

## ORIGINAL ARTICLE

# Cognitive behavioral therapy for insomnia has sustained effects on insomnia, fatigue, and function among people with chronic heart failure and insomnia: the HeartSleep Study

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## Abstract

**Study Objectives:** Insomnia is common among adults with chronic heart failure (HF) and associated with daytime symptoms and decrements in function.

The purpose of this randomized controlled trial (RCT) was to evaluate the sustained effects over one year of CBT-I (Healthy Sleep: HS) compared with HF self-management education (Healthy Hearts; attention control: HH) on insomnia severity, sleep characteristics, symptoms (fatigue, excessive daytime sleepiness, anxiety, depression), and six-minute walk distance at baseline, within one month of treatment, and at 6 and 12 months. The primary outcomes were insomnia severity, actigraph-recorded sleep efficiency, and fatigue.

**Methods:** We randomized adults with stable HF with preserved or reduced ejection fraction who had at least mild insomnia (Insomnia severity index >7) in groups to HS or HH (4 sessions/8 weeks). We obtained wrist actigraphy and measured insomnia severity, self-reported sleep characteristics, symptoms (fatigue, excessive daytime sleepiness, anxiety, depression), and six-minute walk distance at baseline, within one month of treatment, and at 6 and 12 months. We used general linear mixed models (GLMM) and generalized estimating equations (GEE) to evaluate the effects.

**Results:** The sample included 175 participants (M age = 63 ± 12.9 years; 43% women; 18% Black; 68% New York Heart Association Class II or III; 33% LVEF < 45%) randomized to HS (n = 91) or HH (n = 84). HS had sustained effects on insomnia severity, sleep quality, self-reported sleep latency and efficiency, fatigue, excessive daytime sleepiness, and six-minute walk distance at 12 months.

**Conclusions:** CBT-I produced sustained improvements in insomnia, fatigue, daytime sleepiness, and objectively measured physical function among adults with chronic HF, compared with a robust HF self-management program that included sleep hygiene education.

**Clinical Trial Information:** Insomnia Self-Management in Heart Failure; <https://clinicaltrials.gov/ct2/show/NCT02660385>; NCT02660385.

## Statement of Significance

Insomnia, fatigue, sleepiness, and decrements in daytime function are important concerns for adults with chronic heart failure (HF) and limit the quality of life. This randomized controlled trial is the first to document sustained and clinically meaningful effects of cognitive behavioral therapy for insomnia (CBT-I) among adults with chronic heart failure (HF) on insomnia severity, sleep characteristics, fatigue, sleepiness, and objective daytime function, including significant improvement in six-minute walk distance. CBT-I may be a valuable addition to HF disease management programs in addition to standard behavioral and pharmacological approaches. Future studies are needed to determine the effectiveness of CBT-I and best strategies for implementation to improve access for people with heart failure.

**Key words:** self-management; heart failure; insomnia; cognitive behavioral therapy; sleep; fatigue; function; actigraphy

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## Introduction

Almost 75% of heart failure (HF) patients, a population of over 26 million throughout the world [1], have poor sleep quality [2]. They report high levels of daytime symptom burden and functional performance decrements that are not explained by sleep-disordered breathing (SDB), another prevalent sleep disorder in people with HF [3]. HF patients have insomnia symptoms that are associated with disabling symptoms such as fatigue, depression, excessive daytime sleepiness, poor function [3, 4], incident HF, other cardiovascular events, and mortality [5, 6]. Further, the association between insomnia symptoms, daytime symptoms, and function, including Six-Minute Walk Test (6MWT) distance, an objective measure of function, was independent of SDB [7].

HF patients report that insomnia is both significant to their health and infrequently addressed by their health care providers [8]. Patients prefer behavioral treatment to hypnotics that may be associated with adverse daytime effects and cardiac events [8, 9]. Cognitive behavioral therapy for insomnia (CBT-I), a behavioral intervention that is highly efficacious in many groups, including people with chronic comorbid conditions [10], is a behavioral alternative to hypnotic medications. It had significant effects on daytime symptoms and function, as demonstrated in a recent systematic review [11]. However, these prior studies did not include people with HF who have significant symptom burden and generally included self-reports, but not objective measures of function.

A small preliminary efficacy study that compared CBT-I with an attention-control condition [HF self-management education, an intervention that might also improve sleep by improving HF or preventing exacerbations (information on medication management, healthy diet, physical activity, and sleep hygiene instructions)] demonstrated large and statistically significant short-term effects (2 weeks post-treatment) on insomnia severity, actigraph recorded sleep efficiency, fatigue, and self-reported sleep quality [12]. Both CBT-I and HF self-management education were feasible and acceptable [12]. In another small study with no control for time and attention, there were short-term effects on insomnia symptoms, but no improvement in fatigue among people with HF [13]. Improvements in fatigue at six months, compared with HF self-management education, in people with HF who had no evident changes in standard HF treatment suggest that CBT-I has sustained effects, but the sample was small [14], and the longer-term sustained effects are not known.

The purpose of this report is to present the results of the *HeartSleep Study*, a randomized controlled trial (RCT) (NCT02660385 clinical trials.gov) conducted to determine the sustained effects of CBT-I among people with chronic HF and insomnia over one year. We determined the effects of CBT-I ("Healthy Sleep"—HS) compared with HF self-management education ("Healthy Hearts"—HH + sleep hygiene education; attention control condition) on (1) insomnia severity and self-reported and actigraph-recorded sleep characteristics; (2) daytime symptoms, including fatigue, excessive daytime sleepiness, anxiety, and depression; and (3) objectively measured functional performance. The primary outcomes were insomnia severity, actigraph-recorded sleep efficiency, and fatigue. We also evaluated CBT-I's effects on dysfunctional beliefs and cognitions about sleep, an important target for cognitive therapy for insomnia, and determined the effects of CBT-I among people with and without significant SDB.

## Materials and Methods

### Design

The trial protocol was published previously [15]. In brief, the *HeartSleep* study employed a single-center parallel-group randomized controlled trial (RCT) design (NCT02660385 clinical trials.gov). We obtained human subjects' approval, and all participants provided written informed consent. We randomized participants in groups of 4–6 to four bi-weekly face-face group sessions of cognitive-behavioral therapy for insomnia [CBT-I ("Healthy Sleep" + sleep hygiene education – HS)] over eight weeks or an active attention-control comparison group [HF self-management education ("Healthy Hearts"—HH) consistent in format, scheduling, and therapist attention to the CBT-I arm.

### Setting

We recruited participants from the greater New Haven, CT, USA community from the Yale New Haven Health Care System Heart Failure Disease Management Program and the Veterans Affairs Connecticut Health Care System.

### Participants

The sample included people  $\geq 18$  years of age who had chronic HF based on medical record review and clinician report. They were cognitively intact by clinical impression, English speaking, and concerned about sleep for  $\geq 1$  month. They had at least mild insomnia severity, as indicated by a score  $\geq 8$  on the Insomnia Severity Index (ISI) [16]. We included people with both mild and more severe (i.e. clinical) insomnia symptoms because the extent to which people with HF and mild insomnia symptoms may benefit from improvements in sleep, daytime symptoms, or function is not known. We included people with both preserved (HFpEF) or reduced ejection fraction (HFrEF) because left ventricular ejection fraction was not associated with insomnia symptoms in past research [3]. Although chronic insomnia and SDB often co-occur, SDB was not associated with insomnia symptoms or daytime symptoms in people with HF [3] and did not influence older adults' CBT-I outcomes [17, 18]. Therefore, we included people who had no more than mild SDB (apnea-hypopnea index  $\leq 15$ ) and those who were adherent to continuous positive airway pressure (CPAP) for at least four hours/night for six nights per week over the past six months, based on self-report.

We excluded people who had severe depression (Patient Health Questionnaire—PHQ-9 [19]  $> 20$ ), bipolar disorder, seizure disorders, untreated restless legs syndrome, severe sleepiness (Epworth Score  $> 18$ ), narcolepsy, active illicit drug use, end-stage renal failure requiring dialysis, those with night/rotating shift work, travel across  $\geq 2$  time zones within one month of enrollment, or conditions affecting the movement of the arm that may affect wrist actigraph recordings. We excluded people who had more than mild SDB (apnea-hypopnea index  $> 15$ ) based on medical record review, based on a sleep study within the past year, or objective sleep screening conducted for this study unless they were adherent to positive airway therapy for SDB.

### Recruitment

As reported [20], we used multiple recruitment methods. In brief, these included the screening of the electronic health

record (EHR), promotion of the study through the EHR patient portal and the Yale Center for Clinical Investigation (Clinical and Translational Sciences Institute) website, direct contact with patients in the clinical setting, and dissemination of posters, flyers, and brochures in clinical practices. Research assistants approached potential participants in person or by telephone, explained the study, and obtained written informed consent for initial screening.

