chi is a mind-body exercise that combines gentle movement, meditation and deep breathing. Tai chi can be feasibly

administered to diverse groups of older adults and is associated with reduced pain, risk of falling and depressive symptomatology (Kong et al., 2016; Huang, Feng, Li, & Lv, 2017; Chi, Jordan-Marsh, Guo, Xie, & Bai, 2012). Given high rates of physical deconditioning in PLWH (Althoff et al., 2013; Oursler, Sorkin, Smith, & Katzel, 2006), tai chi constitutes a particularly appealing movement-based therapy due to its use of low impact, graded, weight bearing exercises.

Finally, text messaging has recently demonstrated efficacy in reinforcing elements of behavioral interventions, including those directed at changing addictive behaviors (Weitzel, Bernhardt, Usdan, Mays, & Glanz, 2007) and managing chronic pain (Kristjansdottir et al., 2013). Text messaging may also be an acceptable continuing care strategy following intensive treatment for a substance use disorder (Muench, Weiss, Kuerbis, & Morgenstern, 2013) and in reducing problem drinking (Muench, van Stolk-Cooke, Morgenstern, Kuerbis, & Markle, 2017).

We conducted a pilot randomized controlled trial (RCT) to assess the feasibility, acceptability and preliminary efficacy of a multi-component behavioral intervention—a combined CBT and tai chi protocol reinforced with text messaging—to reduce levels of pain and substance use, and improve physical performance among older PLWH. We hypothesized that participants randomized to the intervention arm would demonstrate reductions in substance use, pain-related disability and pain intensity along with improvements in physical performance.

2. Method

2.1 Study Setting

This project was conducted in partnership with APAIT, a non-profit, community-based AIDS service organization that provides mental health and substance use services to an ethnically and racially diverse community in Los Angeles, CA.

2.2 Study Preparation

Prior to the RCT, we conducted focus groups with prospective end-users of the intervention to ascertain their preferences regarding behavioral treatments for pain (Nguyen et al, 2017); developed the integrated intervention and trained APAIT staff to deliver it; and conducted a small (N=9) pilot study, using the results to refine study materials and procedures prior to the current trial. We also obtained supplemental funding to conduct daily diary assessments (DDA) of overall health, pain, behavioral responses to pain, mood, sleep, exercise, drinking and drug use, and social contact among all study participants via their cell phones. These data are reported in a separate paper (Kuerbis et al. in press).

The Institutional Review Boards of all participating institutions approved the study. All participants provided written informed consent and participants assigned to the CBT/TC/TXT arm (described below) granted permission for the CBT sessions to be audiotaped.

2.3 Development of Intervention and Training

2.3.1 CBT development. Study investigators developed an eight session, manualized treatment protocol to be delivered once weekly over 60 minutes in a group format by behavioral health counselors. The eight week, open-group program was adapted from three manualized interventions: 1)

Manage Your Pain (Nicholas et al, 2003); 2) Integrated CBT (Brown et al., 2006); and 3) Mindfulness Based Relapse Prevention (Bowen et al., 2010).

All CBT sessions began with homework review, followed by delivery of didactic materials, coping skills, rehearsal exercises, and a new homework assignment. Therapy content focused on a different theme each week including 1) coping with chronic pain, 2) using mindfulness to cope with pain, 3) understanding and changing problematic patterns of substance use, 4) building motivation for change, 5) stress management and problem solving, 6) coping with negative thoughts and emotions, 7) improving sleep, and 8) building social support. Participants were given a copy of the client manual to facilitate between-session homework practice of coping skills presented in the weekly sessions.

2.3.2 CBT staff training. Three behavioral health counselors, including two members of APAIT's staff, participated in a day-long training led by a Master's level clinician experienced in administering manualized CBT interventions. To maintain fidelity during the trial, a clinical psychologist (SG) provided monthly supervision with review of audiotaped CBT sessions and feedback to counselors.

Ongoing fidelity monitoring was conducted on all CBT sessions using a previously developed fidelity rating scale (NIDA, 1998) that assessed the extent of study therapists' use of CBT-specific skills (e.g., skills training through teaching/rehearsal/modeling, problem solving, and maintaining session structure). Standardized fidelity ratings were made on 50% of randomly selected CBT sessions. These showed acceptable to excellent fidelity on all domains.

2.3.3 Tai Chi component and training. The study employed a Yang-style tai chi delivered weekly for one hour following each CBT session. Each session started with a 10-minute warm-up, stretching and review of tai chi principles followed by 30 minutes of tai chi exercises, including five animal forms, a walking meditation, and a partnered activity known as push hands. Each class ended with a 10-minute cool down and a 5-minute closing that included a review of the material presented.

A tai chi instructor with 18 years of experience trained two APAIT exercise program staff to lead the tai chi exercises. The staff underwent training for 1 hour weekly for 3 months before they began to lead tai chi sessions in the study. The trainer also attended four tai chi study sessions with each of the study instructors during the trial to monitor staff members' instruction and provide feedback and adjustments as needed.

2.3.4 Text message development. Informed by prior studies employing text messaging to facilitate behavior change (Glasner-Edwards et al, 2016, Muench et al, 2014), we developed three types of messages to be delivered weekly over 8 weeks via an automated platform: 1) reminder messages sent one day before each session at 4 pm (e.g., "Remember you have group and tai chi tomorrow at 9 am. See you then."), 2) messages related to the CBT topic of the week sent 1-3 days after each session (e.g., "Don't forget to pace your activities throughout the day."), and 3) messages related to the tai chi exercise sent 4-5 days after each session (e.g., "Keep moving! Exercise is your ticket to maintaining health.")

