Systematic review of cognitive behavior therapy to improve mental health of women living with HIV

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ABSTRACT

Psychological distress is highly prevalent in people living with HIV. Cognitive behavior therapy (CBT) has been associated with improved mental health outcomes in HIV-infected men who have sex with men (MSM); however, little is known of its effect in women living with HIV/AIDS (WLHA). We review current literature on CBT and its effects on depression, anxiety, stress and mental health quality of life (QOL) in WLHA. We undertook a systematic review of the literature indexed in PubMed, Medline, Psychiatry Online and ScienceDirect. Of the 273 relevant studies discovered, 158 contained duplicate data, and 105 studies did not meet the inclusion and exclusion criteria, yielding 10 studies for analysis. Data were independently extracted by each researcher, with differences resolved through discussion and consensus. For WLHA, CBT substantially improved QOL, symptoms of depression and stress, but appeared to have less impact on anxiety. Three of the six studies measuring depression outcomes showed statistically significant decreases in depression. Three of three studies measuring mental health QOL, and three of three studies measuring stress also demonstrated statistically significant improvement. Two of two studies measuring anxiety did not show statistically significant change. CBT is a promising therapy for WLHA. CBT may reduce psychological distress, improving symptoms of depression, stress and QOL. There is a need for additional, better standardized studies that examine CBT for WLHA.

INTRODUCTION

It is estimated that by the end of 2015, over 1.1 million people were living with HIV in the USA alone.[1] While the prevalence of HIV has remained stable over the past several years, there has been a decline in AIDS deaths, with life expectancy approaching that for non-HIV-infected populations for those patients with access to combination antiretroviral therapy (ART).[2] With the increase in life expectancy comes new challenges as HIV/AIDS has become a chronic disease for many, with all of the attendant psychological distress accompanying such a life-long illness.

One common form of treatment is cognitive behavior therapy (CBT), a type of psychotherapy based on the premise that maladaptive cognitive factors lead to the perpetuation of emotional distress and behavioral issues. CBT-AD has demonstrated efficacy in improving medication adherence and depression in HIV-infected injection drug users[3] and others.[4] Nevertheless, the efficacy of CBT for people living with HIV/AIDS (PLHA) has been predominantly characterized in MSM. In this population, CBT has been shown to be effective in improving immune function, depression, stress and quality of life (QOL).

However, globally in 2015, there were an estimated 17.8 million women living with HIV (WLHA), constituting 51% of all adult PLHA; and, less than half of this population is effectively treated. In comparison to men, women are more likely to care for children and experience the stress that accompanies childcare.[5] Additionally, women report higher rates of intimate partner violence compared with men[6], and intimate partner violence has been associated with depression, substance abuse, increased risk of chronic mental illness and other chronic diseases. In studies of MSM living with HIV/AIDS, CBT was found to significantly reduce distress, anxiety and depressed affect.[7 8] With the unique stressors that WLHA face, a tailored CBT may be expected to have a substantial impact on their lives and the course of their illnesses. However, WLHA are underrepresented in clinical trials, and few studies have assessed the effectiveness of CBT for this population.

One systematic review has addressed CBT to improve mental health in PLHA.[9] This review identified 15 studies that evaluated CBT interventions to improve mental health outcomes. Seven studies looked at male-only populations, and only one study had a majority of women. Of the remaining seven studies, the proportion of women ranged from 8% to 36%. This review found that CBT significantly improved four mental health outcomes: depression (d=0.33), anxiety (d=0.30), anger (d=1.00) and stress (d=0.43).