Initial screening included the insomnia severity index, medical record review to screen for study delimitations, the Epworth Sleepiness Scale, the Patient Health Questionnaire (PHQ-9) [19] for depression, and elicitation of the presence of other sleep disorders, such as restless legs syndrome, and circadian rhythm disorders. We used the Apnea Risk Evaluation System (ARES) (Watermark medical, Inc.), a reliable and valid level 3 ambulatory screening device [21] for SDB. Participants completed the sleep screening for two consecutive nights, and the data were scored through the Watermark Medical website to determine the apnea-hypopnea index. If potential participants were evaluated for SDB within one year of recruitment as part of usual care, we reviewed the results of the sleep study in the electronic health record. We included or excluded patients consistent with these results. Because of our interest in the role of insomnia symptoms as contributors to HF outcomes and the preliminary efficacy of this approach in our previous study [12], our focus was on insomnia severity rather than a full ICD-3 diagnosis of insomnia. As noted above, we screened for other sleep disorders and interviewed participants regarding their sleep and other health concerns.

## Randomization

We used block randomization with a computer-generated sequence to assign participants in clusters of four to six each to the CBT-I (Healthy Sleep—HS) or attention-control (Healthy Heart—HH) conditions. Participants were blinded to group assignments until they began the interventions. We did not stratify participants.

## Intervention

We developed interventionist training protocols and participant materials (e.g. workbooks, hand-outs, diaries), and these approaches were feasible and acceptable [12]. The participant materials for both groups were consistent in format, length, reading level, and other characteristics. The interventions were presented in identical formats (i.e. four bi-weekly one-hour sessions with a telephone call on intervening weeks) to control for time and attention. We provided workbooks and bathroom scales for obtaining daily weights, consistent with recommendations for self-management to prevent fluid overload in HF. We initially offered the educational materials and logs for recording sleep skills on a tablet computer provided to participants, but due to participant preferences for the paper format, we subsequently used paper diaries and forms.

Although telehealth and web-based approaches are increasingly used to deliver CBT-I, we used a face-face group approach because participants rated it positively [12], and some had difficulty accessing electronic devices. For each group, we provided scripted telephone boosters of approximately 10 to 15 minutes each on weeks alternate to group sessions to elicit skills use and

give a review, problem-solving, and reminders for the subsequent sessions. We provided make-up sessions for those who missed the face-face sessions by telephone or video conference per participant preference.

**Intervention: CBT-I (Healthy Sleep: HS).** Consistent with standard CBT-I, the intervention was based on the “3-p” model of insomnia [22]. The manualized protocol included stimulus control, sleep restriction, sleep hygiene, cognitive therapy, progressive muscle relaxation, optional hypnotic tapering, and relapse prevention. We provided logs to record the daily use of CBT-I skills in paper or electronic formats. The therapist was a PhD-prepared psychiatric nurse practitioner trained in CBT-I. We offered participants in the HS group the “Healthy Hearts” Guide with information on HF self-management, but we did not discuss these aspects in the group or telephone sessions (See HH condition below). Homework consisted of CBT-I skills practice.

**Attention Control Group: HF self-management (“Healthy Hearts,” HH).** We based the HH intervention on the “Fight against HF Workbook,” [23] to provide education to support HF self-management (explanation of the HF disease process, expected signs and symptoms indicating the need to contact health care providers, HF medications and devices (e.g. pacemakers, internal defibrillators), and information on physical activity, weight management, fluids, diet intake, and stress management [23, 24]. We included brief sleep hygiene education (setting a regular bedtime; obtaining regular exercise, avoiding stimulants, alcohol, and tobacco; sleeping in a quiet bedroom without television or screens; not taking “worries” to bed or going to bed hungry; and developing a bedtime ritual). Sleep hygiene is generally not the active ingredient of CBT-I [25] and was the control condition in some past CBT-I trials [26], but we did not provide individual feedback on participant sleep hygiene behaviors in contrast to the HS group. Participants were informed that improving self-management could improve HF and, in turn, improve sleep along with sleep hygiene behaviors. Homework included HF self-management skills and documenting them in the handbook. A nurse practitioner with experience in the care of HF patients provided the HH sessions.

To promote retention, we provided birthday and holiday cards. Participants received \$25 for the ARES screening and an additional \$275 disbursed over the study milestones. We provided scripted phone calls until the 12-month follow-up to prompt completion of the follow-up measures.

We addressed treatment fidelity by manualizing the protocols for the treatments, provider training, and participant materials. We recorded all sessions and randomly selected 20% to assess consistency. We found that the sessions consistently addressed the protocol, and there was excellent consistency between sessions and therapists. We provided consistent follow-up and scripted telephone calls to promote the enactment of the treatment components by the study participants. For participants who had scheduling difficulties and could not attend face-face meetings or had unreliable transportation, we provided the option to telephone into the group sessions or have telephone make-up sessions with the therapists consistent in format and content with the group sessions.

## Data collection

We measured study outcomes at baseline, 3 months (2–3 weeks postintervention), six months, and 12 months after enrollment.

We conducted interviews and medical record reviews to elicit HF characteristics (NY Heart Association Functional Classification, left ventricular ejection fraction), sleep history, medications, and comorbid conditions and used the Charlson Comorbidity Index [27] to summarize comorbidity.

We used the Insomnia Severity Index, a reliable and valid measure that corresponds to diagnostic criteria for insomnia [16], as the primary measure of the severity of insomnia symptoms. We also used the Pittsburgh Sleep Quality Index (PSQI) [28, 29] and the PROMIS Sleep Disturbance questionnaire to evaluate sleep quality [30, 31]. We used the raw data from the PSQI as self-report measures of sleep latency, sleep duration, and sleep efficiency. All questionnaire measures had acceptable internal consistency levels ( $\alpha > 0.70$ ) computed from data collected for this study.

We obtained 14 days of wrist actigraphy (Respironics Minimitter Actiwatch-2 or Actiwatch Spectrum Plus, devices with equivalent accelerometers) at each time and used Actiware v. 6.0 software to compute sleep duration, efficiency, and minutes of wake after sleep onset (WASO) for each night. Participants completed daily sleep diaries based on the Consensus sleep diary [32]. We used these data to score the lights and lights on data to demarcate time in bed secondary to the use of the event marker or the light meter recordings on the actigraph.

The PROMIS 8-item short-form elicited fatigue and anxious and depressive symptoms. PROMIS measures are based on item-response theory and are responsive to clinical change [33]. The Epworth Sleepiness Scale, a reliable and valid measure, was used to elicit excessive daytime sleepiness [34, 35]. The PROMIS and Epworth Scales had co-efficient alphas exceeding 0.70 in this study.

We used the Six-Minute Walk Test (6MWT), a reliable and valid measure of the distance walked and an indicator of functional performance [36] correlated with maximal V02 [37] and a predictor of death hospitalization [37, 38]. We measured the distance walked on an indoor flat surface in the laboratory or clinical setting with standard methods [39–42].

Two measures elicited sleep-related beliefs and cognitions that are targets of cognitive therapy for insomnia, a CBT-I component. The Dysfunctional Beliefs and Attitudes about Sleep Scale [43, 44] was used to measure maladaptive beliefs about sleep. A higher score reflects higher dysfunctional beliefs and attitudes about sleep. The Sleep Disturbance Questionnaire (SDQ) is a 12-item scale designed to evaluate beliefs about insomnia sources [45]. The SDQ includes four factors that indicate attributions related to insomnia (restlessness/agitation, mental overactivity, consequences of insomnia, and lack of sleep readiness) and was validated in populations with chronic insomnia [45, 46]. Both scales had acceptable reliability, based on coefficient alphas computed for this study ( $\alpha > 0.70$ ).

### Data management and statistical analysis

We used RedCap as the electronic platform for data entry and capture and merged the RedCap data with the wrist actigraph data after cleaning and scoring (Philips Respironics Actiware v.6). We downloaded all cleaned data from the REDCap database and handled missing values on instruments before the data analysis. We assessed missing patterns across questionnaires and imputed missing values using the Markov Chain Monte Carlo (MCMC) approach when non-response across questionnaires

was less than 30% of the total number of questionnaires. All instruments were scored based on scoring guidelines after the single imputations. We performed a descriptive analysis with demographic and clinical characteristics and examined the equivalence between the two assigned groups using two-sided independent t-tests and chi-square tests.