2.4 Randomized Controlled Trial Design and Inclusion Criteria

The trial had three arms: 1) CBT/Tai Chi/Text messaging (CBT/TC/TXT) groups that met weekly over 8 consecutive weeks); 2) support groups (SG) that met weekly over 8 consecutive weeks; and 3) a study assessment only (AO) group. All participants received usual medical care during the study. Enrollment into the groups was conducted on a rolling basis.

2.4.1 Support group. SG arm participants were asked to attend 8 consecutive, weekly, one-hour sessions held at APAIT as part of their regular programming for PLWH. Topics covered included mental health activities, dance, arts and crafts, and various HIV-related topics. Groups were led by APAIT behavioral therapists, some of whom also led the CBT sessions.

2.4.2 Assessment only. Those randomized to this arm completed the baseline and follow-up assessments only.

2.4.3 Inclusion criteria. Participant inclusion criteria were: 1) age ≥ 50 years; 2) able to read and understand English; 3) living with HIV infection; 4) answers yes to the question ”Have you suffered from pain on most days over the past three months?” and answers no to the follow up question “Is your pain due to a cancer?”; 5) at-risk substance use, defined by NIH guidelines (NIDA, 2012), i.e., consuming ≥ 5 drinks on ≥ 1 occasion in the past three months and/or use of any of the following substances at least once weekly and without a prescription or more than prescribed in the past three months: cocaine, amphetamine/methamphetamine, marijuana, opiates/heroin; 6) self-reported ability to participate in a low intensity exercise program; 7) possessed a cell phone that could send and receive text messages; and 8) not currently enrolled in a substance use disorder treatment program.

2.5 Study Participant Recruitment, Study Flow, Randomization and Remuneration

Between November 2015 and April 2016, participants were recruited by a research assistant who distributed flyers at venues serving PLWH, including APAIT, gave presentations at nearby health agencies, and approached potential participants at health centers. A flow diagram (see Figure 1) shows the number of individuals approached, screened, and recruited, as well as losses to follow-up. Randomization was conducted by research staff who used consecutively numbered, sealed envelopes containing assignment information using a computer-generated set of random numbers to select permutated blocks of six. Within each block, equal numbers were assigned to each of the three groups. Participant follow-up concluded in July, 2016.

Participants were compensated for their time via gift cards. Participants in the CBT/TC/TXT arm could be compensated up to $280, those in the SG arm could be compensated up to $200, while subjects in the AO arm could be compensated up to $120. Compensation included $10 for attending each CBT, TC or SG session.

2.6 Data Collection: Measures and Timing

Demographic and health-related data included date of birth, gender, race/ethnicity, education, marital status, housing arrangement, employment status, number of years living with HIV, most recent $CD4^+$ T lymphocyte count and HIV-1 RNA [detectable or undetectable (i.e.,<50 copies/mL)] and number of non-HIV chronic medical conditions. Participants also completed

mental and physical health (SF-12 version 2) (Cronbach α = 0.84) measures (Ware, Koskinki, & Keller, 1996; Gandek et al., 1998).

Substance use data included most often used (preferred) substance and the total number of substances used. Substances included both drugs and alcohol. Substance use measures included the WHO ASSIST-Version 3 (WHO ASSIST, 2002) and the Timeline Followback (TLFB) (Sobell & Sobell, 1992). The TLFB was used to determine the number of days in the past 30 days of a) using a preferred substance; b) using any substance; c) using any drugs; and d) heavy drinking (defined as ≥ 5 drinks for men and ≥ 4 drinks for women).

Pain data included number of years of chronic pain, and medications used to treat pain. Pain measures included two items from the abbreviated Brief Pain Inventory (BPI), i.e., average self-rated pain intensity and percent pain relief in the past 24 hours from pain treatments (Cleeland & Ryan, 1994), the Pain Self-Efficacy Questionnaire (PSEQ) (Cronbach α = 0.90) (Nicholas, 2007), and the modified Roland-Morris Disability Questionnaire (RMDQ) (Cronbach α = 0.89) (Roland & Morris, 1983). Data were collected via self-administered paper and pencil surveys.

Physical performance was assessed with the Short Physical Performance Battery (SPPB) (Guralnik et al., 1994). We calculated a total SBBP score for each participant and determined the percentage of participants with low physical performance (score ≤10) versus high physical performance.

In person assessments were conducted at APAIT at baseline, and at 8- and 12- weeks after the baseline assessment. All measures were collected at

baseline. In addition, the substance use measures based on the TLFB, the pain measures including the BPI, PSEQ and RMDQ and the physical performance measure, the SPPB were collected again at 8- and 12-weeks.

2.7 Qualitative Appraisals

At 8 weeks, participants in the CBT/TC/TXT group were asked if they enjoyed participating in the study and if they had any suggestions for program change.

2.8 Statistical Analyses

Feasibility was assessed by a) success of recruitment and randomization, b) retention and treatment engagement rates, and c) feedback about the study from participants. Bivariate analyses were used to a) compare groups at baseline to assess the success of randomization, b) compare treatment retention and engagement between groups, and c) determine associations between baseline variables, treatment adherence and engagement.

Measures of treatment efficacy included reductions in substance use, pain, and pain-related disability, as well as improvements in physical performance. Changes in outcome variables between baseline and both 8 weeks and 12 weeks are reported as means, standard deviations and medians for each group. Because the data were not normally distributed, we used the non-parametric, Wilcoxon signed rank test in each group to test if the within-individual change in the group was statistically significantly different from zero change.

