Journal of Psychosomatic Research 128 (2020) 109882

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

Manualized cognitive behavioral group therapy to treat vasomotor symptoms for women diagnosed with mood disorders

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ARTICLE INFO

Keywords:
Anxiety - Cognitive behavior therapy
Group
Hot flashes - Menopause
Mood disorders

ABSTRACT

Objective: This 6-week, prospective, single-arm study examined the feasibility, acceptability, and preliminary efficacy of cognitive behavioral group therapy in peri- and postmenopausal women with mood disorders (major depression or bipolar) and problematic vasomotor menopausal symptoms.

Methods: 59 participants from an outpatient clinic with mood disorders and problematic vasomotor symptoms were enrolled. The primary outcomes were change from baseline to 6 weeks in Hot Flush Night Sweat Problem Rating, Hot Flash Related Daily Interference, and Quality of Life. Secondary outcomes were change in Hot Flush Frequency, depression, anxiety, perceived stress, anhedonia, beliefs and cognitive appraisals of menopause. ClinicalTrials.gov [identifier: NCT02860910].

Results: On the Hot Flush Night Sweat Problem Rating, 39.3% improved 2 or more points, which was clinically relevant. Changes in Quality of Life ($p = .001$) and the Hot Flash Related Daily Interference Scale were also significant ($p < .001$). Significant results were found on most secondary outcomes (hot flush frequency on the Hot Flush Daily Diary, depression, anxiety, perceived stress ($p < .001$) and anhedonia ($p = .001$). One of six subscales (control subscale) on the cognitive appraisal of menopause significantly improved ($p < .001$). Three subscales on the beliefs measure did not change significantly ($p = .05$, $p = .91$, and $p = .14$). Six-week study retention was robust ($N = 55$, 93%) and 94.2% of individuals reported that cognitive behavioral group therapy sessions were useful.

Conclusion: This exploratory study suggests that CBGT is acceptable, feasible, and efficacious in women with mood disorders and problematic menopause vasomotor symptoms. Further studies are needed using more rigorous and controlled methods.

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https://doi.org/10.1016/j.jpsychores.2019.109882
Received 5 June 2019; Received in revised form 16 November 2019; Accepted 19 November 2019

1. Objective

Menopause can be an important life transition for women. Physical symptoms may include vasomotor symptoms and irregular menstrual cycles [1]. Vasomotor symptoms also referred to as hot flashes and night sweats (HFNS), are the primary reason why women seek medical attention during menopause. Racial minorities, women with higher BMIs [2–4] and women with lower education levels [4] may be more vulnerable to menopause distress. There is an important link between psychological status and menopause associated with stress, anxiety, or depression [5,6]; and menopause may exacerbate psychiatric symptoms in those with pre-existing mental health conditions. The Study on Women's Health Across the Nation (SWAN) suggested that peri- and early postmenopausal women were at two-to-four-times greater risk for depressive episodes even after controlling for demographic and clinical characteristics [7]. Other risk factors for menopausal symptoms include stressful life events, psychological distress [8,9], higher perceived stress [10], depressive symptoms and negative affect [11]. Negative beliefs about menopause and vasomotor symptom severity have been associated with depressed symptoms during menopause [12,13].

Research on menopause in women with chronic mental illness is sparse. Friedman et al. [14], (N = 91) found that women with schizophrenia/schizoaffective disorder, bipolar disorder (BD), and major depressive disorder (MDD) had relatively high vulnerability to menopause symptoms and psychosocial problems. Women with MDD experienced more vasomotor symptoms during post-menopause compared to women diagnosed with schizophrenia or BD. Sajatovic et al. [15], (N = 91) reported five symptoms most experienced by mentally ill women during menopause: depression, anxiety, fatigue, low energy, and poor memory. Another study by Sajatovic et al. [16], (N = 39) found that women with schizophrenia, BD, or MDD reported that menopause symptoms were affecting their emotional/mental symptoms and/or the emotional symptoms of family members.

Studies using cognitive behavioral therapy (CBT) to treat menopause symptoms have assessed for mood symptoms, with few targeting specifically women with MDD [7]. Cognitive behavioral group therapy (CBGT) interventions have been tested that targeted vasomotor symptoms and/or other menopause symptoms and secondarily depression and anxiety symptoms [18–20]. CBGT has also been used to help with vasomotor symptoms in women with anxiety disorders, remitted mood disorders, and well women [21,22].