We used a modified intent-to-treat design in which we included all participants that completed at least one of the 3 follow-up data collection periods in the analyses. To examine the primary outcomes (insomnia severity, actigraph-recorded sleep efficiency, and fatigue), we separately examined the measurements for the 3-month (primary), 6, and 12-month follow-up. First, we performed the pre-post intervention tests with delta scores (change over 3 months from baseline) within the Healthy Sleep (HS) and Healthy Heart (HH) groups and between the HS and HH groups using paired- and independent t-tests, respectively. We evaluated the longitudinal effects on the continuous outcomes at baseline, 3, and 6 months using the Generalized Linear Mixed Model (GLMM) with random intercepts and unstructured covariances over 6 months. We estimated the changes within groups and time-group interactions to compare the intervention effects between the two groups.

To address the potential for greater change at the 3-month assessment than subsequent follow-ups, we used general linear mixed models (GLMMs). We included the cube root of time, which permits the estimation of flexible nonlinear time patterns. We assessed the residuals for normality and outliers. To comply with the normality assumption, we eliminated observations when the studentized residual was greater than three or smaller than  $-3$ . We analyzed the long-term effects using the GLMM with the outcomes at baseline, 3, 6, and 12 months. We estimated the mean changes over 12 months within the HS and HH groups and tested differences between them using GLMM.

To further examine the treatment effects, we also estimated the changes during postintervention (baseline to 3 months) and longer-term follow-up (3–12 months) period simultaneously using the piecewise regression approach in GLMM. This approach also tests whether the early change at postintervention can be sustained for long-term follow-up. To avoid the inflation of type 1 error, the False Discovery Rate (FDR) was calculated for the postintervention effects on 13 primary outcome variables.

To control inflation associated with type I errors in testing for multiple outcomes simultaneously, we calculated the False Discovery Rate (FDR) for the outcomes based on the p-values from the GLMM for the 12-month follow-up. To evaluate bias due to dropouts, we used the Pattern-Mixture Model (PMM) [47], which corrects bias from dropouts, to confirm the 12-month results. PMM allows for adjusting the intervention effects by averaging the estimates from completers and dropouts.

We used the General Estimating Equation (GEE) to examine the effects of the intervention on changes in dichotomized outcomes in the clinically relevant cutoffs for mild-severe insomnia ( $ISI > 7$ ), excessive daytime sleepiness ( $ESS \geq 10$ ), low sleep quality ( $PSQI \geq 5$ ), and 6MWT distance ( $\geq 1000$  feet) at 3, 6, and 12 months. We estimated the odds ratios and significance for the time effect in each intervention group and the group-time interaction for the intervention effect. We also evaluated the extent to which participants experienced moderate improvement in insomnia based on a decrease in the  $ISI > 7$  [48] at 3, 6, 12 with GEE, including the estimated the odds ratio of a moderate reduction in HS compared to HH. Since the reduction was observed after



the intervention, we examined group difference for intervention effects without the time-group interaction.

In a secondary analysis, we examined the intervention effects separately for people with significant SDB treated with CPAP vs. those with no/mild SDB. The GLMMs at 12 months follow-up were repeated in participants with each condition. Also, we examined the change on each ISI item by dichotomizing the responses (item scores  $\geq 2$ ) and used GEE to examine longitudinal change in these and other binary outcomes.

Power analysis determined that a sample size of 175 has 90% power to detect a median effect size (Cohen's  $D$ ) of 0.5 to compare the primary outcomes between two intervention groups at 3 months using independent  $t$ -tests at a 5% significance level based on our preliminary efficacy study [12]. Powers were calculated for the difference in means between the two groups at multiple time points in the longitudinal models, assuming within-subjects correlations over time. With scenarios of within-subject correlations of 0.6, 0.7, and 0.8, the sample size of 84 per group could detect the same difference of means (i.e. Cohen's  $D = 0.50$ ) between the two groups at 3, 6, and 12 months with 93% or greater powers in the longitudinal model. The sample size was somewhat smaller for the 6MWT, for which there was missing data at 3 months due to the inability of some to complete the walk due to physical issues or come to the laboratory. The sample size of 140 for the 6MWT at 3 months has 84% power to detect the same effect size.

## Results

The consort diagram appears in Figure 1. In total, we prescreened 10 291 medical records; 3724 patients were eligible to receive an invitation to screen. We were unable to contact 2263, and 1461 were invited to screen for eligibility [20]. Of those invited, 304 were assessed for eligibility, and 195 enrolled. Six participants dropped out prior to randomization, and 189 were randomized to HH and HS conditions. Fourteen completed the intervention or control condition but dropped out or died before follow-up assessments began (see Figure 1). Nine of these were randomized to HS. There was no difference between dropouts and those retained on gender or comorbidity. Dropouts were slightly older [ $M = 65.2$  (12.4) vs.  $M = 63.0$  (12.9) years] and had slightly more severe insomnia symptoms [ISI: ( $M = 17.8$  (4.1)) vs.  $M = 15.0$  (4.6)], but these differences were not statistically significant. There were no statistically significant differences in these characteristics between the dropouts in the HH and HS.

Attendance levels were high, and dropout rates during the intervention were low. Participants who dropped out reported being too busy with medical appointments, family responsibilities, or work or were no longer interested in participating after receiving the intervention. Some did not wish to complete study measures at follow-up. Participants with baseline data ( $n = 175$ ) and at least one follow-up (3 months) were included in the overall analysis of sustained effects.

The clinical and demographic characteristics of the sample appear in Table 1. The mean age was 63 years. The sample includes 57% men and 17.9% Black participants. The majority were overweight or obese and had an average score of 2.7 on the Charlson Comorbidity Index. Half used CPAP for SDB. The majority had New York Heart Association Class II or III HF with preserved ejection fraction (HFpEF). There were no statistically significant differences between the HS and HH groups on the

clinical or demographic characteristics, except for the prevalence of diabetes mellitus and the Charlson Comorbidity Index that were higher in the HH group. Prescription hypnotic use was 11.3% in the HS group and 4.2% in the HH group at baseline.

The sleep, symptom, and functional variables were similar at baseline for both groups (Table 2). The average insomnia severity was consistent with levels suggesting clinical insomnia [16], and participants overall had poor sleep quality, prolonged sleep latency, and low levels of sleep efficiency. PROMIS measures of sleep disturbance, fatigue, and anxiety were higher than the  $T$ -scores of 50 that reflect population norms.

There were both short-term (3 months) and sustained (6 and 12 months) the group-time interaction effects on insomnia severity (Tables 2 & 3). The decrease of more than six points in the ISI was sustained at 6 and 12 months (Figure 2). These changes were of similar magnitude in the piecewise GLMM (Supplementary Table 4). There was a statistically significant improvement in the HH group that was about half as large as in the HS group. The percentage of participants with "clinical" levels of insomnia severity (ISI  $>15$ ) decreased from 60.4% to 12.7% in the HS group compared to a decrease from 48.8% to 24.3% in the HH group ( $p = .0005$ ). Among the HS group, 38% were in remission (ISI  $>7$ ) at one year, compared to 25% in the HH group. Within groups, but not group-time interaction effects were statistically significant. (Table 4; Figure 3). Using the estimate of a "moderate" improvement in insomnia of  $>7$  points [48], 31 (38%) of participants in the HS had a moderate decrease at 3 months that was sustained at 12 months, compared to the HH group, among whom 15 (18.7%) had moderate decreases at 3 months and 20 (28.6%) had moderate decreases at 12 months. There was a significant group difference ( $p = .0239$ ) in these changes.

We examined the single items from the ISI to further understand specific improvements in insomnia symptoms (Supplementary Table 1). There were statistically significant group-time effects on difficulty falling asleep, worry/distress about sleep, and interference of sleep with daily functioning (all  $p < .05$ ), and a trend suggesting that participants in the HS group were less likely to report sleep-impaired quality of life ( $p = .0639$ ). There were no group differences in difficulty staying asleep, waking too early, or satisfaction with current sleep. The proportion who reported dissatisfaction with sleep decreased in both groups, but over 70% continued to report at least moderate dissatisfaction with sleep at 12 months.