To assess the preliminary efficacy of the intervention, we conducted an intention-to-treat analysis-all individuals randomized in the study were

included in the analyses whether they received treatment or not-using baseline, 8-, and 12-week follow-up data for each dependent variable. Linear, mixed-effects models were used (with random intercept at the individual level to account for within-individual correlations in the repeated measures of the outcome) to evaluate the five continuously scaled outcomes (average pain, percent pain relief, PSES score, RMDS, SPPB), with treatment group (CBT/TC/TXT, SG, AO) as a between-individuals factor (to capture differences between the groups at baseline), time as a within-individuals factor (to capture change over time), and a group-by-time interaction to examine differences in the magnitude of change between groups. A parallel mixed-effects, logistic regression model was used for the dichotomous outcome (low physical performance). Poisson regression models were used for the four count outcomes (days of using preferred substance in the past 30 days, days of any substance in the past 30 days, days of using drugs in the past 30 days, and days of heavy drinking).

From the fitted model, to estimate treatment effects, we evaluated three between-group pairwise comparisons (CBT/TC/TXT vs AO, SG vs AO, CBT/TC/TXT vs SG) of change over time. Poisson regression models (for count outcomes: substance use measures) estimate within-group change as a count ratio (CR), and the treatment effect estimate is the ratio of two CRs. The treatment effect estimates from the linear regression models (for continuous outcomes: pain measures and SPPB) are between-group differences in the magnitude of the change from baseline (difference of differences). The logistic regression model (for the binary outcome: low physical performance) estimates within-group change as an odds ratio (OR),

and the treatment effect estimate is the ratio of two ORs. Since change at 12 weeks was greater than the change at 8 weeks for most outcomes, we treated time as a continuous variable: actual number of days elapsed from baseline to the date of the follow-up, divided by 30 (to get the average change per month). These models were adjusted for baseline number of different types of substances used (range 1-8) because 12-week follow-up participation rates varied significantly by baseline values of this variable (i.e., the baseline numbers of substances used for non-responders were 3.6 and for responders was 2.5 with p=0.0356.)

3. Results

3.1 Baseline Participant Characteristics

3.1.1 Demographic and health-related characteristics. Table 1 shows that participants' had a mean age of 55. Most were male, non-Hispanic black, had completed some college or more education, were never married, had stable housing, and were not employed. The CBT/TC/TXT group had a higher mean SF-12 mental health score compared to the other groups.

3.1.2 Substance use, pain-related and physical performance variables. Most used substances included alcohol, cannabis and stimulants, and the mean (SD) number of substances used by each participant was 2.69 (1.36). ASSIST scores indicated that most participants had moderate or high risk substance use. On average, in the prior 30 days, participants reported using their preferred substance, any substance, and drugs on more than half of the days, as well as 3.2 days of heavy drinking (Table 1). Participants reported having chronic pain an average of 10.6 years. The mean pain intensity score (on a 0-10 scale) was 6.9, and percent pain relief provided by any treatment in the past 24 hours was 50.7%. The mean score on the Short Physical Performance Battery (SPPB) was 8.0 and the percentage of those with low physical performance on the SPPB was 48%.

3.1.3 Randomization. There were no statistically significant between-group differences at baseline for any variable, aside from SF-12 Mental Health Score (p=0.04) and percentage of pain relief provided by any treatment (p=0.04) (Table 1).

3.2 Outcomes

3.2.1 Feasibility/Adherence with Follow-Up Assessments. Of the 55 participants, 40 (73%) completed the 8-week and 46 (84%) completed the 12-week assessment. At 8 weeks, the non-response rates for the CBT/TC/TXT, SG and AO arms were 11%, 26%, and 44% respectively, p=0.08. At 12 weeks they were 17%, 16%, and 17%, p=0.99.

3.2.2 Acceptability/Treatment engagement. The mean number of sessions attended for CBT, tai chi and SG were 5.6, 5.5 and 5.1, respectively. Of the 18 CBT/TC/TXT participants, 12 (67%) attended ≥6 CBT sessions, and 11 (61%) attended ≥6 tai chi sessions. Of the 19 SG participants, 11 (63%) attended ≥6 sessions. There were no associations between any of the baseline variables and treatment engagement (data not shown).

3.2.3 Within group outcomes/Changes over time in primary outcomes. In Table 2, we present the unadjusted means, standard deviations and medians for within-group change scores from baseline to 8 weeks and from baseline to 12 weeks for all primary outcomes. Of note, the mean and median are quite different in most cases and the standard deviations are large, most likely due to the small sample size and heterogeneity within the sample.

3.2.3.1 Substance use outcomes. From baseline to 12 weeks, the CBT/TC/TXT group had statistically significant reductions in all four substance use outcomes: days of using preferred substance in the past 30 days (median reduction of 6 days), days of using any substance in past 30 days (median reduction of 9 days), days of using drugs in past 30 days (median reduction of 6 days), and days of heavy drinking in past 30 days (median change =0 but signed rank sums are statistically different, $p = 0.047$, indicating the within-individual change in the group was non zero). The support group also showed a statistically significant reduction in the number of days of preferred substance use in the past 30 days, from baseline to 12 weeks (median reduction of 5 days).

3.2.3.2 Pain outcomes. A statistically significant reduction in median pain intensity occurred in the SG from baseline to 12 weeks, and in the AO group from baseline to 8 weeks (median reduction of 1 point in both groups). For the CBT/TC/TXT group, median percent pain relief increased significantly (30%) from baseline to 12 weeks.

3.2.3.3. Physical performance outcomes. Statistically significant improvements were observed in both physical performance outcomes in the CBT/TC/TXT group from baseline to 8 weeks and from baseline to 12 weeks (median increase of 2 points in SPPB at each time point). The median change in % with low physical performance was 0 but the signed rank sums are statistically different at each time point. The SG showed a statistically significant improvement in SPPB score from baseline to 12 weeks (median increase of 1 point).

3.2.4 Between group outcomes/Adjusted treatment effects. Table 3 shows the adjusted between-group pairwise comparisons of change scores. These results are exploratory given that this is a pilot study with a small sample. Because there were baseline differences in baseline SF-12 Mental Health Score and % Pain relief across groups, we conducted a sensitivity analysis including these two variables as covariates and observed nonsignificant changes in the change scores (data not shown).

