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Telephone interventions for co-morbid insomnia and osteoarthritis pain: The OsteoArthritis and Therapy for Sleep (OATS) randomized trial design

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ABSTRACT

The OsteoArthritis and Therapy for Sleep (OATS) study is a population-based randomized controlled trial of cognitive behavioral therapy for insomnia (CBT–I) with four innovative methodological aims. These are to: (1) Enroll representative participants across Washington state, including those from medically underserved communities; (2) Enroll persons with persistent insomnia and chronic osteoarthritis (OA) pain; (3) Test a scalable CBT-I intervention; and (4) Evaluate patient-reported outcomes (insomnia, pain severity, fatigue, depression) and cost-effectiveness over one year. This paper describes progress towards achieving these aims. The target population was persons age 60+ who had received OA care within the Kaiser Permanente Washington (KPW) health care system. We employed a two-phase screening via mail survey and telephone follow-up, with a 3-week interval between screens to exclude persons with spontaneous improvement in sleep or pain symptoms. Participants were randomized to a 6-session telephone-delivered CBT-I intervention or a 6-session telephone education only control condition (EOC). Blinded outcome assessments (completed online or on mailed paper forms) included primary and secondary sleep and pain outcome measures and quality of life measures. We obtained healthcare utilization from administrative claims data. Intent to treat analyses, including all participants randomized when they scheduled the first telephone session, will be conducted to compare CBT-I and EOC outcomes. The trial will be the largest experimental evaluation of telephone CBT-I to date, and the first to evaluate its cost-effectiveness.

Trial registration: ClinicalTrials.gov identifier: NCT02946957.

1. Introduction

Osteoarthritis (OA) is extremely common in older adults, affecting almost 50% of people aged 65 or older, a significant proportion of whom complain of significantly disturbed sleep [1]. Insomnia comorbid with pain is associated with increased psychoactive medication use, health care utilization, and costs in primary care settings [2–4]. Evidence-based treatments to improve sleep such as cognitive-behavioral therapy for insomnia (CBT–I) are available and have been shown to be efficacious for older adults, including those with OA [5–8]. However, delivery models for CBT-I need to be enhanced to enable large-scale dissemination, particularly to populations lacking access to specialty sleep clinics such as older adults with difficulties attending in-person CBT–I, and persons living in rural and other medically underserved areas.

Traditional CBT-I is typically offered in 6–8 face-to-face, 60-min individual or group sessions [9–11]. To increase accessibility and cost-effectiveness of CBT–I, alternative treatment modalities are emerging, including video telehealth [12], internet delivery [13,14], and mobile phone-delivered apps [15,16]. Telephone-delivered CBT-I has the additional advantage of giving patients access to individualized CBT-I interventions from home, with professional guidance and support

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similar to face-to-face delivery that is essential for maximizing adherence and treatment effects [17–19]. While telephone-delivered CBT for psychological disorders has been found effective [20], no large randomized trials have assessed initial and long-term effectiveness of telephone CBT—I, its impact on comorbid symptoms such as pain, fatigue, and depression, or whether it can be delivered in a cost-effective manner to diverse populations of older adults in a general health care system.

The OsteoArthritis and Therapy for Sleep (OATS) study is the largest test of telephone CBT-I to date (n = 327) and will be the first to evaluate its cost-effectiveness. Participants were randomized into telephone-delivered CBT-I or education only attention control (EOC). We employed double-screening to target patients with persistent and severe OA-related sleep and pain symptoms. Telephone intervention allowed us to enroll large numbers of patients across Washington State, affording access to minority and underserved populations, and to rural communities and patients with limited mobility or access to services for insomnia. In addition to assessing treatment efficacy and cost-effectiveness, the trial will provide an opportunity to learn about mediators and moderators of treatment effects, adding to the limited published research available on who benefits from treatment, and through what mechanisms CBT-I works. If the trial is successful and cost-effectiveness is established, telephone CBT-I has potential for national dissemination to reduce the substantial personal and economic burdens of OA-related insomnia and related symptoms on patients and society.