Since this prior review, we identified 10 studies that specifically addressed the efficacy of CBT in WLHA. In this systematic review, we analyzed current literature to determine
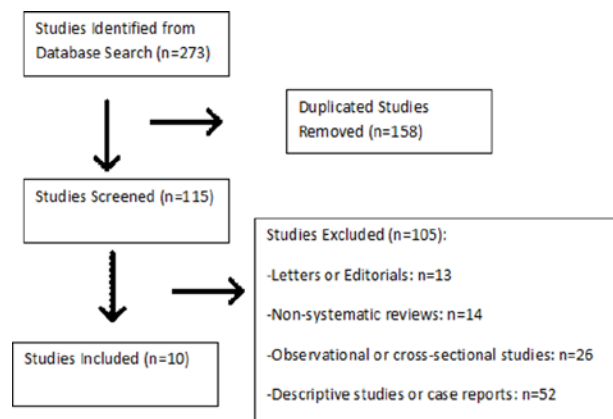
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Figure 1 Flow diagram depicting the study selection process.

whether CBT improves mental health QOL, depression, anxiety and stress in WLHA.

METHODS
Database and search strategy
A systematic review of the literature was conducted, and this report follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[10] This comprehensive search of journal and trial databases including PubMed, Medline, Psychiatry Online and ScienceDirect was conducted in July 2014. The search identified interventions that were in English language and published in a peer-reviewed journal between July 1981 and July 2014. We used the following search terms: cognitive behavior therapy, CBT, women, HIV, HIV+, AIDS, stress, depression, QOL and anxietyfigure 1.

Trial selection
Studies were included if they met the following criteria: controlled trials with CBT as the main intervention; participants were WLHA, aged 18 years and older; the study included separate data analysis for WLHA; outcomes included depression, stress, mental health QOL or anxiety and were written in English language. Interventions were excluded if they were letters, editorials, non-systematic reviews, observational studies, cross-sectional study designs, descriptive studies or case reports. Data were independently extracted by each researcher, with differences resolved through discussion and consensus. Of 273 studies originally identified from the database search, 158 duplicate studies were initially removed. A hand search of the remaining articles identified no additional papers of relevance. The remaining 115 studies were screened, of which 105 were excluded based on the above criteria, leaving 10 studies for review and analysis.

Data abstraction
Our final data extraction yielded four spreadsheets, with each of three researchers independently creating a set. Spreadsheet 1 included general study and subject demographic characteristics (ie, location, dates of study, sample size, HIV+/AIDS status, mean age, ethnicity), allowing restriction of studies to those assessing depressive symptoms, measurement times, medications and other sample

criteria. Spreadsheet 2 included evaluation of study design, control and follow-up (ie, retention percentage, intervention features, sessions, duration, social support component/individual, homework and session leader). Spreadsheet 3 included features related to outcome measurement (ie, instrument, preintervention and postintervention assessment and effect size). Spreadsheet 4 included sources of bias (ie, allocation concealment bias, blinding bias, incomplete outcome data/attrition bias, selective reporting bias), along with each investigator's support for each judgment. When differences were found in assessment of bias, they were resolved by discussion and consensus.

Analytical approach
We used data from the studies for effect size calculation. For studies which had multiple follow-ups, we used the first postintervention assessment for analyzing intervention effects. Studies used different measures for assessing similar outcomes, making meta-analysis impossible. The Beck Depression Inventory (BDI) and the Coping Orientation to Problems Experienced (COPE) inventory for stress were among the most commonly used measures, and were used by three studies each. Effect sizes were calculated for individual studies' data, but comparison of effect sizes within an outcome was not performed due to the differences in measures.

Effect size calculation
Effect size was calculated for each control group and intervention group. The means compared were the baseline score and the postintervention score. Effect size was also calculated for the postintervention score comparing the means of the control group with the experimental group. Effect sizes were calculated using the formula Cohen's $d = M_1 - M_2 / s_{pooled}$, where $s_{pooled} = \sqrt{[(s_1^2 + s_2^2)/2]}$.[11]

Assessment of risk bias in included studies
Assessment of risk bias was performed by each author. During the preliminary data abstraction, limitations of the studies were assessed. During a more detailed data abstraction, risk of bias was evaluated in each of the following categories: allocation concealment, blinding, attrition and selective reporting.