In studies using CBGT, intervention methods vary. Some studies combined cognitive restructuringpsycho-education and slow-paced/deep breathing [20,24]. Other studies combined cognitive restructuring, progressive muscle relaxation, psycho-education and group discussions [20,25]. Hunter and Smith [24,26–27], developed an eight-session CBGT intervention, delivered over four to six weeks, that has been effective for breast cancer survivors [27–29] and well women [24,30]. This manualized treatment has been adapted to different formats such as the web [28] and for different populations, such as for working women [31]. Green et al.'s pilot study, an eight-week CBGT intervention that found positive results with a reduction in anxiety, depression, and vasomotor symptoms [21], provided evidence for Green et al.'s randomized clinical trial/RCT [22]. Green et al.'s RCT tested a 24 h manualized CBGT intervention delivered over 12 weeks, including sessions to manage depression and anxiety [22,23]. While Green et al. did not specifically target women with vasomotor symptoms and MDD or BD, at least mild (but not severe) depressive symptoms were additional inclusion criteria [22]. The intervention by Green et al. reduced self-reported vasomotor and depressive symptoms, sleep difficulties and sexual-related concerns.

Though the efficacy of various CBT programs has been well-established as noted in the studies above, there were limited data on manualized CBGT specifically targeting women diagnosed with MDD and BD. Therefore, we conducted a non-randomized exploratory study to evaluate the feasibility, acceptability, and preliminary efficacy of a manualized CBGT treatment for peri- and postmenopausal women with chronic, remitting and relapsing mood disorders, with or without anxiety disorder and problematic vasomotor symptoms. While Green et al.'s [22] 12-week program potentially could have targeted mood and problematic vasomotor symptoms, participant burden was balanced by using the six-week program by Hunter et al. [26].

For the primary outcomes, we hypothesized that this manualized CBGT treatment would significantly reduce HFNS problem rating, reduce daily interference related to hot flashes, and improve quality of life. We also hypothesized that this CBGT treatment would significantly reduce hot flush frequency, mood, anxiety, perceived stress and anhedonia, increase positive beliefs about hot flushes, and improve cognitive appraisals (i.e., Menopause Representations Questionnaire) about menopause. This study also explored which independent variables were significant predictors of the outcomes and assessed for participant satisfaction.

2. Methods

Ethical approval for this study was obtained from University Hospitals Cleveland Medical Center's Institutional Review Board (IRB number: 04-16-11). Informed consent was obtained from all participants. The study was registered with ClinicalTrials.gov [identifier: NCT02860910] and amended after initial clinical trials registration with respect to primary and secondary outcomes. Predictor values included both baseline and end-of-study values.

2.1. Study population and eligibility criteria

The study included 59 women. Participants were recruited between December 2016 and August 2018 from outpatient clinics of the Departments of Psychiatry and Reproductive Biology at an academic medical center. Participants were assigned consecutively and based on availability. Criteria for inclusion were 40–65 year-old women with current or lifetime mood disorders who were peri- or postmenopausal with at least one bothersome hot flash or night sweat per day. North American Menopause Society (NAMS) practice guidelines [17,31] for stages of reproductive aging determined menopause status. The MINI International Neuropsychiatric Interview (MINI) confirmed current or lifetime DSM-V diagnoses of major depressive (MDD) or bipolar disorder (BD) with scores of > 7 on the Montgomery-Asberg Depression Rating Scale (MADRS). No participants were taking HT for vasomotor symptoms. All were stable on psychotropic medications for at least eight weeks prior to intervention and were agreeable to remaining on current doses of psychotropic medications until the study concluded.

Participants self-identified as black or white, reflecting the majority of women in this mid-western U.S. study site. Since some previous studies suggested that black women have more vasomotor symptoms than white women [2–4] we considered race as a predictor of primary outcomes. Other racial groups were excluded from the study. The study also excluded women with psychotic disorder, borderline personality disorder, active substance use disorder in the last 12 months, serious suicidal risk, acute mania (score > 15 on the Young Mania Rating Scale YMRS), those on HT for vasomotor symptoms, or women on chemotherapy and/or tamoxifen. Women with scores > 4 at baseline or screening on item 10, (suicidal thoughts) were excluded. Fig. 1 displays a CONSORT diagram of study flow.

2.2. Operational definitions

Feasibility was operationalized as the percentage of participants who completed the study and who were lost to follow-up after enrollment (i.e., retention). Acceptability was assessed via a questionnaire asking participants to rate perceived helpfulness/usefulness of the study. Preliminary efficacy was assessed by determining whether the study significantly reduced menopause and clinically related burden