3.2.4.1 Substance use outcomes. Significantly greater reductions were observed in the CBT/TC/TXT group, relative to the AO group in three of the four substance use outcomes (Table 3). As compared to the AO group, the CBT/TC/TXT group had a 2% greater relative reduction per month (effect estimate=0.98) in the number of days of using their preferred substance, a

4% greater relative reduction per month (effect estimate =0.96) in the number of days of using drugs in the past 30 days, and a 19% greater per-month reduction (effect estimate=0.81) in number of days of heavy drinking in the past 30 days. We observed similar findings when comparing the CBT/TC/TXT group to the SG (Table 3).

3.2.4.2 Pain outcomes. No statistically significant differences were observed among the groups for any of the pain-related outcomes except for percent pain relief. The CBT/TC/TXT group had a 13% greater per-month absolute improvement in percent pain relief as compared to the SG.

3.2.4.3 Physical performance outcomes. Statistically significantly greater improvements in SPPB score were found in the CBT/TC/TXT group versus AO group and SG. On the 12-point SPPB scale, the average per-month improvement in the CBT/TC/TXT group was nearly one point greater than that in the AO group ($p < 0.001$) and a half point greater than in the SG ($p = 0.04$).

3.3 Participant feedback/Qualitative data. Sixteen CBT/TC/TXT participants (89%) provided feedback about the study. Overall feedback was very favorable; two-thirds wished that the eight-week program and the one-hour sessions (CBT and tai chi) lasted longer, while the remainder thought the individual program components and session length were adequate. Most rated the CBT group and tai chi sessions as extremely useful (75% and 88%, respectively) and enjoyed working with the therapist/instructor (94 and 100%, respectively). About 70% of the CBT/TC/TXT participants indicated that they would definitely attend this type of group therapy if it were offered by APAIT with no compensation and not as part of a study. Suggestions for

additional topics to address included stigma, HIV and aging, and more education about various medical conditions. Two (male) participants suggested including a male facilitator living with HIV and one suggested having the groups available in Spanish. Related to the text messaging component, 69% reported it was extremely important in helping them to make or maintain a change. Fifty-six percent would have liked to receive the messages for longer than 8 weeks, and 50% thought two motivational texts a week was not enough.

4. Discussion

This study demonstrated that a multi-component behavioral intervention addressing substance use, pain, and physical performance in older PLWH with comorbid substance use and pain disorder conducted in partnership with a community-based agency is feasible, acceptable and has preliminary efficacy. Importantly, our enrolled population used multiple substances, had ASSIST scores indicating moderate to high risk substance use, long term chronic pain and high rates of low physical performance at baseline. Feasibility and acceptability indicators showed moderate levels of participant enrollment (62% of those eligible agreed to participate), excellent 12-week assessment completion (84%), acceptable to excellent CBT treatment fidelity ratings, and high attendance at CBT and tai chi sessions (67% and 61%, respectively attended at least 6 sessions). Our qualitative data highlight overall positive program feedback and provide suggestions for changes to study procedures to enhance study efficacy. Anecdotally, we also learned from study staff about some of the barriers to attending the group-based sessions including illness, drug use, lack of stable housing, and

transportation issues. We also learned that most participants did not complete the homework assigned to them as part of the CBT component.

We hypothesized that the intervention would lead to reductions in substance use and pain outcomes and improve physical performance. Looking first at within-group changes, statistically significant improvements from baseline to 12 weeks were observed in the CBT/TC/TXT group for all four substance use outcomes, one pain outcome (percent pain relief) and both physical performance measures. In the SG, from baseline to 12 weeks, statistically significant improvements were seen for one substance use (days of use preferred substance) and one pain (pain intensity) and one physical performance (SPPB) outcome. In the AO group, no statistically significant within group improvements were observed from baseline to 12 weeks.

Looking next at between-group changes, we observed several statistically significant between-group changes, most importantly in days of heavy drinking and in the SPPB score. The substance use change scores were modest (≤ 6%) except for days of heavy drinking in which, compared to the AO group, the CBT/TC/TXT group and SG had large relative reductions (19% and 13%, respectively).

We also observed a significant between group treatment effect with respect to perceived relief obtained from pain treatments over the past 24 hours suggesting that the intervention may improve quality of pain management. This is important given that both the mean and median self-rated pain intensity among participants at the time of enrollment was moderately severe (i.e., 7 on a 10 point scale). We did not, however, observe any meaningful treatment-related reductions in pain intensity or perceived

disability due to pain. Possible explanations for these latter findings include that most participants' pain was of a neuropathic origin, which has not been shown to respond to psychological interventions when used as stand-alone therapy (Eccleston, Hearn & Williams 2015). In addition, our intervention merged elements of pain and substance use behavioral treatments such that the dose of pain coping skills training, behavioral activation, and cognitive restructuring may have been insufficient. Also as participants did not complete the homework exercises, which serve to reinforce the use of the techniques and suggests that adoption of the behavioral strategies to manage pain both during and after the intervention period was limited.

With respect to the physical performance outcomes, SPPB score improved in the CBT/TC/TXT group relative to both the AO and SG of a magnitude indicative of meaningful improvement (Kwon et al., 2009). These results provide strong support for future research that evaluates the role of movement therapies such as tai chi in reducing risk of falls, mobility-related disability and frailty occurrence in older PLWH.