RESULTS
Sample characteristics (table 1)
The 10 studies selected included WLHA with ages ranging from 30 to 45 years. Six studies included women who were HIV+, but had not progressed to AIDS; three included women diagnosed with AIDS, and one included both. Women from all races were included, with predominance of African-American women (range=53%–90%). Four studies included women with a history of depression or other psychiatric illness, some of whom were prescribed psychiatric medications.

Effect of intervention
Three studies examined mental health QOL, generally described as the individual's perception of aspects of her life being satisfactory (table 2). This can include emotional state, affect, mood and other symptoms. These studies used

Table 1 Sample characteristics

Study	HIV+ or AIDS	Age (mean)	Sample size intervention (I); control (C)	African-American (%)	Baseline depression/ HX of psychiatric disorder	Outcome measured
Jones et al[19]	AIDS	Data not provided	I=92 C=82	Data not provided	Data not provided	Stress
Lechner et al[12]	AIDS	39.6	I=150 C=180	59%	No	Quality of life
Sikkema et al[13]	Both	40.3	I=52 C=33	53%	Yes	Depression, quality of life and anxiety
LaPerriere et al[14]	AIDS	38.0	I=74 C=80	67%	Yes	Depression
Jones et al[17]	HIV+	Data not provided	I=88 C=89	Data not provided	Data not provided	Stress
Antoni et al[16]	HIV+	Data not provided	I=21 C=18	Data not provided	Data not provided	Stress
Futterman et al[15]	HIV+	Data not provided	I=83 C=77	Data not provided	Yes	Depression and stress
Jones et al[20]	HIV+	38.6	I=212 C=239	68%	No	Depression and anxiety
Brown et al[18]	HIV+	44.7	I=30 C=30	70%	Yes	Depression and stress
Jensen et al[11]	HIV+	31.21	I=46 C=26	90%	No	Depression, quality of life

a variety of measures such as Grief Reaction Index (GRI), profile of mood states, Medical Outcome Study HIV 30, Benefit Finding Scale and other measures of positive and negative affect. All studies found a significant improvement in mental health QOL for WLHA. One showed a significant increase in positive affect and positive state of mind, with Cohen's d effect sizes of the intervention group ranging from 0.118 to 0.301, thus indicating a small-to-medium effect of the CBT intervention.[11] Another study showed a significant increase in mental health QOL for the intervention group.[12] A third study demonstrated significant improvement in GRI score for women in the intervention condition compared with the control,[13] along with a significant difference between the treatment group and control group in Symptom Checklist 907 Revised ($p < 0.05$). Effect sizes were −0.455 for the GRI and −0.360 for the SCL, indicating a medium effect size for CBT on mental health QOL.

Six studies examined depression (table 3). Three different scales were used to measure changes in depression: BDI, Hamilton Depression Scale (HAM-D) and the Center for Epidemiological Studies Depression Scale (CES-D). Three of the six studies showed a significant decrease in depression. One study used the BDI ($p < 0.001$, $d = -0.654$),[14] another the HAM-D ($p < 0.01$; $d = -0.527$)[13] and the third used the CES-D ($p < 0.01$; $d = -1.445$).[15] These effect sizes indicate a medium to large effect of CBT on depression. The other three studies showed no significant difference in scores for the intervention group.

Table 2 Quality of life

Study	Evaluation design	Description of intervention	Instrument used for assessment	Relevant outcomes	Cohen's d
Jensen et al[11]	RCT; control—1 day workshop; 45% attrition at 9 months	Group; 10 sessions; 135 min each; weekly homework; delivered by doctoral trainees, post doc fellow and psychologists	► Total positive affect ► Positive states of mind scale ► Spiritual well-being ► Total negative affect	There was a significant increase in positive affect and positive state of mind ($p < 0.05$) but no significant change in Beck Depression Inventory or negative affect.	0.118; 0.151; 0.207; 0.301;
Lechner et al[12]	RCT; control—individual video-tape session; 25% attrition for intervention, 13% for control	Group; 10 sessions; 90 min stress management, 30 min relaxation; delivered by trained leader	► Medical outcomes study HIV 30	There was a significant increase in mental health QOL for the intervention group ($p < 0.05$).	Not enough data reported
Sikkema et al[13]	RCT; control—individual mental health and psychiatric services; 44% completed full intervention	Group; 12 sessions; 90 min each; delivered by two males and two female therapists—one doctoral psychologist, two masters of social work, one nurse practitioner	► Grief Reaction Index ► Symptom Checklist 907 Revised (SCL-907R)	There was a significant improvement in GRI score for women in the intervention condition compared with the control ($p < 0.01$) and a significant difference between the treatment and control SCL-907R ($p < 0.05$).	−0.455; −0.360