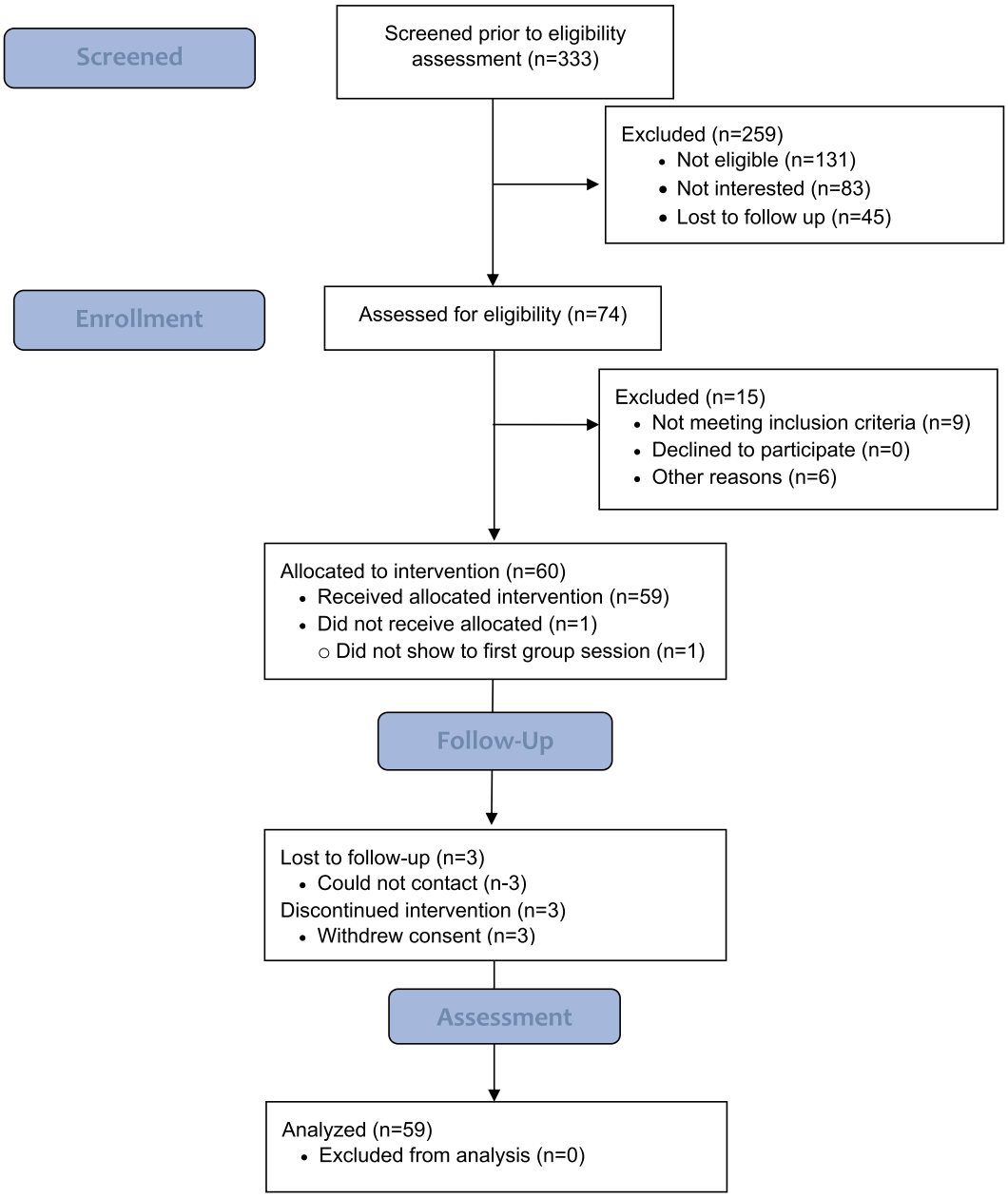

Fig. 1. CONSORT Diagram.

Session 1: Psycho-education and the cognitive behavioral model
Session 2: Stress management, improving wellbeing and identifying precipitants
Session 3: Managing hot flashes using a cognitive behavioral approach
Session 4: Managing night sweats and improving sleep (part one)
Session 5: Managing night sweats and improving sleep (part two)
Session 6: Review, maintaining changes, and dealing with setbacks. Open discussion about other menopause-related health topics. Choices included weight changes, sexual functioning, and/or cognitive functioning.

Fig. 2. CBGT Intervention.
Note: Session 6 adapted for the population. Additional open discussion topics included psychoeducation about menopause and MDD, major depressive disorder or depressive symptoms; BD, bipolar disorder; or AD, anxiety disorder. The breast cancer topic was removed.

and improved participants' quality of life.

2.3. Intervention

The CBGT was delivered in six consecutive, weekly 90 min groups in an outpatient setting. There were 11 groups of four-to-seven participants, mean 5.36 (SD 1.21). Session content is noted in Fig. 2. Sessions were led by study staff. Homework assignments were given between sessions, as instructed in the manualized protocol. Participants were given an introductory audio recording explaining hot flushes and night sweats, the role of stress, and how to relax. To help manage hot flushes and night sweats, participants were given two audio recordings: a short relaxation and breathing exercise and a deep muscle relaxation training and paced breathing. Participants selected one of the relaxation trainings to practice daily. Audio recordings were pre-recorded and part of the manualized protocol.