This study has several strengths. This is the first study, to our knowledge, employing a multicomponent behavioral intervention to address both chronic pain and substance use in older PLWH. Another strength is that we conducted the study in partnership with a community-based agency serving PLWH, and trained its staff to deliver the multicomponent intervention, so our model of implementation was pragmatic by design. Several limitations, however, warrant attention. We enrolled English-speaking participants only, therefore the extent to which the results generalize to non-English speaking patients remains unclear. The same

person conducted recruitment and all study assessments and was therefore not blinded to group assignment. We elected to have rolling enrollment of the groups and this may have affected group cohesion and reduced the efficacy of the CBT protocol. Some of the staff who led the CBT group sessions also led the support groups which could have contributed to some of the beneficial effects observed in the latter group through contamination bias. We also compensated participants to attend the CBT, TC and SG sessions, which likely enhanced participation rates and reduces generalizability, as this is not feasible in non-study settings. It may also be challenging to implement the tai chi component of the intervention with fidelity in community-based settings as skilled instructors may be difficult to find, depending on location, and therefore using other modalities such as technologies to facilitate remote tai chi could enhance real world implementation.

In conclusion, this pilot study demonstrates the feasibility and acceptability of a combined behavioral therapy in a vulnerable and understudied population, as well its preliminary efficacy in reducing substance use and improving physical performance. Suggestions for improvements to the CBT component of the intervention and inclusion of additional text messages will be addressed in a larger study to enhance the intervention's potential efficacy in further reducing substance use and pain. The next steps, to refine the intervention and test it in a larger RCT, are warranted by the data and needed to facilitate effective and accessible interventions to address substance use, pain and physical performance in the growing population of older PLWH.

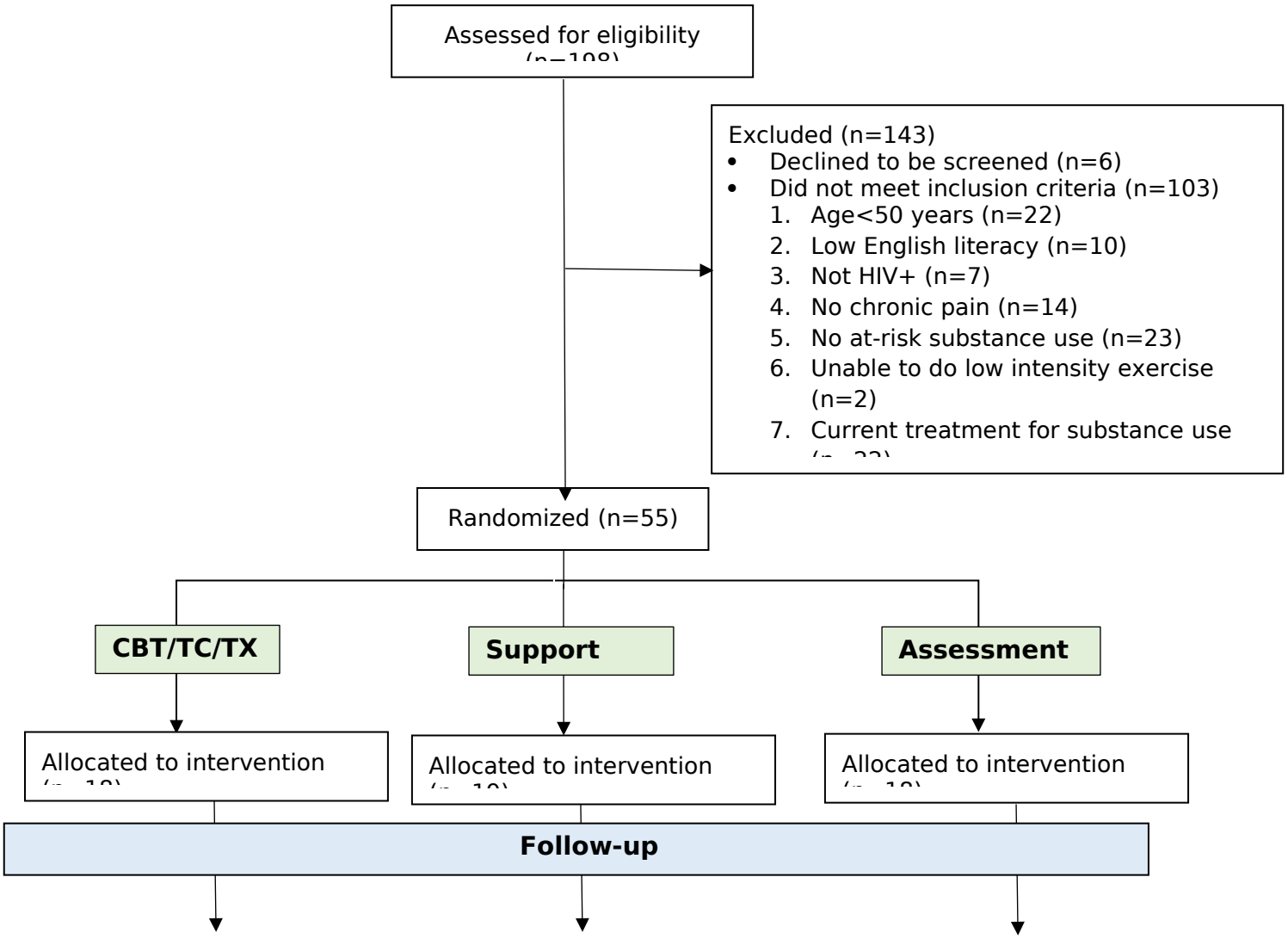
Assessed for eligibility
Excluded (n=143)
• Declined to be screened (n=6)
• Did not meet inclusion criteria (n=103)
1. Age<50 years (n=22)
2. Low English literacy (n=10)
3. Not HIV+ (n=7)
4. No chronic pain (n=14)
5. No at-risk substance use (n=23)
6. Unable to do low intensity exercise (n=2)
7. Current treatment for substance use
Randomized (n=55)
CBT/TC/TX
Support
Assessment
Allocated to intervention
Allocated to intervention
Allocated to intervention
Follow-up
8 week follow-up (n=16)
• non-response (n=2)
12 week follow-up (n=15)
• non-response (n=3)
8 week follow-up (n=14)
• non-response (n=5)
12 week follow-up (n=16)
• non-response (n=3)
8 week follow-up (n=10)
• non-response (n=8)
12 week follow-up (n=15)
• non-response (n=3)