RCT, randomised controlled trial.

Table 3 Depression

Study	Evaluation design	Description of intervention	Instrument used for assessment	Relevant outcomes	Cohen's d
Jensen et al[11]	See table 1	See table 1	▶ Beck Depression Inventory (BDI)	No significant change in BDI or negative affect.	No data reported.
Laperriere et al[14]	RCT; control—10 weekly individual videotape sessions on stress management, relaxation, coping and entertainment; 28% attrition at 6 months	Group; 10 sessions; 120 min each; delivered by doctoral level psychologist and post doc fellows	▶ BDI	CBSM intervention showed a significant decrease in BDI for up to 1 year (p<0.001).	−0.654
Sikkema et al[13]	See table 1	See table 1	▶ Hamilton Depression Scale	There was a significant difference from baseline to postintervention for the intervention group (p<0.01).	−0.527
Brown et al[18]	See table 1	See table 1	▶ Center for Epidemiological Studies Depression Scale (CES-D)	There was no significant change in CES-D scores.	−0.043
Jones et al[20]	RCT; control—individual information session; 53% attrition at 12 months	Group; 10 sessions; 120 min each; weekly homework	▶ BDI	There was no significant difference in depression score for the intervention group.	−0.079
Futterman et al[15]	See table 2	See table 2	▶ CES-D	There was a significant decrease in CES-D scores for women in the intervention compared with the control (p<0.01).	−1.445

CBSM, cognitive behavioral stress management; RCT, randomised controlled trial.

Five studies examined stress (table 4). Three of the studies showed improvement in stress-related outcomes. One study showed a decrease in life stress events measured by the Life Experiences Survey (p<0.05, d=−0.315).[16] Another used the COPE inventory, and showed a significant decrease in overall stress scores for up to 6 months (p<0.05).[17] A third showed a significant increase in stress management knowledge (p<0.01; d=0.730).[18] These effect sizes indicate a small effect on life stress events, and a large effect on stress management knowledge. Two studies used the COPE inventory to measure stress, and neither showed a significant improvement in scores.[15 19]

Two of the studies examined anxiety (table 5). They used the State Trait Anxiety Inventory and the Hamilton Rating Scale for Anxiety. Neither of the studies showed a

Table 4 Stress

Study	Evaluation design	Description of intervention	Instrument used for assessment	Relevant outcomes	Cohen's d
Antoni et al[16]	RCT; control—1 day 5 hour CBSM workshop; 55% attrition at 9 months	Group; 10 session; 135 min each; delivered by doctoral trainees, postdoctoral fellows and licensed psychologists	Life Experiences Survey	The intervention group had a significant decrease in life stress events (p<0.05).	−0.15
Jones et al[17]	RCT; control—individual information session; 28% attrition at 6 months	Group; 10 sessions; 120 min; weekly homework; delivered by therapist	Positive stress coping: COPE	The intervention group's scores were significantly improved compared with the control participants (p<0.05). This effect lasted up to 6 months.	Not enough data reported.
Jones et al[19]	RCT; control—individual information sessions	Group; 10 sessions; 120 min each; weekly homework; delivered by therapist	COPE	The intervention group did not significantly improve on 'behavioral disengagement coping strategies'.	Not enough data reported.
Futterman et al[15]	RCT; control—standard care; 44% retention rate at 6-month follow-up	Mothers2Mothers (M2M) mentors and group therapy; eight sessions; weekly homework; delivered by an M2M mentor trained in CBI	COPE	The intervention group did not significantly improve positive coping from baseline to follow-up.	0.283
Brown et al[18]	See table 1	See table 1	▶ Perceived Stress Scale ▶ HIV-Related Life Stressor Burden Questionnaire ▶ Stress Management Knowledge	The intervention significantly increased stress management knowledge (p<0.01).	−0.223; −0.218; 0.730

CBI, cognitive behaviour intervention; RCT, randomised controlled trial.