Fidelity to the manualized intervention was assessed either in-person or via review of audio-recordings by study staff using a standardized fidelity checklist for session numbers 1–5. Each group chose one to three topics to discuss during session 6. Topics for session 6 were adapted versions of the CBGT approach developed and described by Hunter and Smith [26] to meet the needs of the study population. Please see the variation in Fig. 2.

2.4. Study assessments

One week prior to beginning CBGT, participants were assessed at screening for inclusion criteria and eligibility confirmation. Once enrolled, participants were assessed on demographic and clinical variables.

3. Primary outcomes

3.1. Hot Flush night Sweat (HFNS) problem rating

The five-item Hot Flush Rating Scale rating scale assessed hot flush frequency and problematic hot flushes and night sweats. It used two subscales: Hot Flush (HF) Frequency (2-items) and HFNS Problem Rating (3-items). The former served as a secondary outcome (described further below) while the latter served as a primary outcome.

The problem rating items were rated on a 1-to-10-point scale and assessed whether hot flushes were regarded as problematic or distressing and how much they interfered with daily routines. To calculate HFNS Problem Rating, the total score (ranging from 3 to 30), was divided by 3. The test-retest reliability and internal consistency for the HFRS are (r = 0.8) and (α = 0.87), respectively [32].

3.2. The hot flash related daily interference scale (HFRDIS)

This 10-item rating scale assessed the degree to which hot flashes interfered with daily functioning in nine areas: work, social activities, leisure activities, sleep, mood, concentration, relations with others, sexuality, and life enjoyment (scoring ranging 0–90). This study included a 10th item designed to assess the degree to which hot flashes interfered with overall quality of life. The Quality of Life (QOL) measure in this study (score ranging 0–10). Each item was rated 0–10 from "did not interfere" to "completely interfered." Higher scores indicated more hot flash interference with daily functioning. Internal consistency of this scale was high (α = 0.96) [33].

4. Secondary outcomes

4.1. Hot Flush Frequency (HF Frequency)

The Hot Flush Rating Scale (HFRS) assessed for HF Frequency over the previous week.

4.2. The Hot Flush daily diary

Participants rated daily hot flushes and night sweats on a 3-point scale (mild, moderate, and severe) [22]. Incidents of daily hot flushes and night sweats were added to calculate weekly totals. The Daily Diary, given one week before the baseline visit and at all-time points, was collected weekly. Recording hot flush frequency was highly correlated with hot flushes (r = 0.97, p < .001) and night sweats (r = 0.94, p < .001) [34].

4.3. Snaith-Hamilton pleasure scale (SHAPS)

Anhedonia, the inability to experience pleasure, is a hallmark symptom of depression [29]. This is a 14-item, clinician-rated assessment rated on a 4-point scale from "strongly disagree" to "strongly agree." Higher scores (range 0–42) indicate more severe symptoms. Test-retest reliability ranges from 0.80–0.92 and 0.84–0.97, respectively [35].

4.4. Montgomery-Asberg depression rating scale (MADRS)

This 10-item clinician-rated measurement queried for symptoms of depression. Higher scores (range 0–60) suggested more severe depression [30]. Inter-rater reliability ranged from 0.89 to 0.97 [36].

4.5. The structured interview guide for the Hamilton anxiety rating scale (SIGH-A)

This 14-item clinician-rated measurement assessed for anxiety severity. Items were rated from 0 = "None" to 4 = "Constant or nearly constant significant impairment." Internal consistency was (α = 0.92). Test-retest reliability was (r = 0.75) [37].

4.6. The Quick inventory of depression symptomatology-self report (QIDS-SR-16)

This 16-item scale, administered at all-time points, measured depression severity. Items were rated from 0 to 3, with scores ranging from 0 to 48. The internal consistency was (α = 0.81 to 0.94) [38].

4.7. The menopause representations questionnaire (MRQ)

This 17-item scale assessed the cognitive appraisal of menopause. It consists of two sections (identity and beliefs sub-scales), with six belief subscales scored on a Likert scale from Strongly Agree (5) to Strongly Disagree (1). The scales, alphas, and retest reliability were: Relief α = 0.63, 0.82; New Phase α = 0.60, 0.80; Negative Impact α = 0.78, 0.84; Control α = 0.63, 0.92; Short timeline α = 0.72, 0.54; and Long Timeline α = 0.60, 0.55 [39].