Figure. 1. Study flow diagram

Table 1. Baseline Characteristics [a]

	Total N=55	CBT/TC/TXT N=18	Support group N=19	Assessment only N=18
Demographics				
Age, Mean (SD), Range[b]	55.1 (5.4), 49-71	53.3 (4.8), 49-65	55.2 (5.0), 49-67	56.8 (6.0), 50-71
Gender				
Male	42 (76)	14 (77)	14 (74)	14 (78)
Female	8 (15)	2 (11)	3 (16)	3 (17)
Transgender, male-to-female	5 (9)	2 (11)	2 (11)	1 (6)
Ethnicity / Race				
Hispanic	17 (31)	7 (39)	6 (32)	4 (22)
Non-Hispanic, black	29 (53)	9 (40)	11 (58)	9 (50)
Non-Hispanic, other	9 (16)	2 (11)	2 (11)	5 (28)
Education				
High school or less	21 (38)	7 (39)	9 (47)	5 (28)
Some college or more	34 (62)	11 (61)	10 (53)	13 (73)
Marital Status				
Married/Partner	9 (16)	2 (11)	4 (21)	3 (17)
Divorced/Separated	11 (20)	4 (22)	3 (16)	4 (22)
Widowed	4 (7)	0 (0)	3 (16)	1 (6)
Never married	31 (56)	12 (67)	9 (47)	10 (56)
Housing Arrangement[c]				
Stable housing	42 (76)	15 (83)	14 (74)	13 (72)
Unstable housing	13 (24)	3 (17)	5 (26)	5 (28)
Employment				
Working full time or part time	5 (9)	2 (11)	1 (20)	2 (11)
Unemployed or disabled	49 (91)	16 (89)	17 (94)	16 (89)
HIV				
Years of being HIV positive, Mean (SD)	17.4 (8.1), Range 0.6-32	16.2 (8.4) Range 4-32	15.6 (7.2), Range 1-26	20.5 (8.3) Range 0.6-32
Most recent CD4, Mean (SD)	597 (363) Range 34-1600	582 (357) Range 37-1600	698 (342) Range 34-1282	611 (380) Range 52-1400
HIV viral load				
Undetectable[d]	34 (63)	10 (56)	12 (63)	12 (71)
Detectable	20 (37)	8 (44)	7 (37)	5 (29)
Comorbidities				
Number of non-HIV chronic conditions. (range 0 to 8), Mean (SD)	3.1 (1.7)	2.8 (1.6)	3.1 (1.8)	3.3 (1.7)
Physical and Mental Health (SF-12))				
Physical Health Score, Mean (SD)	34.1 (9.3)	32.2 (11.1)	36.4 (8.4)	33.7 (8.1)
Mental Health Score,[e] Mean (SD)	37.9 (11.3)	43.5 (10.9)	34.9(12.0)	35.6 (9.4)
Substance Use				
Most often used (preferred) substance	17 (31)	8 (44)	4 (21)	5 (28)
Alcohol	16 (29)	6 (33)	4 (21)	6 (33)
Cannabis	18 (33)	4 (22)	9 (47)	6 (28)
Stimulant	4 (7)	0 (0)	2 (11)	2 (11)

	Total N=55	**CBT/TC/TXT N=18**	**Support group N=19**	**Assessment only N=18**
Demographics				
(Cocaine/Amphetamine-like) Pain killers (more than prescribed or w/o Rx)				
Number of substances used, Mean (SD)	2.69 (1.36)	2.56 (1.20)	2.37 (1.16)	3.17 (1.62)
WHO ASSIST score[f]				
Alcoholic beverages				
Low risk	21 (38)	5 (28)	10 (53)	6 (33)
Moderate risk	15 (27)	6 (33)	3 (16)	6 (33)
High risk	18 (35)	7 (39)	6 (32)	6 (33)
Cannabis				
Low risk	24 (44)	9 (50)	10 (53)	5 (28)
Moderate risk	23 (42)	6 (33)	8 (42)	9 (50)
High risk	8 (15)	3 (17)	1 (5)	4 (22)
Cocaine				
Low risk	31 (56)	12 (67)	9 (47)	10 (56)
Moderate risk	14 (25)	4 (22)	5 (26)	5 (28)
High risk	10 (18)	2 (11)	5 (26)	3 (17)
Amphetamine type stimulants				
Low risk	31 (56)	8 (44)	11 (58)	12 (67)
Moderate risk	11 (20)	6 (33)	4 (21)	1 (6)
High risk	13 (24)	4 (22)	4 (21)	5 (28)
Inhalants				
Low risk	48 (87)	17 (94)	17 (89)	14 (78)
Moderate risk	5 (9)	1 (6)	1 (5)	3 (17)
High risk	2 (4)	0 (0)	1 (5)	1 (6)
Sedatives or sleeping pills				
Low risk	41 (75)	15 (83)	15 (79)	11 (61)
Moderate risk	9 (16)	2 (11)	2 (11)	5 (28)
High risk	5 (9)	1 (6)	2 (11)	2 (11)
Hallucinogens				
Low risk	51 (93)	17 (94)	18 (95)	16 (89)
Moderate risk	3 (5)	1 (6)	0 (0)	2 (11)
High risk	1 (2)	0 (0)	1 (5)	0 (0)
Opioids				
Low risk	30 (55)	12 (67)	11 (58)	7 (39)
Moderate risk	17 (31)	4 (22)	7 (37)	6 (33)
High risk	8 (15)	2 (11)	1 (5)	5 (28)
Substance Use in Past 30 Days, Mean (SD),median				
Days of using preferred substance	18.8 (10.8), 20	16.4 (9.1), 14	21.2 (10.8), 29	18.6 (12.1), 21
Days of using any substance	22.3 (9.5), 29	18.5 (9.2), 16	23.1 (9.2), 30	24.9 (9.6). 30
Days of using drugs	18.7 (12.3), 23	14.5 (11.9), 12	19.6 (12.8), 29	21.7 (11.8), 30
Days of heavy drinking	3.2 (7.7), 0	5.1 (9.0), 0	3.8 (9.4), 0	0.9 (2.2), 0
Pain				
Years of chronic pain, Mean (SD), Range	10.6 (8.9), 0.5-31	10.8 (3.8), 2-30	12.4 (9.3), 0.5-30	8.5 (9.1), 0.6-31
Medications used to treat pain				
Neuropathic pain (NP) medication	4 (7) 12 (22)	2 (11) 4(22)	1 (5) 4 (21)	1 (6) 4(22)
NSAIDs	9 (16)	3 (17)	2 (11)	4 (22)