There were statistically significant group-time interaction effects on sleep quality measured by the PSQI, with sustained effects at one year (Tables 2 and 3; Figure 2; Supplementary Table 4), and there was some improvement in PSQI in HH, but the overall improvement in the HS continued to be significantly higher with larger improvement in this group over 12 months ( $p = .0057$ ). Based on the dichotomized PSQI score, 74.7% of the HS and 82.9% of the HH group had residual poor sleep quality at 12 months (Table 4; Figure 3). There were clinically meaningful and sustained decreases in the PROMIS sleep disturbance scale of a mean 6 points delta at postintervention. This change was 5.41 points at postintervention in the piecewise GLMM and 5.58 points at 12 months in the GLMM in the HS group up to 12 months. There were small within-groups improvements in the HH group. The measure of improvements indicated as a range from 0 to 1 (1 represents no change from baseline, 0 represents change to 2 times of standard deviation), in multiple sleep characteristics in the HH and HS groups appear in

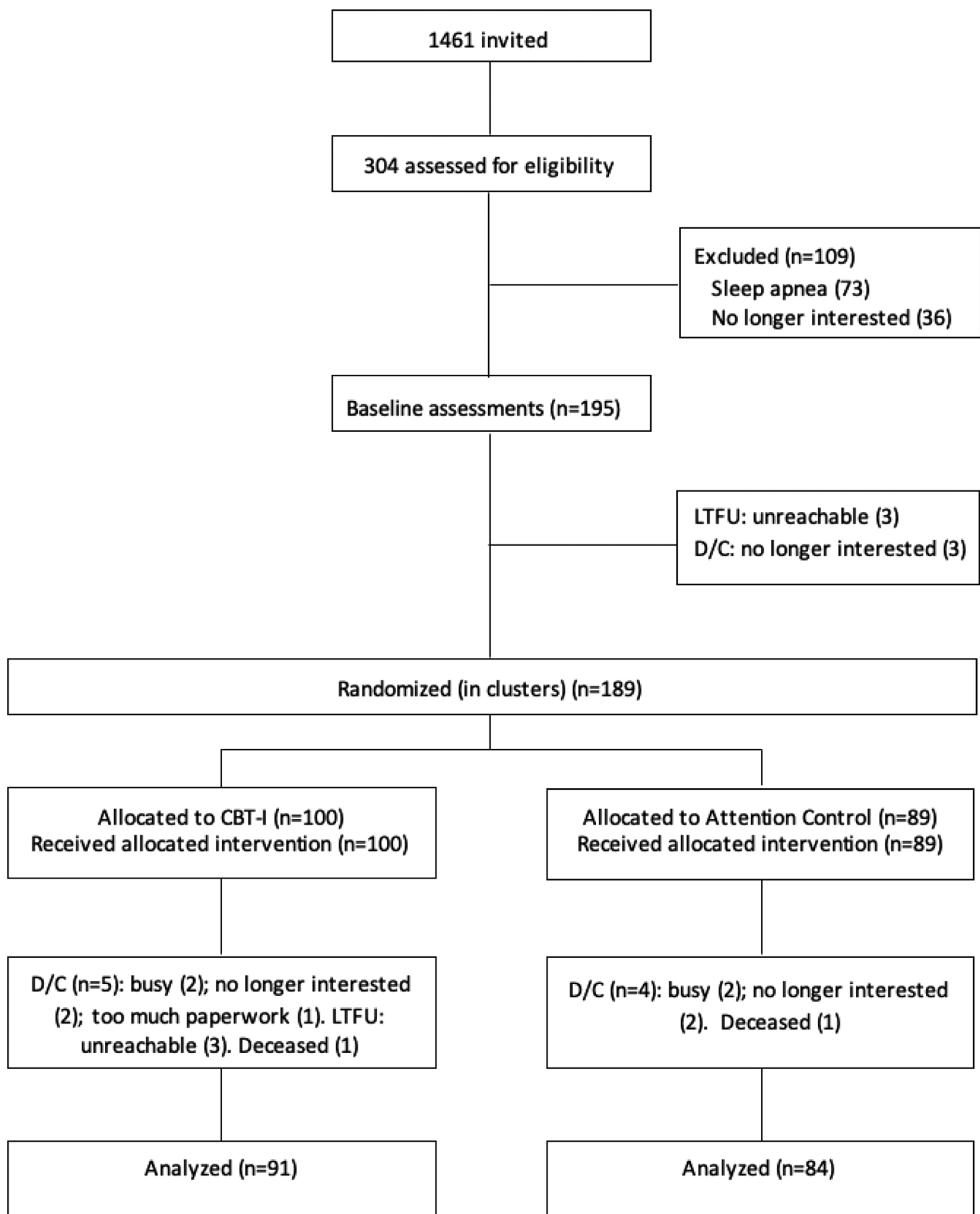


Figure 1. Consort diagram.

**Supplementary Figure 1.** The spiderweb shape shrinks to show improvements in sleep characteristics from baseline. More shrinkages in HS represents better improvement in sleep characteristics compared to HH.

Self-reported sleep latency decreased by about 14 minutes at 6 months in the HS group but did not improve in the HH group, and the difference remained statistically significant at 12 months (Table 3). Actigraph-recorded, but not self-reported

**Table 1.** Demographic and clinical characteristics of the sample (N = 175)

Variables	Mean (SD)/N (%)	Healthy Sleep N = 91	Healthy Heart N = 84
		Mean (SD)/N (%)	Mean (SD)/N (%)
Age	63.0 (12.9)	62.0 (13.1)	64.1 (12.6)
Gender: male	100 (57.1%)	53 (58.2%)	47 (55.9%)
Race			
White	133 (76.0%)	69 (75.8%)	64 (76.2%)
African American	28 (16.0%)	14 (15.4%)	14 (16.7%)
Native American	1 (0.6%)	0	1 (1.2%)
Asian	1 (0.6%)	0	1 (1.2%)
Other	12 (6.9%)	8 (8.8%)	4 (4.8%)
Ethnicity: Hispanic	9 (5.2%)	5 (5.5%)	4 (4.8%)
Veterans	20 (11.4%)	10 (11.0%)	10 (11.9%)
Body Mass Index (BMI)	31.9 (8.4)	31.3 (8.3)	32.4 (8.6)
<18.5	3 (1.8%)	3 (3.4%)	0
18.5–<25	35 (20.6%)	18 (20.7%)	17 (20.5%)
25–<30	42 (24.7%)	24 (27.6%)	18 (21.7%)
30+	90 (52.9%)	42 (48.3%)	48 (57.8%)
New York Heart Association (NYHA) Classification			
I	51 (29.3%)	26 (28.6%)	25 (30.1%)
II	83 (47.7%)	43 (47.2%)	40 (48.2%)
III	36 (20.7%)	18 (19.8%)	18 (21.7%)
IV	4 (2.3%)	4 (4.4%)	0
Ejection Fraction (EF) % s—SHFM	49.4 (15.3)	49.0 (15.3)	49.8 (15.5)
EF < 45	58 (33.5%)	33 (36.3%)	25 (30.5%)
Charlson Comorbidity Index (CCI)*	2.7 (1.9)	2.4 (1.8)	3.0 (1.9)
Health history			
Diabetes*	56 (32.4%)	23 (25.3%)	33 (40.2%)
Hypertension	107 (62.9%)	51 (57.3%)	56 (69.1%)
COPD	40 (23.3%)	20 (22.2%)	20 (24.4%)
Peripheral Vascular Disease	26 (15.8%)	15 (17.4%)	11 (13.9%)
Myocardial Infarction	46 (28.4%)	20 (24.4%)	26 (32.5%)
Sleep Apnea / CPAP Use	91 (52.0%)	46 (50.5%)	45 (53.6%)
Pacemaker	44 (25.4%)	23 (25.3%)	21 (25.6%)
LVAD	3 (1.9%)	1 (1.2%)	2 (2.6%)
Hypnotic medications	12 (7.9%)	9 (11.3%)	3 (4.2%)
Heart failure medications			
ACE or ARB	87 (49.7%)	46 (50.5%)	41 (48.8%)
Beta blocker	115 (65.7%)	55 (60.4%)	60 (71.4%)
Statin	106 (60.6%)	56 (61.5%)	50 (59.5%)
HCTZ	7 (5.6%)	5 (7.6%)	2 (3.3%)
Loop diuretic	111 (71.6%)	52 (66.7%)	59 (76.6%)
Insomnia Severity Index (ISI)	15.0 (4.6)	15.3 (4.5)	15.0 (4.6)
Mild (ISI: 7–14)	80 (45.6%)	36 (39.6%)	44 (52.4%)
Clinical Insomnia (ISI:15–28)	95 (54.3%)	55 (60.4%)	40 (47.6%)

Loop diuretic indicates use of any loop diuretic e.g. Bumex, Demadex, and Lasix.

\*\*\* statistically significant difference between two intervention groups with p-values <.001, <.01, and <.05 respectively. Healthy Sleep = CBT-I Group; Healthy Hearts = Heart Failure Self-Management Group (Healthy Control).

sleep duration, increased by about 14 minutes (0.24 hours) in the HS group and decreased by about 26 minutes (0.44 hours) in the HH group at 3 months, and these differences were sustained at 6 months, but there were no group-related differences at 12 months (Tables 2 & 3) and no group-related difference from 3 to 12 months in the piecewise approach (Supplementary Table 4). Sleep duration returned to the baseline level in the HS group while it remained shorter than baseline in the HH group at 12 months (Table 3). There were no statistically significant changes in actigraph-recorded sleep efficiency, but the level of sleep efficiency was low overall, but there were sustained improvements of approximately 5 minutes in self-reported sleep efficiency.