4.8. The hot flushes beliefs scale (HFBS)

This 27-item measure assessed the cognitive appraisal of women experiencing hot flushes and night sweats [40]. It consisted of three subscales: 1) beliefs about self in social context, 2) beliefs about coping with hot flushes, and 3) beliefs about coping with night sweats. This scale was coded from 0 to 5 (strongly disagree to strongly agree). Higher numbers represented more negative beliefs. Alphas ranged from 0.78 to 0.93, and test-retest reliability ranged from 0.74 to 0.78 [41].

4.9. The perceived stress scale (PSS-10)

This self-rated psychological assessment measured participants' perceptions of their ability to cope with perceived stress [28]. The 10 items were scored from 0 = "Never" to 4 = "Very often" [42]. Internal and test-retest reliability were > 0.70 [43].

4.10. The Managing menopausal symptoms: Evaluation of groups

This survey was administered to participants towards the study's end. When asked, “How did you find the group sessions?” participants were given individual responses to rate (e.g., “useful” on a scale ranging from “not at all” to “extremely”, or “How often” queries with a range of time responses) [44, 45].

4.11. Study staff training and fidelity

Study staff who administered clinician-rated assessments received quarterly inter-rater reliability training. Cronbach's alpha was between 0.97 and 0.99 for the (MADRS)/depression, the (YMRS)/mania and the SIGH-A/anxiety. Group facilitators adhered to the treatment protocol 100% across all five sessions. The primary investigator trained study staff on additional psychoeducation topics added to session 6.

4.12. Statistical analyses

Descriptive statistics were calculated for clinical and demographic characteristics. Chi-square was used to analyze categorical variables. Paired *t*-tests assessed change between the T0 (baseline) and T1 (end of study) visits for primary and secondary outcomes. For primary outcomes, analyses were accompanied by Pearson correlations between the change scores of all three measures.

Multiple regression models were conducted to determine associations between demographic and clinical variables and study outcomes. The predicator variables assessed were BMI, education, race, level of PSS-10/stress, manic symptoms on the YMRS, HFBS/beliefs, MRQ/cognitive appraisal of menopause, mood (MDD/BD) and anxiety disorder comorbidity (DSM-V), and psychotropic medications affecting vasomotor symptoms. To adjust for multiple comparisons, *p*-values of 0.01 were considered significant.

5. Results

5.1. Enrollment

Feasibility measures: Of the 59 participants, 86.4% ($N = 51$) attended all six sessions, 3.4% ($N = 2$) attended five sessions, and 6.8% ($N = 4$) attended four sessions. Of the two (3.5%) participants lost to follow up, one attended three sessions and one attended only one. Attendance included make-up sessions, if a group session was missed. The number of CBGT sessions was 66. The number of individual make-up sessions (one-to-one by phone or in-person) was 35. This study had excellent retention, with 93% ($N = 55$) of the participants completing the study and 5% ($N = 3$) lost to follow-up after enrollment. There were no adverse effects.

5.2. Baseline sample description

Table 1 shows sample demographic and clinical characteristics. In addition, thirty-seven (62.7%) had comorbidity with generalized anxiety disorder, 21 (35.6%) with other pertinent comorbid diagnoses, and 10 (16.9%) had no comorbid diagnoses. Other pertinent diagnoses included anxiety disorder not otherwise specified and specific phobia.

5.3. Primary outcomes

Most of the primary and secondary outcomes were chosen based on previous research studies (noted in the objectives section). Additional outcomes were used (i.e., anhedonia) due to the population and the exploratory nature of this study.

As seen in Table 2, the HFNS Problem Rating decreased significantly over time from T0 to T1 visit ($p = .001$). Thirty-six (64.3%) of participants reported improvements, while 22/56 participants (39.3%) reported improvements of 2 or more points, which is considered clinically on the 10-point Problem Rating scale. Scores were significantly reduced from T0 to T1 for QOL ($p = .001$) and the HFRDIS ($p < .001$).

Correlations between change scores from T0 to T1 were significant for the reductions in the HFRDIS and QOL improvement, such that as HFRDIS was reduced, QOL increased, $r = -0.77$, $p < .001$. QOL improvement also was related to reduction in HFNS Problem Rating, such that HFNS Problem Rating decreased as QOL improved, $r = -0.42$, $p = .003$. Change scores between the HFNS Problem Rating and HFRDIS were not significantly associated, $r = 0.16$, $p = .28$.

Table 1
Demographic and Clinical Characteristics of the Sample. Selective serotonin reuptake inhibitors (SSRIs); serotonin-norepinephrine reuptake inhibitors (SNRIs).