	Total N=55	CBT/TC/TXT N=18	Support group N=19	Assessment only N=18
Demographics				
Opioids Use any NP, NSAID, or Opioid	23 (42)	9 (50)	7 (37)	7 (39)
Pain intensity on average (0-10), Mean (SD), median	6.9 (2.0), 7	6.4 (2.2), 7	7.0 (1.9) 8	7.4 (1.9) 7
% Pain relief in past 24 hours, provided by any treatment[e] Mean (SD), median	50.7 (30.4), 50	41.7 (33.2), 35	64.7 (21.2), 70	45.0 (31.7), 45
Pain Self-Efficacy Questionnaire (PSEQ)[g] score (0-60), Mean (SD) median	33.6 (13.1), 34	38.2 (13.6), 42	30.4 (12.5), 31	32.3 (12.6), 29.
Roland-Morris Disability Questionnaire (RMDQ)[h] score (0-24),Mean (SD), median	16.7 (5.6), 17	15.7 (6.9), 17	17.3 (5.2), 17	17.1 (4.5), 17
Physical Performance				
Short Physical Performance Battery (SPPB)[i] score (0-12), Mean (SD), median	8.0 (2.4), 8	8.2 (2.7), 8	8.1 (2.1), 8	7.8 (2.4), 8
Low physical performance (SPPB<=10), % Mean	48 (87)	14 (78)	17 (89)	17 (94)

Abbreviation: SD, Standard Deviation

[a] Data are presented as No. (%) unless otherwise indicated.

[b] Three individuals who were enrolled reported they were age 50 at the time of the screening assessment when actually they were turning 50 in the coming year.

[c] Stable housing was defined as living in an apartment/house alone or with a family member, friend or roommate. Unstable housing was defined as living in a foster or group home, boarding/halfway house, shelter, welfare hotel, on the street, vacant lot, abandoned building, park, or car.

[d] Undetectable means fewer than 50 copies of HIV per milliliter of blood (<50 copies/mL). In California, PLWH must carry with them a “diagnosis form” which lists their most recent HIV-1 RNA levels completed within the last 90 days.

[e] P=0.04 across the three study groups.

[f] ASSIST defines risk scores differently for alcohol and other substances. For alcohol low risk is 0 to 10, moderate risk is 11 to 26, high risk is >=27; for the other substances, low risk is 0 to 3, moderate risk is 4 to 26, high risk is >=27.

[g] PSEQ: Higher score indicates stronger self-efficacy beliefs.

[h] RMDQ is composed of 24 yes/no questions designed to assess back pain as experienced by the patient in the last 24 hours. Yes items are scored to yield a total score where 0 = no disability to 24 = maximum disability.

[i] SPPB: Higher score indicates better physical performance.

Table 2. Descriptive Statistics for Within Group Changes in Outcomes from Study Baseline to 8 Weeks and 12 Weeks

	CBT/TC/TXT N=18		Support Group N=19		Assessment Only N=18	
Outcomes	**Mean±SD, Median**	**P value***	**Mean±SD, Median**	**P value***	**Mean±SD, Median**	**P value***
Substance Use in past 30 days						
Days of using preferred substance						
BA to 8 weeks	-1.4±15.3, -2	0.678	-8.5±15.7, -1	0.147	2.3±12.4, -1	0.891
BA to 12 weeks	-7.3±12.7, -6	**0.043**	-10.1±15.0, -5	**0.032**	-1.7±10.0, 0	0.594
Days of using any substance						
BA to 8 weeks	-3.2±15.6, -4	0.511	-7.9±15.7, -1	0.227	-2.6±10.6, 0	0.438
BA to 12 weeks	-9.5±12.9, -9	**0.021**	-9.7±15.5, -2	0.087	-5.4±10.4, 0	0.078
Days of using drugs						
BA to 8 weeks	-3.8±14.0, -2	0.221	-4.8±16.7, 0	0.445	-1.3±9.0, 0	1.000
BA to 12 weeks	-9.8±9.8, -6	**<0.001**	-6.9±16.9, 0	0.251	-4.3±10.8, 0	0.266
Days of heavy drinking						
BA to 8 weeks	-3.9±9.2, 0	0.086	-0.1±11.8, 0	1.000	1.1±2.7, 0	0.313
BA to 12 weeks	-4.8±9.4, 0	**0.047**	-2.3±7.5, 0	0.125	0.8±3.4, 0	0.750
Pain						
Pain intensity (range, 0-10)						
BA to 8 weeks	-0.1±2.2, 0	0.952	-1.3±2.4, -1	0.063	-1.3±1.5, -1	**0.039**
BA to 12 weeks	-0.1±2.0, 0	0.800	-1.4±1.7, -1	**0.010**	-1.2±2.7, -2	0.159
Percent pain relief (range, 0-100)						
BA to 8 weeks	5.6±33.3, 10	0.506	-7.1±40.8, 0	0.680	1.0±38.1, 0	0.844
BA to 12 weeks	28.0±42.8, 30	**0.032**	-13.1±40.8, -15	0.202	2.7±35.6, 10	0.845
Pain Self-Efficacy Questionnaire score (range, 0-60)						
BA to 8 weeks	1.3±16.4, 1	0.659	0.6±14.0, -1	0.933	4.4±13.5, 4	0.250
BA to 12 weeks	-5.4±13.1, -4	0.236	-2.1±11.5, -2	0.366	-3.1±14.5, -3	0.516
Roland-Morris Disability Questionnaire score (range, 0-24)						
BA to 8 weeks	-0.9±7.9, -1	0.416	-1.9±4.5, -1	0.194	-4.1±3.8, -3	**0.004**