There was a statistically significant decrease in fatigue at 3 months in the HS group and no change in the HH group. The interaction effect was not statistically significant at 3 months ( $p = .07$ ) (Table 2). However, fatigue continued to improve, and the HS effect was sustained, and the group-time interaction is statistically significant at 12 months on the GLMM. (Table 3) This was confirmed in the pattern mixture analysis conducted with the 12-month data to address the potential for bias based on dropouts. (Supplementary Table 2) and the piecewise regression indicated that fatigue continued to decrease from 3 to 12 months in HS vs. HH (Supplementary Table 4).

As shown in Table 2, a greater decrease in excessive daytime sleepiness was observed in the HS compared to the HH with a

**Table 2.** Effects of healthy sleep (CBT-I) compared with healthy hearts (attention control) interventions at one month postintervention (3 months postbaseline) on insomnia and sleep characteristics, daytime symptoms and function

	Change in Healthy Sleep (N = 91)		Change in Healthy Heart (N = 84)		Difference in delta	Effect size
	Baseline		Baseline		H0: $\Delta_{HS} = \Delta_{HH}$	$(\Delta_{HS} - \Delta_{HH})/$
	Mean (SD)	$\Delta_{HS}$ (SD)	Mean (SD)	$\Delta_{HH}$ (SD)	(P)	pooled SD
Insomnia and sleep characteristics						
Insomnia Severity (ISI)	15.3 (4.5)	***-6.60 (5.23)	14.6 (4.6)	***-3.46 (5.18)	.0002	-0.60
Sleep Quality (PSQI)	9.7 (3.7)	***-2.78 (3.16)	9.8 (4.0)	-0.51 (3.31)	<.0001	-0.70
Sleep Disturbance (PROMIS)	55.5 (6.6)	***-6.06 (7.54)	55.1 (8.1)	-1.20 (7.64)	<.0001	-0.64
Sleep Latency (PSQI) (minutes)	31.9 (30.2)	-4.39 (43.97)	36.7 (43.4)	-2.11 (44.28)	.7496	-0.05
Sleep Efficiency (PSQI) (%)	79.3 (14.3)	*4.87 (17.41)	77.8 (15.0)	-1.96 (15.41)	.0110	0.42
Sleep Duration (Actigraphy) (hours)	7.5 (1.4)	0.24 (1.73)	7.9 (1.9)	-0.44 (2.11)	.0318	0.35
Sleep Efficiency (Actigraphy)(%)	79.3 (9.1)	-0.5 (5.8)	80.9 (9.2)	0.3 (7.2)	.4356	-0.12
WASO (Actigraphy) (minutes)	62.7 (31.5)	2.37 (26.86)	61.0 (33.2)	-5.67 (34.36)	.1101	0.26
Daytime symptoms						
Fatigue (PROMIS)	55.1 (7.5)	***-3.24 (6.53)	54.4 (9.7)	-1.13 (8.05)	.0723	-0.29
Depression (PROMIS)	49.7 (8.4)	** -1.93 (6.38)	51.5 (8.3)	***-2.50 (6.37)	.5781	0.09
Anxiety (PROMIS)	51.4 (8.6)	** -2.08 (5.98)	51.5 (8.8)	-0.32 (7.16)	.0954	-0.27
Excessive daytime sleepiness	8.0 (4.6)	** -1.39 (4.21)	8.1 (5.0)	-0.23 (3.37)	.0558	-0.30
Daytime function						
Six minute walk distance	1090 (486)	*74.7 (236.2)	1101 (371)	**61.6 (156.3)	.7028	0.07
Sleep-related cognitions and beliefs						
Sleep Disturbance (SDQ)^	2.9 (0.7)	** -0.48 (0.61)	2.8 (0.7)	-0.11 (0.69)	.0005	-0.57
Dysfunctional Beliefs & Attitudes about Sleep (DBAS)^	5.2 (1.5)	***-1.2 (1.29)	5.2 (1.4)	*-0.27 (1.15)	<.0001	-0.76

ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index (higher score = poorer sleep quality); WASO: Wake after Sleep Onset; SDQ: Sleep Disturbance Questionnaire; DBAS: Dysfunctional Beliefs & Attitudes about Sleep Scale; PROMIS™ = Patient Reported Outcomes Measurement System.

$\Delta_{HS}$  and  $\Delta_{HH}$ , the pre-post changes at 3 months from baseline in Healthy Sleep and Healthy Heart, were tested with paired t-test.

\*\*\*, \*\*, \* indicate p-values <.001, .01, and .05 respectively. Differences between  $\Delta_{HS}$  and  $\Delta_{HH}$  were examined with two-sample independent t-tests.

^DBAS and SDQ are secondary outcomes.

marginal *p*-value of .0558 obtained from independent t-test, but this postintervention effect was statistically significant, and the decrease was sustained for follow-up in the piecewise GLMM (Supplementary Table 4). The group-time interaction on excessive daytime sleepiness was significant at 6 and 12 months in the GLMM (Table 3) that was confirmed in the pattern mixture analysis (Supplementary Table 2). The proportion of the sample with excessive daytime sleepiness decreased from 40.7% to 20.2% in the HS group, but there was no statistically significant decrease in the HH group (36.9% to 32.9%) (Table 4 and Figure 3).

There were slight decreases in anxious and depressive symptoms in both groups, but no group-time interaction effects. The within-group effects on depressive symptoms were somewhat larger in the HH than the HS group.

There were statistically significant improvements in 6MWT distance in both groups, with the largest sustained effects at 12 months in the HS group. The group-time interaction effects were statistically significant at 6 and 12 months, with the greatest increases at 12 months (117.4 vs. 61.3 feet in the HS and HH groups, respectively) (Table 3). Although the difference was large, these trends were not statistically significant in the pattern mixture analysis (Supplementary Table 2). The continued improvement in the SMWT from 3 to 12 months was confirmed in the piecewise GLMM (Supplementary Table 4). After dichotomizing the scores at  $\geq 1000$  feet (consistent with the 300-meter estimate of risk for poor outcomes) [37], there was an increase at 12 months in the proportion of participants who walked  $\geq 1000$  feet in the HS group (68.55% to 86.0%) compared with the HH group (76.8% to 82.8%), *p* = .024 (Table 4 and Figure 3).

There were statistically significant decreases in dysfunctional beliefs and cognitions about sleep, measured with the DBAS and SDQ, with sustained effects at 12 months and significant group-time interaction effects across the year. Both groups improved but the improvements in HS were larger (Tables 2 and 3 and Supplementary Table 4).

As a secondary analysis, we evaluated differences in HS and HH's effects between people with and without CPAP-treated sleep apnea. There were statistically different improvements in the HS vs. the HH group in people with treated sleep apnea in insomnia severity, sleep quality, fatigue, sleepiness, and six-minute walk distance, and these differences were similar in people with no-mild SDB. Sleep duration improved in HS (0.29 hours) but not in the H group (-0.10 hours) among people with sleep apnea (*p* = .0608) over 12 months, while actigraph-recorded sleep duration decreased in both the HS (-0.27 hours) and HH (-0.35 hours) groups among people with non-mild sleep apnea over 12 months (Supplementary Table 3).