Variable	Entire sample ($N = 59$)
Age (Mean, SD)	53.9 (5.6)
Race	
Black	34 (57.6)
White	25 (42.4)
Marital status	
Currently married	24 (40.7)
Not Currently married	13 (22.0)
Never married	22 (37.3)
Highest level of education (N, %)	
No college/technical/business school	11 (18.6)
Some college/technical/business school	48 (81.4)
Years of education completed (Mean, SD)	15.1 (2.3)
Employment status (N, %)	
Employed part-time	10 (16.9)
Employed full-time	27 (45.8)
Other	22 (37.3)
BMI (Mean, SD)	31.1 (7.2)
Smoking status (N, %)	24 (40.7)
Primary diagnosis (N, %)	
Major depressive disorder	48 (81.4)
Bipolar disorder (Type 1 and Type 2)	11 (18.6)
Menopause type (N, %)	
Natural	38 (64.4)
Surgically or medically induced	21 (35.6)
Menopause status (N, %)	
Perimenopause	25 (42.4)
Post-menopause	34 (57.6)
Psychiatric medication (N, %)	
SSRIs	20 (33.9)
SNRIs	11 (18.6)
Mood stabilizer	6 (10.2)
Gabapentin	6 (10.2)
Anti-hypertensive	1 (1.7)
Clonidine	1 (1.7)
Tricyclic	3 (5.1)
Antidepressant	37 (62.7)
Bupropion	10 (16.9)
Mirtazapine	1 (1.7)
Other psych meds	27 (45.8)
Total number of women on a psychiatric medication that reduces vasomotor symptoms	38 (64.4)
Total number of women taking more than one psych meds	28 (47.5)
Total number of women not taking a psych med	13 (22.0)

5.4. Secondary outcomes

HF Frequency on the HFRS did not change significantly between T0 and T1 visits ($p = .46$). Scores were significantly reduced from T0 to T1 on the Daily Diary, anxiety (SIGH-A) perceived stress (PSS-10) ($p < .001$) and anhedonia ($p = .001$). Average weekly hot flushes and night sweats were also reduced on the Daily Diary, (T0 = 71 and T1 = 36). Scores were significantly increased between T0 and T1 for the control subscale of the cognitive appraisal of menopause (MRQ) ($p < .001$) all other subscales on the MRQ did not significantly

Table 2
Mean Differences on Primary and Secondary Outcomes for All women at T0 (baseline) and T1 (end of study).

Measurement	T0	T1	*t*	df	*p*	Cohen's d
HFNS Problem Rating	5.58 ± 2.18	4.53 ± 3.11	0.75	54	0.008*	0.37
Hot Flush Frequency	44.71 ± 45.51	40.58 ± 43.95	2.74	54	0.46	0.10
Hot Flush Daily Diary	69.91 ± 73.56	36.01 ± 29.17	3.50	50	< 0.001*	0.59
Quality of Life	4.27 ± 3.11	2.90 ± 2.82	3.36	51	0.001*	0.49
HFRDIS	47.25 ± 28.22	31.73 ± 21.94	3.99	51	< 0.001*	0.61
Depression MADRS	15.69 ± 7.24	12.20 ± 13.58	1.65	55	0.10	0.27
QIDS-SR-16	9.14 ± 4.54	7.09 ± 4.22	3.76	53	< 0.001*	0.50
Anhedonia (SHAPS)	26.47 ± 6.29	23.88 ± 7.49	3.43	49	0.001*	0.39
Anxiety (SIGH-A)	17.81 ± 7.30	15.86 ± 6.36	4.15	54	< 0.001*	0.53
MRQ Subscales						
Relief	7.58 ± 1.96	7.79 ± 1.89	1.11	52	0.27	0.14
New Phase	5.31 ± 1.61	5.77 ± 1.22	1.71	52	0.09	0.31
Negative Impact	16.69 ± 3.63	16.08 ± 3.54	1.37	49	0.18	0.20
Control	12.98 ± 2.56	16.23 ± 2.56	7.02	52	< 0.001*	1.21
Short Timeline	4.19 ± 1.73	4.68 ± 1.63	2.10	50	0.04	0.28
Long Timeline	7.32 ± 1.17	7.53 ± 1.30	1.00	52	0.32	0.16
HFBS						
Subscale 1	2.13 ± 1.15	1.83 ± 1.01	2.04	51	0.05	0.27
Subscale 2	2.57 ± 0.55	2.59 ± 0.59	0.12	52	0.91	0.02
Subscale 3	2.40 ± 0.66	2.33 ± 0.63	1.50	52	0.14	0.23
PSS-10	21.02 ± 6.39	17.81 ± 7.30	4.06	51	< 0.001*	0.47

Note: HFNS, Hot Flush Night Sweats Problem Rating; HFRDIS, Hot Flash Related Daily Interference Scale; MADRS, Montgomery-Asberg Depression Rating Scale; QIDS-SR-16, Quick Inventory of Depression Symptomatology-Self Report; SHAPS, Snaith-Hamilton Pleasure Scale; SIGH-A, Structured Interview Guide for the Hamilton Anxiety Rating Scale; MRQ, Menopause Representations Questionnaire; HFBS, Hot Flushes Beliefs Scale; PSS-10, Perceived Stress Scale-10. HFBS subscale 1, beliefs about self in a social context; HFBS subscale 2, beliefs about coping with hot flushes; HFBS subscale 3, beliefs about coping with night sweats.

change. The three subscales on the beliefs measure (HFBS) did not change significantly between T0 and T1 ($p = .05$, $p = .91$, and $p = .14$), respectively.