	CBT/TC/TXT N=18		Support Group N=19		Assessment Only N=18	
Outcomes	**Mean±SD, Median**	**P value***	**Mean±SD, Median**	**P value***	**Mean±SD, Median**	**P value***
BA to 12 weeks	-1.4±7.2, 1	0.570	-1.1±4.9, 0	0.541	-1.9±4.9, -1	0.152
Physical Performance						
Short Physical Performance Battery (range 0-12)						
BA to 8 weeks	2.1±1.6, 2	**<0.001**	0.1±2.6, 2	0.630	0.4±2.6, 1	0.539
BA to 12 weeks	2.1±1.6, 2	**<0.001**	0.9±1.7, 1	**0.044**	-0.5±2.6, 0	0.563
Low physical performance (SPPB<=10), %						
BA to 8 weeks	-43.8 (51.2), 0	**0.016**	-21.4 (42.6), 0	0.250	-30.0 (48.3), 0	0.250
BA to 12 weeks	-40.0 (50.7), 0	**0.031**	-25.0 (44.7), 0	0.125	-6.7 (45.8), 0	1.000

BA= baseline; SD = standard deviation

*Signed rank test was used to test statistical significance of within-group change; P values <0.05 are bolded.

Table 3. Treatment Effects (between group pairwise comparisons of change over time) estimated from Mixed Effects Models*

	CBT/TC/TXT vs. Assessment Only		**Support Group vs. Assessment Only**		**CBT/TC/TXT vs. Support Group**	
Outcomes	**Effect Estimate** (95% CI)**	**p**	**Effect Estimate** (95% CI)**	**p**	**Effect Estimate** (95% CI)**	**p**
Substance Use						
Days of using preferred substance in past 30 days	0.98 (0.96, 1.00)	**0.018**	0.96 (0.94, 0.98)	**<0.001**	1.02 (1.00, 1.04)	**0.045**
Days of using any substance in past 30 days	0.98 (0.96, 1.00)	*0.071*	0.98 (0.96, 1.00)	**0.031**	1.00 (0.98, 1.02)	0.799
Days of using drugs in past 30 days	0.96 (0.93, 0.98)	**<0.001**	0.99 (0.97, 1.01)	0.192	0.97 (0.95, 0.99)	**0.003**
Days of heavy drinking in past 30 days	0.81 (0.76, 0.86)	**<0.001**	0.87 (0.81, 0.93)	**<0.001**	0.94 (0.88, 0.99)	**0.019**
Pain						
Pain intensity on average (0-10)	0.39 (-0.13, 0.90)	0.139	-0.03 (-0.54, 0.49)	0.922	0.41 (-0.09, 0.92)	0.109
Percent pain relief	8.27 (-0.76, 17.30)	*0.072*	-4.73 (-13.75, 4.28)	0.299	13.01 (4.08, 21.93)	**0.005**
Pain Self-Efficacy Scale score (0-60)	-0.05 (-3.54, 3.43)	0.976	0.01 (-3.42, 3.45)	0.993	-0.07 (-3.48, 3.35)	0.968
Roland-Morris Disability Questionnaire score (0-24)	0.16 (-1.22, 1.55)	0.815	0.31 (-1.07, 1.69)	0.652	-0.15 (-1.51, 1.21)	0.827
Physical Performance						
Short Physical Performance Battery score (SPPB, 0-12)	0.91 (0.41, 1.41)	**<0.001**	0.4 (-0.10, 0.89)	0.117	0.51 (0.02, 1.01)	**0.040**
Low physical performance (SPPB<=10)	0.52 (0.18, 1.51)	0.223	0.72 (0.24, 2.16)	0.557	0.71 (0.27, 1.88)	0.490

* Poisson regression models (for count outcomes: substance use measures) estimate within-group change as a count ratio (CR), and the treatment effect estimate is the ratio of two CRs. The treatment effect estimates from the linear regression models (for continuous outcomes: pain measures and SPPB) are between-group differences in the magnitude of the change from baseline (difference of differences). The logistic regression model (for the binary outcome: low physical performance) estimates within-group change as an odds ratio (OR), and the treatment effect estimate is the ratio of two ORs.

** Treatment effect is the ratio of the count ratio (or odds ratio) in arm 1 vs arm 2 for count outcomes and binary outcomes (e.g., in the first column this is the ratio of the count (or

odds) ratio in CBT/TC/TXT arm vs. AO arm. For continuous outcomes, treatment effect is the change in arm1 minus the change in arm 2. P values between 0.05 and 0.1 are italicized; p values <0.05 are bolded

Acknowledgements

We would like to acknowledge the support of APAIT, without whom we could not have done this project. Thanks also to Suzanne Hughes, PhD, and Rebecca Zipfel, for their assistance with manuscript preparation.

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