## Discussion

This is the first RCT to examine the sustained effects of CBT-I among adults with chronic HF and insomnia symptoms [49]. CBT-I had sustained and significant effects on insomnia severity, sleep quality, self-reported latency and efficiency, fatigue, excessive daytime sleepiness, and objectively measured physical function compared with a robust attention control group that included HF self-management and sleep hygiene education. These findings extend previous studies of the short-term



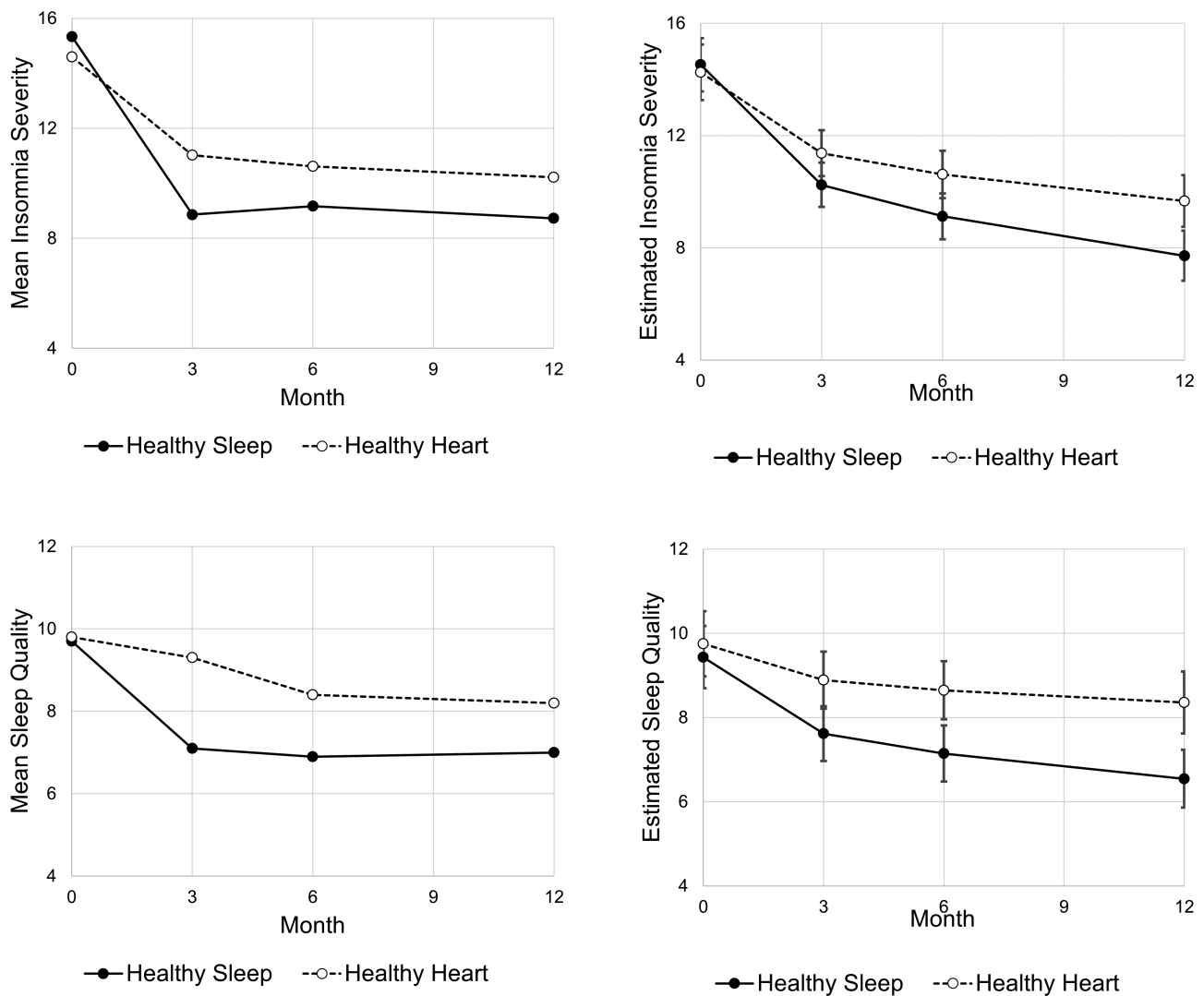


Figure 2. Means and estimated means from the mixed effects models of the effects of insomnia (ISI) and sleep quality (Pittsburgh Sleep Quality Index) between the healthy sleep (CBT-I) and the healthy hearts (Attention control) interventions from baseline through 12 months.

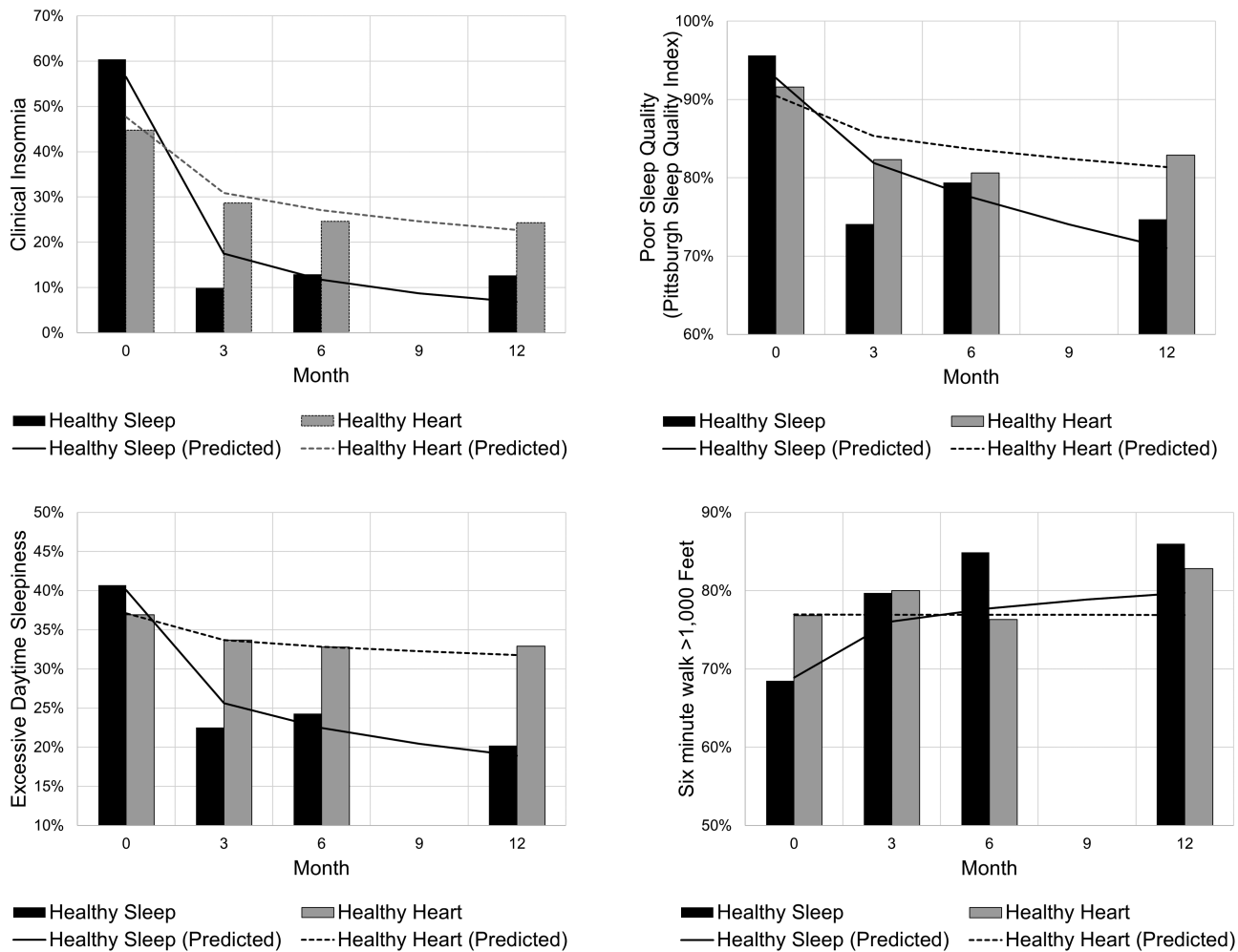
effects of CBT-I among people with HF [12, 13] and people with other forms of cardiovascular disease [50] and a meta-analysis of the short-term effects of CBT-I vs. active controls on insomnia comorbid with medical conditions [10].

The sustained effects on 6MWT distance, an objective measure of functional performance that also has prognostic significance for people with HF [51, 52], are especially notable, and these findings extend past studies focused on self-report measures [11]. The magnitude of the effects is clinically meaningful [37, 53] and greater than the effects of some medications [37] and cardiac rehabilitation [54] among people with cardiovascular disorders.

CBT-I effects on fatigue and sleepiness are clinically meaningful [55, 56] and consistent with short-term and six-month effects in a preliminary efficacy study [12, 14]. Although a recent systematic review found small-moderate effects of CBT-I on daytime symptoms [11], it did not include people with HF, a group at exceptionally high risk for fatigue, a predominant and distressing symptom for people with this condition. The decline from 40% to 20% of participants with excessive daytime sleepiness indicates a large improvement in the HS group. Excessive

daytime sleepiness is also a hallmark of SDB, a condition present in about half of the sample, and participants with both insomnia and SDB treated with CPAP had large improvements in this outcome.

Improvements in fatigue, sleepiness, and especially six-minute walk distance, with CBT-I suggest the potential importance of understanding the biological mechanisms for these improvements [49], especially given the contributions of insomnia to incident HF, death [5], and cardiac events [6]. CBT-I improved inflammatory processes among older adults with insomnia, among whom a significant proportion had heart disease [57], although a small study of HF patients revealed no effects of CBT-I on cortisol or catecholamines [58], possibly due to lack of statistical power. However, increases in the ratio between day and night cortisol over six months were associated with improvements in fatigue, depression, sleep duration, and sleep-related cognitions in people who had CBT-I. Although CBT-I did not influence early markers of cardiovascular disease in a small trial [59], the latter studies were not fully powered to address the effects on these biomarkers.