The average depression score (QIDS-SR-16) fell in the high mild range at T0 and fell in the low mild range at T1 ($p < .001$). The depression scores on the MADRS did not change significantly between T0 and T1 ($p = .10$).

Correlations were used to identify potentially relevant predictors for change in the primary outcomes of QOL, HFRDIS, and HFNS Problem Rating from T0 to T1 using the predictors: race, BMI, beliefs (HFBS), cognitive appraisal of menopause (MRQ), stress (PSS-10), mania (YMRS), mood disorder diagnoses (MDD/BD), anxiety comorbidity, use of SSRIs or SNRIs, and years of education. Using a cutoff value of $p \leq .10$, HFBS subscale 1 (beliefs about self in social context) and the cognitive appraisal of menopause (MRQ) subscale of relief were identified as potential predictors for changes in QOL. For changes in the HFNS Problem Rating subscale, the cognitive appraisal of menopause (MRQ) subscale of long-term timeline and the presence of depression vs. bipolar disorder were identified as potential predictors. No potential predictors were identified for HFRDIS changes.

Multivariate regression models using the stepwise method were conducted for changes in the HFNS Problem Rating Scale and in QOL using the covariates identified in the previous correlations as potential predictors. At the $p < .01$ level, the beliefs (HFBS) were not significant predictors of change in QOL, $\beta = -0.29$ (-1.45, -0.06), $p = .04$, and the fit of the model was not significantly improved by including the relief subscale of the Menopause Representations Questionnaire (MRQ), $F = 0.30$. For changes in the HFNS Problem Rating, subscale 1 of the HFBS/beliefs was not a significant predictor, $\beta = 0.15$ (-0.45, 1.29), $p = .34$, and the fit of the model was not significantly improved by the presence or absence of depression or bipolar disorder, $F = 0.33$. Thus, no significant predictors were identified for changes in QOL, the HFNS Problem Rating subscale, or the HFRDIS.

5.5. Acceptability

Participants typically responded with values between "moderately" and "extremely" to questions such as whether group sessions were useful or helped reduce stress (94.2%). One reverse-coded item asked whether participants found the group sessions "upsetting;" 81.8% responded, "Not at all." Cumulatively, participants, on average, had more positive than negative opinions about these groups, rating the groups as very much or extremely helpful in coping with hot flashes (82%) and night sweats (70.5%).

6. Discussion

This non-randomized, exploratory study described a novel use of CGBT, targeting 40–65-year-old women with mood disorders (MDD and BD) and bothersome menopause symptoms. The primary aims of this study were to evaluate the feasibility, acceptability, and efficacy of a manualized CBGT treatment for women with mood disorders and changes over time in HFNS Problem Rating, daily interference (HFRDIS), and QOL. Secondary aims were to evaluate secondary outcomes (Hot Flush Frequency, depression, anxiety, perceived stress, anhedonia, beliefs and cognitive appraisals of menopause) over time and identify potentially relevant predictors for primary change outcomes.

This study had excellent retention (please refer to Fig. 1) and acceptability (perceived usefulness/helpfulness of CBGT 94.2%). There were no adverse side effects. Comparable to previous menopausal studies [21,22,24], in this exploratory study, group CBGT improved mood, anxiety, and overall quality of life. Like the Green et al. and MENOS2 studies [22,24], participants perceived the intervention as useful [22,24,44,45] and improved their levels of control or ability to cope with HFNS [24,44,45]. Changes over time for individual HF Problem Rating, daily interference (HFRDIS), QOL on the HFRDIS, depression (QIDS-SR-16), anxiety (SIGH-A), anhedonia (SHAPS), stress (PSS-10) and increased control over hot flushes and night sweats (MRQ) subscale showed preliminary efficacy for the manualized CBGT treatment used in this study for a mood disorders population.

The percentage of women reporting a 2-point decrease in HFNS Problem Rating was 39.3% compared to > 60% with studies using the same CBGT protocol [24, 27–28]. Previous studies also found that

mood, anxiety and stress were correlated with HFNS Problem Rating [13]. The current study found that improvement in QOL was correlated with reductions in HFNS Problem Rating and daily interference (HFRDIS). In general, participants with MDD or BD have tended to have undue burdens in the life domains assessed by the HFRDIS/daily interference, which would seem to lend some explanation to the association between improved QOL and reduced daily interference.