2. Methods

2.1. Conceptual framework

The OATS trial was designed to test a CBT-I intervention for older adults with persistent and severe insomnia and chronic OA pain, building upon a psychobiological model of good sleep [21]. Poor coping with OA-related sleep disturbances leads to non-restorative sleep, negative mood and reduced quality of life, and increased pain, fatigue, and health care costs. CBT-I is designed to teach more appropriate coping responses that lead to more restorative sleep, and ultimately improvements in mood, pain, fatigue, and reduced costs (Fig. 1).

2.2. Study design overview and aims

The OATS study is a randomized controlled trial of individual telephone-delivered CBT-I vs. placebo telephone EOC in 327 OA patients aged 60 + with persistent and severe insomnia symptoms and OA pain. The trial is being conducted by a multi-disciplinary team from the University of Washington (UW) and Kaiser Permanente Washington Health Research Institute (KPWHRI). KPW is a non-profit, integrated managed health care organization in Washington State. The study protocol and methods were reviewed and approved by the University of Washington Institutional Review Board.

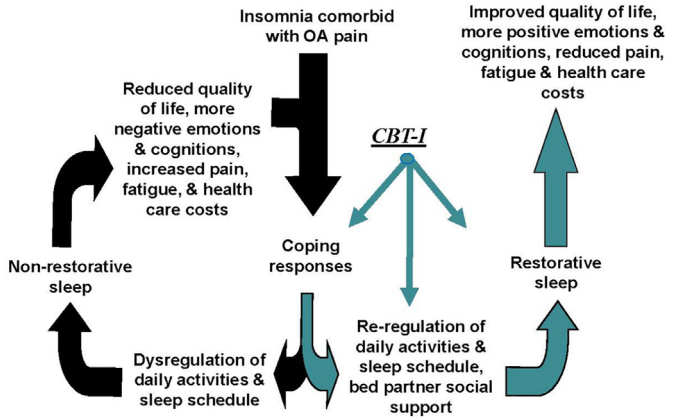

Fig. 1. Conceptual model: Impact of Cognitive-Behavioral Therapy for Insomnia (CBT—I) in OA Patients.

Baseline, post-treatment (2 month), and longitudinal (12-month) follow-ups will assess short- and long-term effects on insomnia severity, and secondary outcomes of sleep quality, pain, fatigue, mood, and quality of life. The cost-effectiveness of CBT-I will also be evaluated. The primary study questions in this trial are whether:

1) Telephone-delivered CBT-I improves post-treatment and long-term insomnia severity outcomes relative to telephone-delivered EOC;
2) Secondary benefits associated with improved insomnia outcomes include improvements in sleep quality, pain severity, fatigue, and depression;
3) CBT-I is cost-effective (i.e., improves quality of life for OA patients with comorbid insomnia at acceptable cost) evaluated from the perspective of healthcare insurers; and
4) CBT-I effects on insomnia are moderated by baseline insomnia, pain, or depression symptom severity, or whether changes in insomnia severity mediate the effects of CBT-I on secondary outcomes (pain severity, fatigue, depression, health care use).

2.3. Methodological innovations

The OATS trial includes several scientifically significant and innovative elements not previously applied in evaluating CBT—I. First, through the use of a telephone-delivered assessment and intervention protocol, we were able to provide outreach to participants from medically underserved populations across the state of Washington. Second, we used a two-stage screening procedure over a three week interval to identify patients with persistent and severe insomnia and OA pain, screening out those with spontaneous improvement in pain or insomnia symptoms. Double screening was important because our prior data suggested that CBT-I effects may be greatest and most durable in targeted patients with more severe and persistent symptoms [22]. Lastly, the OATS trial is the largest trial of telephone-delivered CBT-I to date, and the first to assess its cost-effectiveness in a large health care system.