**Figure 3.** Observed and estimated proportions of participants with clinical insomnia (Insomnia Severity Index  $\geq 15$ ), daytime sleepiness (Epworth Sleepiness Scale  $> 10$ ), poor sleep quality (Pittsburgh Sleep Quality Index—PSQI  $> 5$ ), and six-minute walk distance  $> 1000$  feet between the healthy sleep and healthy heart interventions over 12 months.

The sustained effects of CBT-I on sleepiness, fatigue, and six-minute walk distance are especially notable given that the elements of the HH active control (e.g. medication adherence, diet, daily activity, symptom monitoring) are components of standard care for HF, designed to improve HF outcomes such as function and symptoms. Improvements in HF due to daily self-management may also contribute to improved sleep, and there were small within-group improvements in the HH group at 12 months and small improvements in depressive symptoms.

The effects of HS compared to HH on mean levels of insomnia severity were statistically large at 3 months and the change of more than 6 points over the 6 through 12-month follow-ups was consistent with a clinically meaningful change defined as 6 points in primary insomnia [60] and with change in insomnia severity in a small study of people with coronary heart disease at 3 months [50], but did not overall achieve the change of more than 7 points indicating a moderate change determined in another study of people with clinical insomnia [48]. However, the percentage of the group that experienced moderate change in insomnia severity was significantly greater in the CBT-I group, especially at 3 months, when the rate was approximately twice as large as in the HH group.

Notably, 38% of the HS group, compared to about 24% of the HH group achieved remission from insomnia at 12 months—a rate similar to the 36% remission rate reported in a meta-analysis of CBT-I trials [61] conducted with people with insomnia and comorbid psychiatric or medical disorders. However, only one of these trials [62] included people with heart disease among others; none included people with HF; and few studies followed participants for a long as one year. Despite our positive outcomes, it is possible that individual components of CBT-I may be more beneficial than others or that other strategies focused on HF self-care may provide added benefits for insomnia treatment when tailored to individual needs.

Although about 75% of the CBT-I group continued to have poor global sleep quality (PSQI  $> 5$ ) as determined by the Pittsburgh Sleep Quality Index (PSQI), these findings may be explained by the fact that the PSQI includes questions on nocturia, difficulty breathing during sleep, pain, and “enthusiasm” about daytime activities—all of which may be influenced by HF itself and are not direct indicators of sleep itself, but rather, influencing factors.

The effects of CBT-I on sleep and the large effects on six-minute walk and fatigue suggest the importance of CBT-I for people with HF, but further research is needed to determine a

**Table 3.** Effects of healthy sleep (CBT-I) compared with healthy hearts (attention control) interventions at six and twelve months on insomnia and sleep characteristics, daytime symptoms, function, and sleep-related beliefs and cognitions: general linear mixed model with false discovery rate for the primary outcome variables

	Change in Healthy Sleep group (N = 91)	Change in HH group (N = 84)	Group × Time interaction	
	Estimate ± SE	Estimate ± SE	P	False Discovery Rate (12 months)
<b>Insomnia and sleep characteristics</b>				
Insomnia Severity (ISI)				
6 months	***-6.63 ± 0.48	***-4.06 ± 0.49	.0002	
12 months	***-6.69 ± 0.47	***-4.57 ± 0.50	.0023	0.0130
Sleep Quality (PSQI)				
6 months	***-3.02 ± 0.31	**-.092 ± 0.32	<.0001	
12 months	***-2.89 ± 0.32	***-1.36 ± 0.34	.0013	0.0130
Sleep Disturbance (PROMIS)				
6 months	***-5.87 ± 0.75	*-1.72 ± 0.77	.0001	
12 months	***-5.58 ± 0.74	***-2.62 ± 0.77	.0057	0.0148
Sleep Duration (Actigraphy) (hours)				
6 months	0.21 ± 0.12	-0.18 ± 0.12	.0236	
12 months	0.03 ± 0.11	-0.18 ± 0.12	.2094	0.2722
Sleep Latency (PSQI) (minutes)				
6 months	***-14.06 ± 2.24	-0.17 ± 2.30	<.0001	
12 months	***-10.86 ± 2.09	-1.83 ± 2.19	.0030	0.0130
Sleep Efficiency (PSQI) (%)				
6 months	***5.21 ± 1.51	0.91 ± 1.52	.0456	
12 months	***4.91 ± 1.43	1.17 ± 1.49	.0713	0.1159
Sleep Efficiency (Actigraphy) (%)				
6 months	-0.53 ± 0.51	0.17 ± 0.57	.3786	
12 months	-0.44 ± 0.58	0.01 ± 0.59	.5869	0.6358
Wake After Sleep Onset (Actigraphy) (minutes)				
6 months	1.31 ± 2.29	-1.17 ± 2.34	.3631	
12 months	0.29 ± 2.13	-1.16 ± 2.19	.6377	0.6377
<b>Daytime symptoms</b>				
Fatigue (PROMIS)				
6 months	***-3.16 ± 0.70	-1.37 ± 0.72	.0757	
12 months	***-4.26 ± 0.67	*-1.49 ± 0.72	.0051	0.0148
Depression (PROMIS)				
6 months	*-1.55 ± 0.66	***-2.549 ± 0.68	.3186	
12 months	-1.11 ± 0.64	***-2.71 ± 0.68	.0857	0.1238
Anxiety (PROMIS)				
6 months	***-2.73 ± 0.73	*-1.67 ± 0.74	.3087	
12 months	***-2.85 ± 0.71	*-1.90 ± 0.74	.3571	0.4220
Excessive Daytime Sleepiness (ESS)				
6 months	***-1.99 ± 0.37	---0.68 ± 0.37	.0136	
12 months	***-2.15 ± 0.35	***-0.84 ± 0.36	.0106	0.0230
<b>Daytime function</b>				
Six minute walk distance (feet)				
6 months	***101.0 ± 17.0	**44.0 ± 16.6	.0172	
12 months	***117.4 ± 18.1	**61.3 ± 17.7	.0274	0.0509
<b>Sleep-related beliefs and cognitions ^</b>				
Sleep Disturbance (SDQ)^				
6 months	***-0.45 ± 0.07	***0.23 ± 0.06	.0064	
12 months	***-0.42 ± 0.05	***-0.26 ± 0.06	.0419	—
Dysfunctional Beliefs and Attitudes About Sleep (DBAS)^				
6 months	***-1.15 ± 0.12	***-0.43 ± 0.13	<.0001	
12 months	***-0.99 ± 0.13	***-0.59 ± 0.13	.0286	—

ISI: Insomnia Severity Index; PSQI: Pittsburgh Sleep Quality Index (higher score = poorer sleep quality); ESS: Epworth Sleepiness Scale. WASO: Wake after Sleep Onset; SDQ: Sleep Disturbance Questionnaire; DBAS: Dysfunctional Beliefs & Attitudes about Sleep Scale; PROMIS™: Patient Reported Outcomes Measurement System; HS: Healthy Sleep; HH: Healthy Heart.

The estimates are the average change for 6 months which are computed from GLMMs with random intercepts and unstructured covariance for the outcomes at baseline, 3, and 6 months, and the "Time × Group Interaction" represents the intervention effects of HS compared to HH.

\*\*\*, \*\*, \* indicate significant change within group sat 0.001, 0.01, and 0.05 significance levels, respectively. FDR: False Discovery Rate was calculated only for the primary outcome variables (excluding SDQ and DBAS – process variables^).