Though our studies were not a direct comparison due to the different analyses, a study by Norton, Chilcot, & Hunter found that CBT treatment effects on HFNS problem rating were mediated by changes in beliefs about the ability to cope/control vasomotor symptoms [13]. This study's findings did not show beliefs (HFBS) as a predictor of change in problematic HFNS; nor did (HFBS) beliefs change significantly over time, as expected based on the above study. It was expected that the six subscales on the cognitive appraisal of menopause (MRQ) would also improve by the end of treatment. Only the control subscale changed significantly over time. In addition, we anticipated that race would be a significant predictor of change based on previous studies that showed that racial minorities have more bothersome vasomotor symptoms [2–4]. However, our findings did not support this.

Similar to the Green, Haber, McCabe, & Soares [21] pilot study and the RCT by Green et al. [22], significant results were found for the HFRDIS/daily interference and anxiety/SIGH-A using paired *t*-tests. Unlike the Green studies [21,22], depressive symptom severity did not reduce significantly from baseline on the MADRS, a clinician-rated assessment. In contrast, in this exploratory study, depressive symptom severity decreased significantly over time on the self-rated QIDS-SR-16. Since anhedonia is a hallmark symptom of depression, this study also included an anhedonia measure (SHAPS). We are not aware of this construct in previous studies examining CBGT treatment for mood and vasomotor symptoms.

For this current study, the reduction in HF Frequency on the HFRS (9.5% from T0 to T1) was insignificant over time. In the MENOS1 study by Mann et al. [27], HF Frequency was also found insignificant with 21% and 24% reductions in frequency rating from T0 to nine weeks in two groups (CBGT and usual treatment) respectively.

In summation, this manualized CBGT treatment by Hunter and Smith [26] was acceptable, feasible, and showed preliminary efficacy in reducing menopause-related burden, improving quality of life, and reducing symptoms related to anxiety, depression, and perceived stress in 40–65-year-old women with mood disorders and bothersome menopause symptoms.

7. Limitations and future research

There were several limitations to this exploratory study: absence of a control group and follow-up visits, and a relatively small sample size. Though two of the six sessions focused on improving sleep, no measurements assessed changes in sleep quality. Correlations in changes over time between the HFRDIS and QOL should be interpreted with caution, as both assessments measure daily interference while the QOL consists of one item.

We did not collect data on any concomitant psychotherapy to treat participants' mood or anxiety disorders, which may have influenced outcomes and generalizability. We did not differentiate subcategories of surgically induced menopause (i.e., hysterectomy verses bilateral oophorectomy).

In spite of these limitations, our findings are of potential use to investigators interested in advancing care for women with mood disorders and bothersome menopause symptoms. Building upon our preliminary findings of reasonable feasibility and efficacy, future studies should include a control group, long-term follow up visits, and additional information that may influence generalizability. It may be helpful to include enough participants with bipolar type II disorder to compare outcomes to those of participants with major depression and to conduct a mediation analysis by including beliefs as a predictor variable (design in this study does not facilitate a formal mediational analysis).

8. Relevance to clinical practice

Despite methodological limitations, exploratory study findings have relevance to clinical practice. Menopause symptoms complicate, co-occur, and overlap with depression [46] and other mental health conditions. CBGT is well tolerated and can reduce both menopause burdens and mood symptoms in women with mood disorders. With the growing population of women between the ages of 40–65, it is a critical time to develop practical and effective interventions to help women with mood disorders cope with the menopause transition.

Contributors

All contributors commented on and approved the final draft of this paper.

Funding

This work was supported by University Hospitals Cleveland Medical Center's Office of Community Impact, Equity, Diversity, and Inclusion, Cleveland, Ohio, USA. Minority Faculty Leadership Development Award number P0305.

Declaration of Competing Interest

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf and the authors declare they have no competing interests to report'.

Acknowledgements

We would like to thank Dr. Myra Hunter, Professor of Clinical Health Psychology, Department of Psychology, King's College London who served as an advisor and provided consultation to the PI via phone and email exchanges. Joseph Calabrese, MD, Professor of Psychiatry Case Western Reserve University School of medicine, Director Mood Disorders Program, University Hospitals Cleveland Medical Center; Corinne Bazella, MD, NCMP, University Hospitals MacDonald Women's Hospital and Associate Professor Obstetrics and Gynecology, Case Western University School of Medicine; and Jean Marino MSN, APRN-CNP, NCMP, IF, Department of Obstetrics and Gynecology, University Hospitals MacDonald Women's Hospital provided valuable consultation throughout this project. Thank you to Mandy Neudecker, Librarian at University Hospitals, UHMSO who was instrumental in helping to guide the literature search.

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