2.4. Recruitment and participants

Recruitment began in September 2016 and ended December 2018. Participant screening and recruitment was population-based, employing KPW electronic health care records. Potential participants were identified across Washington State. All participants had a diagnosis of osteoarthritis (715xx) on at least one health care visit in the three years prior to the date of screening initiation. Persons eligible for screening were 60 years or older and had been continuously enrolled at KPW for at least one year. Invitations to participate included all available and eligible racial/ethnic minorities.

We excluded persons with a number of health care conditions identified in electronic health care data from the past three years that are known to impact sleep and that would not be expected to respond to a CBT-I intervention. These conditions included: rheumatoid arthritis; primary sleep disorders (obstructive sleep apnea, periodic leg movement disorder, restless leg syndrome, sleep-wake cycle disturbance, rapid eye movement behavior disorder); dementia or receiving cholinesterase inhibitors; Parkinson's disease; cancer diagnosis in the past year and receiving chemotherapy or radiation therapy in the past year; or inpatient treatment for congestive heart failure within the prior six months. Since the prevalence of comorbid chronic medical conditions is high among seniors and the implications for ability to participate vary, we did not exclude patients with other chronic diseases, nor did we exclude persons receiving prescription or over-the-counter sleep or pain medications. These criteria were consistent with our earlier studies [23] and designed to enhance the interpretability and generalizability of study results.

2.5. Prescreening

Potentially eligible participants received a mailed invitation explaining the study with a $2 cash pre-incentive, followed by a screening telephone call from a KPWHRI survey program interviewer. Those who were interested were screened using a 4-item version of the Insomnia Severity Index (ISI) [10] and the Brief Pain Inventory (BPI) [24] pain intensity and interference subscales. Persons with ISI ≥ 6 and two 0–10 pain ratings (BPI average pain intensity and interference) with a summed score ≥ 9 were invited to participate. (In our previous Lifestyles study [22], a 4-item ISI score of > 6 predicted a subsequent full ISI score 2 months later of 11 or greater with an area under the ROC curve of 0.777 for the 4-item ISI screener versus 0.784 for the full ISI.) The KPWHRI interviewer asked participants with elevated insomnia and pain symptoms for permission to use their electronic health records for study purposes, and for consent to send their contact information to UW study staff.

Three weeks later, a UW research coordinator re-contacted consenting subjects by telephone to confirm eligibility and interest in participation. Subjects with a score of 7 or greater on the Blessed Short Orientation Memory and Concentration Test [25] (indicating cognitive impairment), and those who reported they had a prior primary sleep disorder diagnosis (other than insomnia) or who were using a CPAP machine were excluded. During this follow-up call, potential participants were re-screened with the full 7-item ISI as well as the BPI. Participants with an ISI score ≥ 11 and a two item BPI sum score ≥ 9, and who had no planned surgery in the upcoming year were invited to participate. Those invited were mailed a study consent and HIPAA form to sign and return. They also completed a one-week sleep diary and baseline assessment packet, either on mailed paper forms or online.

2.6. Randomization

The OATS trial used a permuted block randomization with random block sizes and patients were randomly assigned to the intervention and control groups within each block. This design helped ensure approximate balance of intervention and control participants over the entire course of recruitment. Random block sizes were used to avoid detection of patterns in the randomization; blocks of size 2, 4 and 6 were sampled in a 6:3:1 ratio. A password-protected randomization form was created that the study clinical supervisor (SMM) accessed after participants 1) completed and returned the diary, baseline assessment packet, signed consent and HIPAA forms, and 2) scheduled an initial telephone treatment session with the assigned study interventionist (called "coach" hereafter). After randomization, appropriate study materials (CBT-I or EOC) were mailed to enrolled participants, timed such that they were received before the initial telephone session.

2.7. Baseline and post-assessments

Blinded assessments included primary and secondary measures of insomnia, pain severity and interference, depression, and fatigue. Additional ratings of clinical improvement and processes of change as well as quality of life, health care use, and costs will also be analyzed. Assessments were collected at baseline (before randomization), post treatment (2 months), and longitudinal (12-month) follow-up. Treatment satisfaction was measured after the first telephone session and again at 12 months. Additional information on medications, health care utilization, and costs will be obtained from KPW electronic health care records.