Table 5 Anxiety

Study	Sample characteristics	Description of intervention	Instrument used for assessment	Relevant outcomes	Cohen's d
Jones *et al*[20]	451 HIV+ women; M age 38.6; 68% AA, 11% Caucasian; 16% hour, 5% other	Group; 10 sessions; 120 min each; no weekly homework; delivered by NR	State Trait Anxiety Inventory	The intervention did not significantly improve anxiety scores.	−0.158
				Women in intervention group who increased self-efficacy scores improved anxiety scores significantly.	−0.131
Sikkema *et al*[13]	85 HIV+ women; M age 40.3; 59% AA, 16% hour, 10% Caucasian, 15% other; 53% AA, 28% white, 13% hour, 6% other. HIV+ or AIDS+ women with a history of psychiatric disorders	Group; 12 sessions; 90 min each; with/no exercises between sessions, Delivered by therapists, doctoral psychologist, masters of social works and nurse practitioner	Hamilton Rating Scale for Anxiety	The intervention did not significantly improve anxiety scores. Women in intervention group exhibited the 'greatest positive change'.	−0.385

AA, African-American.

significant change in anxiety scores. However, both studies noted that women in the intervention group demonstrated the greatest improvement in anxiety scores.

Risk of bias
Except for one study,[15] all included papers in this study were randomized controlled trials, typically performed with a random number generator, although in many studies this procedure was not specifically described. However, control and treatment groups had similar demographic distributions, indicating a low likelihood of bias for allocation. Futterman separated treatment conditions by location, with one location for the control group and one for the intervention group. Attrition rates were substantial in all the studies analyzed. Furthermore, in some studies attrition rates tended to be higher among intervention groups.[14 16 18] Treatment groups required participants to return weekly for 8–12 weeks of therapy. In addition, two studies showed a higher attrition rate for the group intervention rather than individuals.[12 17] Demographic analysis by these studies of the participants who were lost to follow-up compared with those who completed the final assessment could give valuable information on the reasons behind the attrition, future success of such CBT programmes and whether the skewed attrition rates affected the final assessment groups.

The studies made little effort to discuss allocation concealment and blinding biases. Most studies were randomized controlled studies, but few mentioned any blinding procedures during the administration of measures. Due to the nature of the therapy, patients and treatment providers could not be blinded to the treatment. Blinding during the assessment phase was described in only some studies.[11 12 16 18 20] In all the studies, assessors and treatment providers were different individuals. Therefore, allocation bias was minimized but not entirely eliminated in the nine controlled trials.

Quality of the evidence
While most of the studies had large sample sizes (>100), they also had significant attrition rates ranging from a 3% to 56%. Many of these large studies assessed multiple outcomes. Another challenge with CBT is that the therapy is given over multiple sessions. For studies with these long CBT interventions, many participants did not attend all of the sessions. Individuals that did not complete the intervention but attended the follow-up measurement were included in data analysis.

DISCUSSION
Overall, 10 studies were identified that met the criteria for reporting data from studies of WLHA and CBT. The four outcomes we focused on were measured with various methodologies by each study. Many of these studies were also subanalyses of a single larger data set, while two studies[11 16] analyzed different outcomes in the same study. Four studies[12 14 19 20] all analyzed different outcomes from the SMART/EST Women's Project I. The effectiveness of CBT on the four outcomes was appraised based on effect sizes that were calculated across the ten studies. The relatively small number of available studies limited the opportunity to draw definitive conclusions.