**Table 4.** Proportions of participants with mild insomnia, clinical insomnia, excessive daytime sleepiness, poor sleep quality, and six minute walk distance  $\geq 1000$  feet over 12 months from baseline in the healthy sleep (CBT-I) compared with the healthy hearts groups (attention control) based on the generalized estimating equation (GEE)

		Follow ups				GEE for longitudinal test	
		Baseline	3 months	6 months	12 months	Odds ratio [95% CI]	Group × Time interaction
Mild-Severe Insomnia (Insomnia Severity Index >7)							
Healthy Sleep	N (%)	91 (100.0%)	53 (65.4%)	50 (71.4%)	49 (62.0%)	***0.05 [0.03, 0.09]	0.4715
Healthy Heart	N (%)	84 (100.0%)	63 (78.7%)	54 (78.3%)	53 (75.7%)	***0.07 [0.04, 0.14]	
Clinical Insomnia (Insomnia Severity Index ≥15)							
Healthy Sleep	N (%)	55 (60.4%)	8 (9.9%)	9 (12.9%)	10 (12.7%)	***0.06 [0.03, 0.12]	0.0005
Healthy Heart	N (%)	41 (48.8%)	23 (28.7%)	17 (24.6%)	17 (24.3%)	***0.32 [0.18, 0.57]	
Excessive Daytime Sleepiness (Epworth Sleepiness Scale ≥10)							
Healthy Sleep	N (%)	37 (40.7%)	18 (22.5%)	17 (24.3%)	6 (20.2%)	***0.35 [0.21, 0.58]	0.0204
Healthy Heart	N (%)	31 (36.9%)	27 (33.7%)	22 (32.8%)	23 (32.9%)	0.79 [0.50, 1.25]	
Poor Sleep Quality (Pittsburgh Sleep Quality Index ≥5)							
Healthy Sleep	N (%)	86 (95.6%)	60 (74.1%)	54 (79.4%)	59 (74.7%)	***0.19 [0.10, 0.39]	0.0440
Healthy Heart	N (%)	76 (91.6%)	65 (82.3%)	54 (80.6%)	58 (82.9%)	***0.46 [0.28, 0.75]	
Six Minute Walk Distance (≥1000 feet)							
Healthy Sleep	N (%)	61 (68.5%)	55 (79.7%)	45 (84.9%)	49 (86.0%)	*1.77 [1.11, 2.84]	0.0516
Healthy Heart	N (%)	63 (76.8%)	56 (80.0%)	45 (76.3%)	53 (82.8%)	0.99 [0.71, 1.40]	

The Generalized Estimating Equation (GEE) was used to examine the difference in changes in the proportion of the sample with mild-severe insomnia (Insomnia Severity Index—ISI  $>7$ ); clinical insomnia (ISI  $\geq 15$ ), excessive daytime sleepiness daytime sleepiness (Epworth Sleepiness Scale—ESS  $\geq 10$ ), poor sleep quality (Pittsburgh Sleep Quality Index—PSQI  $\geq 5$ ) and six-minute walk Distance ( $\geq 1000$  feet) between HS and HH. The odds ratios were estimated for reductions of the problematic responses in each group over 12 months, and the “Time  $\times$  Group Interaction” represents the intervention effects of HS compared to HH.

“, ”, \* indicates significant change within group at  $p < .001$ , .01, and .05 significance levels, respectively.

specific metric for clinically meaningful change in insomnia severity in these patients. Previous estimates of clinically meaningful change were not specifically developed for people with HF or others with comorbid medical disorders that are associated with significant daytime symptoms such as fatigue and poor daytime function that may be improved with CBT-I. Additionally, our focus was on insomnia symptoms and not a clinical diagnosis of insomnia per se. Therefore, further research is needed regarding the metrics for clinically meaningful change in these participants to guide future translational efforts.

Consistent with a “stepped care” approach to insomnia [63], it is possible that the HF self-management components, including sleep hygiene education, may be sufficient to improve sleep and related outcomes in those with mild insomnia symptoms, and this should be considered in future studies. The social support benefits of group participation may also contribute to improved outcomes.

To address the potential effects of treatment expectancy that may explain differences in the sleep outcomes, we provided sleep hygiene education to the HH group and explained that improvement in HF symptoms through self-care strategies taught to this group (e.g. medication adherence, avoiding a high sodium diet, exercise) may also improve insomnia. This was consistent with common perceptions among HF clinicians and some people with HF about the contributors of HF exacerbations and sleep. Indeed, the HH group showed improvements, albeit smaller improvements, than those in the HS group.

Cognitive therapy, a component of CBT-I, targets misperceptions and distorted cognitions and thoughts about sleep that contribute to insomnia. The effects of CBT-I are consistent with a past study of people with HF [64] and a recent systematic review [65]. Our current findings, the mediational role of sleep-related cognitions in HF, and the correspondence between

improvements in dysfunctional cognitions and improved symptoms in a past study [64], further underscore the importance of cognitions.

Our findings, coupled with concerns from people with HF that health care providers often do not assess or treat their sleep [8], suggest the importance of including sleep disorders screening and follow-up with treatment into HF care. The current study addressed the effects of CBT-I provided in a face-to-face group format based on earlier preliminary data suggesting its feasibility and acceptability. However, brief behavioral therapy for insomnia, web, “app,” or telehealth approaches are efficacious in many groups and are likely more feasible and accessible, given the shortage of trained behavioral sleep specialists. Future studies should address the effectiveness of these modalities among people with HF, especially given anecdotal resistance noted early in our study to technology-delivered approaches.

People with HF often experience both insomnia and SDB [3, 7]. Large improvements in insomnia severity, sleep quality, sleep latency, and efficiency in people with both CPAP-treated SDB and insomnia are consistent with outcomes in a broad population of people with these conditions [66]. Large improvements in fatigue, sleepiness, and six-minute walk distance in people with insomnia and SDB further extend this work to the HF population and suggest the importance of treating both comorbid insomnia and SDB [67]. In other studies, combined use of PAP and CBT-I improved insomnia outcomes [66] and improved the apnea-hypopnea index [68]. In our trial, we screened out many participants who had untreated moderate-severe comorbid SDB. Although we provided a referral for SDB treatment, a large percentage of these participants were reluctant to follow up due to concerns about the use of CPAP. Future studies are needed that address comorbid sleep apnea and insomnia (COMISA) among people with HF who have both sleep disorders.



Strengths of this study, the first to our knowledge to examine the sustained effects of CBT-I among people with HF, included its randomized design; inclusion of a robust attention control that is often a component of standard care; standardized measures; a full year of follow-up; and careful attention to intervention fidelity. We used rigorous statistical approaches, including GLMM and a piecewise approach to examine changes over time—approaches that provide different perspectives but were generally in accordance with one another. We addressed possible bias due to drop-outs and avoided the inflation of type I error due to multiple outcomes with the false discovery rate. A strength of our power analysis was based on our preliminary efficacy trial [12] that included the identical intervention and control condition and insomnia measures to the current trial and baseline and 3-month follow-up data. In addition, we performed the power analysis to detect the mean difference on repeated measures by assuming correlations within-subjects. This power calculation was not performed for GLMM but shows approximate powers for longitudinal models.

There are several limitations. As noted above, we screened out many participants who had untreated moderate to severe SDB, and therefore the findings cannot be generalized to this group. Due to cost, participant burden, and recommendations that electrophysiological measures of sleep are not needed to diagnose insomnia, we did not conduct polysomnographic sleep measurements. However, we conducted objective screening for sleep apnea and excluded participants with other sleep disorders, such as restless legs syndrome or untreated obstructive sleep apnea to eliminate these as potential confounding influences.

We randomized 195 participants and included all participants who had at least one follow-up in the analyses ( $n = 175$ ). Although we did not include participants who were randomized but had no follow-ups, the rate of drop-out was similar between the HH and HS groups and there were no significant differences in the clinical or demographic differences between those who dropped out and those retained. We lost participants to follow-up due to death or exacerbation of HF and desire not to complete the follow-up measurements. For individuals who missed specific milestones due to hospitalization or other issues, we resumed data collection subsequently if possible. Of note, 12-month follow-ups for some study participants occurred after the onset of the Covid-19 pandemic. This contributed to some missing data on the 6MWT due to the need to conduct it in the clinic or laboratory and may have contributed to insomnia severity. Except for the six-minute walk distance, effects remained statistically significant when addressed with pattern mixture analysis to address potential confounding due to missing data/dropouts.

The study was designed to include face-face group sessions, and some participants were not able to attend. We provided make-up telephone sessions for these individuals, but it is possible that this also influenced the study outcomes. Given the differences in approach to CBT-I vs. the attention-control condition, it is also possible that treatment expectancy influenced the study outcomes. However, we did not see a differential rate of attrition between these groups, and the attention control also improved on insomnia, albeit to a lesser extent than the CBT-I group. Inclusion of sleep hygiene information and small improvements in sleep due to HF self-management suggest that it is unlikely that treatment expectancy contributed to these outcomes.

The findings of this study suggest the sustained efficacy of CBT-I, compared with HF self-management education among people with HF and chronic insomnia symptoms, including improvements in insomnia severity, sleep characteristics, and significant daytime outcomes, including fatigue, excessive daytime sleepiness, and six-minute walk distance—important HF outcomes. These results have important implications for the clinical care of people with HF, as standard device and drug therapy do not consistently improve these outcomes. Future research is needed on the best ways to provide access to CBT-I for HF patients and to determine its effectiveness when delivered within HF disease management settings.

## Supplementary Material

Supplementary material is available at *SLEEP* online.

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## Disclosure Statement

None declared.

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