For self-report outcomes, participants had the option of either completing paper/pencil forms mailed to them with a prepaid return envelope, or entering the assessments online into a secure REDCap study database. Participants who failed to complete their post-treatment or 12-month assessments within 4 weeks of the scheduled receipt date received two calls (one from the UW research coordinator, one from the study coach), followed by a second mailed assessment packet and letter encouraging their participation. The principal investigators not involved in clinical supervision of study trainers (MVV, MVK), research staff involved in baseline and follow-up data collection, and staff responsible for data preparation remained blinded to the group assignments throughout recruitment, intervention, and follow-up.

2.7.1. Baseline characteristics

Variables include age, race, education, marital status, and duration of pain and sleep disturbances (duration dichotomized to having been present less than six months versus longer).

2.7.2. Primary outcome

The primary study outcome is the Insomnia Severity Index total item score. The ISI includes seven items (sleep onset, sleep maintenance, early morning awakening, satisfaction with current sleep pattern, interference with daily functioning, impairment attributed to sleep problems, distress caused by sleep problems) [10]. Each item is rated for the prior 2 weeks on a five-point Likert scale *(0 = no problem, 4 = severe problem)*. The ISI has good internal consistency and is sensitive to changes in sleep of older adults following behavioral treatment for insomnia [26].

2.7.3. Secondary outcomes

Pain – Arthritis pain intensity and interference with activities were measured using the Brief Pain Inventory-short form (BPI-sf) [24]. The BPI-sf is a validated, widely used questionnaire that rates pain intensity (4 items) and interference (7 items) from 0 to 10. It has been validated for use in clinical trials with OA pain patients [27].

Depression – Depression was measured using the Patient Health Questionnaire (PHQ-8) [28], a reliable, valid, dimensional measure of depression symptom severity. The PHQ-8 rates frequency of occurrence of 8 depressive symptoms on a 4-point scale. Scores of 5–9 indicate mild or subclinical depression; 10 or greater indicate depression [29,30].

Fatigue – Fatigue was measured using the Flinders Fatigue Scale (FFS) [31], a 7-item self-report questionnaire to measure fatigue level in a variety of situations. The FFS has strong internal reliability and validity [31], and been used to measure fatigue in CBT-I trials with older adults [32,33].

2.7.4. Clinical improvement and processes of change

Sleep –The Pittsburgh Sleep Quality Index (PSQI) [34] measures self-ratings of overall sleep quality using seven sleep components. A PSQI global score > 5 is highly sensitive and specific for distinguishing good and poor sleepers [35,36]. The Sleep Hygiene Index (SHI) [37] is a 13-item scale that rates how often participants engage in specific sleep hygiene related behaviors, including continued adherence to CBT-I recommendations over time. Higher scores indicate worse sleep hygiene. The Sleep Problem Acceptance Questionnaire (CPAQ) [38] is an 8-item scale that rates willingness to experience insomnia symptoms and activities engagement. Higher scores indicate more willingness and engagement.

Pain – The Chronic Pain Acceptance Questionnaire (CPAQ-8) was used to rate willingness to experience pain symptoms and activities engagement [39,40]. Higher scores indicate more willingness and engagement.

Quality of life – The EuroQol 5D (EQ-5D) [41,42] rates health status on five dimensions and overall health status from 0 to 100. The EQ-5D is the most widely used measure in clinical trials assessing general quality of life of OA patients [43], and was recommended by the U.S. Agency for Healthcare Research and Quality for assessing health state preference values [44]. Additionally, we collected data from the 24-item Western Ontario and McMaster Universities Arthritis Index (WOMAC) [45], which rates arthritis pain, stiffness, and physical functioning in everyday activities. It is the most widely used condition-specific quality of life measure for arthritis cost-effectiveness studies

Table 1
Overview and comparison of CBT-I and EOC treatment protocol session content.