A greater number of studies showed a significant CBT impact on QOL and stress than studies that did not; however, QOL studies included a wide range of measures, including grief and positive affect. As QOL was broadly defined, a wider range of studies was included, which may have contributed to a higher likelihood of finding a significant result. Similarly, stress was broadly defined. Of the five studies evaluating stress, one of the studies only found a significant impact on stress management knowledge, rather than an actual decrease of stress levels. One of the recurrent challenges in analyzing these studies is the wide range of definitions and assessment tools used for measuring mental health outcomes. Only two studies analyzed anxiety, and neither found a significant impact for CBT.

Depression had the largest number of studies for analysis, and many of the studies used the BDI. However, only three of six studies found a significant improvement in depression scores. Each study that found a significant impact used a different measurement tool, suggesting that the measurement tool chosen did not appear to bias the outcome. It is important to note that two studies[14 20] were subanalyses of the SMART/EST Women's Project I; therefore, their data overlap. However, both studies were included because

one[14] limited data to participants with a BDI score >10 at baseline, while the other[20] evaluated the entire study population. The comparison of these two analyses provided valuable insight into improving the design of future studies, since the former[14] found a significant improvement in BDI scores, while the latter[20] did not. This difference may be attributed to the fact that the BDI scores in the latter were much lower at baseline; and, CBT may be less likely to have an impact on depression scores of women with lower risk of depression. Of the studies that analyzed depression, only two restricted the study to participants with clinical depression at baseline.[13 14] Both studies found that CBT showed significant improvement in depression scores. Therefore, future studies may do well to restrict enrollment to women with diagnosed depression or high BDI scores.

General characteristics of CBT sessions were provided in the selected articles, including the number of sessions and length of each session. The various types of CBT may have different efficacy based on the setting. Differences in effect could potentially be attributable to the heterogeneity of the interventions, but deconstructing components that worked specifically for WLHA was not possible since studies which demonstrated improvement shared many of the same general characteristics as studies that showed no change.

One major challenge in analyzing the evidence was the use of a variety of outcome measurement tools. While it did not seem that any one tool skewed the results, it would be beneficial to the field for future studies to standardize outcome measurements in order to permit more direct comparisons and enable meta-analysis. A limitation of this current systematic review is that due to the heterogeneity of study measurements, we were unable to pool the data for meta-analysis.

There were also discrepancies between studies that analyzed the same populations. For example, one study[11] clearly stated that the report is a subanalysis of the data found in another.[16] However, the former had two additional participants in the CBT treatment condition than did the latter. The studies that analyzed data from SMART/EST Women's Project I also had varying numbers of study participants, and it was not always clear how the specific population number was chosen for each study. Efforts were made to contact the study researchers, but no additional information was obtained.

Whereas statistically significant differences in outcomes favoring CBT were found in the majority of studies examining three of four measures (ie, depression, QOL and stress), the possibility of bias introduced by the selective publication of studies reporting favorable versus less favorable outcomes (ie, file drawer effect), may have influenced these results. Nevertheless, this systematic review of mental health outcomes in largely minority WLHA extends the findings of earlier work, largely reflecting data obtained in MSM, demonstrating a beneficial impact for CBT.

Conclusions and implications for future research
CBT appears to be a promising therapy WLHA, and there is a clear need for more rigorous research on its impact. CBT for WLHA leads to improved stress levels and possibly decreased symptoms of depression. A greater number of studies focusing on CBT for WLHA is needed to fully establish its benefit. Standardization of outcome measurements and analysis of specific subpopulations would clarify which individuals would most likely benefit from CBT. Future studies showing improvement in medication adherence, viral load and CD4 count would cement CBT as a necessary intervention for these women, and can lead to clarification regarding specific CBT protocols which are more effective. As the nature of HIV management changes with improved antiretroviral treatment and awareness, so must behavioral science research progress in order to keep pace, and to permit optimal benefit for WLHA.

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