Session	CBT-I	Education only control
1	Information on insomnia and sleep Behavioral/scheduling: Stimulus control	Introduction to OA pain and sleep Sleep hygiene strategies
2	Behavioral/scheduling: Bed restriction	Tools for protecting your joints Stages of sleep
3	Information on sleep and aging	Prescription medication treatments for pain and sleep
4	Constructive worry Relaxation/mindfulness	Exercise for pain and sleep
5	Sleep hygiene recommendations Adopting beliefs/attitudes that foster good sleep	Using nutrition to help reduce pain and improve sleep
6	Review of behavioral and cognitive strategies Maintaining treatment gains/relapse prevention	Over-the-counter medications and supplements

Table 2
Induction and assessment of intervention fidelity across delivery, reception and enactment phases.

	Fidelity induction	Fidelity assessment
Delivery	Comprehensive treatment manual Intervention delivery checklist Coach training	Supervision Audiotape review
Receipt	Multiple channels for conveying key intervention elements to participants Repetition and practice of key intervention content with participants	Participant pre- and post-treatment ratings of intervention delivery and efficacy
Enactment (CBT-I only)	Explicit behavioral goals set Problem-solving enactment barriers Environmental cues employed as reminders	Coach tracking of adherence to sleep scheduling recommendations

[46].

2.8. Interventions

2.8.1. Study coaches and training

In the OATS trial, all participants had contact with a CBT-I interventionist (study "sleep coach") six times over eight weeks. All contacts were by telephone. Coaches included an MS-level psychologist, a PhD nurse, and a PhD social worker. Coaches received one-day trainings for each intervention condition, led by experts in CBT-I (SMM) and osteoarthritis and pain education (MT). An overview of the content for CBT-I and EOC is shown in Table 1.

2.8.2. CBT for insomnia (CBT−I)

The telephone CBT-I protocol followed a standardized telephone-delivered CBT-I manual used in previous studies by the investigative team [18,19,47]. Participants were instructed to lie awake in bed at night for no more than 15 min before getting up and to then spend time doing quiet activities in a dimly lit room until they felt sleepy. Study coaches guided participants to follow a bed and rising time schedule intended to reduce the number and/or duration of nighttime awakenings, and to decrease overall time spent awake during the night. Nightly bed restriction was set initially to match the average sleep time reported by participants in their Week 1 sleep diary, with a minimum of 6.0 h in-bed duration. In-bed time was then extended over the treatment course by 15 min per week if sufficient sleep improvement occurred, defined as achieving 85% sleep efficiency (percent time asleep divided by time in bed) or greater in the previous week. Participants were encouraged to work with bed partners to develop sleep plans that partners would support. Cognitive techniques included instruction in constructive worry techniques and mindfulness practice to reduce cognitive and physiological arousal at night, and education about age-related sleep changes and realistic expectations regarding sleep. During each session call, coaches reviewed the previous week's sleep diary with participants to develop and revise individualized sleep scheduling plans.

2.8.3. Education-only control (EOC)

The telephone EOC protocol was modeled after a well-accepted group EOC condition developed for our previous clinical trial for older adults with OA pain and insomnia [23,48]. EOC is credible to participants because it provides general information about insomnia and OA pain as well as symptom management strategies. Information from the NIAMS "Osteoarthritis" handout on health booklet [49] and additional sleep and OA handouts developed for this study were reviewed along with the daily sleep logs. EOC was designed to control for nonspecific treatment effects (e.g., social support and education). It did not contain hypothesized CBT-I active ingredients (bed restriction, stimulus control, cognitive techniques) or behavioral change homework assignments.

2.8.4. Intervention fidelity

Based on Lichstein's treatment implementation model [50], three intervention phases were differentiated: *delivery* by the provider; *receipt* by the participant; and *enactment* by the participant. Within each intervention phase, attention was paid to both *induction* and *assessment* of intervention fidelity. Table 2 summarizes steps taken to induce and assess intervention fidelity.

All three coaches delivered both interventions; all telephone sessions were recorded. Training included fidelity review by one of the PIs (SMM) of all six recordings for three pilot cases (two CBT−I, one EOC) for each coach. Thereafter, two sessions for each participant were reviewed to maintain treatment fidelity and to ensure there was no contamination between the delivery of treatment conditions. Although participants were aware of the content of the intervention they received, they were not told whether they were receiving an active or a control intervention, nor were they told anything about the content of the alternative intervention. Coaches completed weekly content checklists to ensure adherence to key session components. Feedback on reviewed audio-recordings was provided on a weekly basis.

2.8.5. Health care costs

Intervention costs – We measured the time required for coaches to conduct the CBT-I intervention including length of the telephone sessions and pre- and post-call duties (e.g. scheduling future calls, note-

taking, and mailings). We will calculate coaching costs by assigning hourly compensation estimates to the coaches based on U.S. Bureau of Labor Statistics data [51].

Health Care Use and Costs – Information on medications (opioid, sedative, and antidepressant use), health care visits (ambulatory and surgical joint replacements), and costs of study participants will be collected from KPW electronic health care (EHR) data. Intervention group differences in rates of health care visits for pain, sleep and other non-specific symptoms, and rates of filling prescriptions for pain and sleep medications will be compared, as well as differences in overall costs of ambulatory health care. We will separately examine group differences in rates of joint replacement surgery. We will assign costs to each unit of healthcare utilization by applying a Medicare fee-for-service fee schedule using the validated Standardized Relative Resource Cost Algorithm [51].

2.9. Data analyses

2.9.1. Planned RCT data analysis methods

The difference in the primary outcome, insomnia severity as measured by the ISI, between the CBT-I and EOC groups at the post-treatment and 12-month follow-ups will be estimated in a single model using generalized estimating equations (GEE) with working independence to account for correlation within individuals. We will fit a linear model (ANCOVA) where the dependent variable is the change in ISI at each follow up time and the primary independent variables are baseline ISI, an indicator of treatment group, an indicator of follow up time (post-treatment or 12 months), and an interaction between treatment group and follow up time. Additionally, we will adjust for baseline age, pain, depression, cognitive status, use of opioids, use of hypnotics, and any other baseline variables that are imbalanced between the treatment groups or predictive of missingness in the ISI at the post-treatment and/or 12-month follow ups. A similar approach will be used for all continuous secondary outcomes and clinical improvement/processes of change variables. In addition to estimating the difference in the change in ISI post-treatment and at 12-months between the treatment groups, we will also estimate the proportion of individuals that experience a 30% reduction in ISI insomnia severity at both time points, as well as the relative proportion comparing the treatment and control groups. Adjusted estimates will be obtained using a modified Poisson regression within the GEE framework [52].

The proposed semiparametric modeling approach assumes that data are missing completely at random (MCAR) [53]. We will carefully evaluate the amount of missing data both overall and by treatment group, the sources of missing data (e.g., death and study dropout), and the relationship between missingness and measured covariates. If we find evidence that missingness is related to measured covariates (i.e., that data are missing at random [MAR] rather than MCAR), we may turn to weighted or likelihood-based estimation approaches that are valid for data under MAR, such as weighted GEE [54] or random-effects models [55]. While the MAR assumption underlying random effects models is less stringent than the MCAR assumption underlying GEEs, additional assumptions are required. We will carefully evaluate the assumptions required by each analytic method and will select an appropriate modeling framework accordingly. Because analytic approaches to missing data are evolving, we will review the most recent literature before analysis and will consider approaches including multiple-imputation [56,57], weighting [58], principal stratification [59] and methods for non-ignorable missingness [60].

Exploratory moderator analyses will assess whether CBT-I effects on insomnia differ by baseline insomnia severity, pain severity, and depression symptom severity. If there are intervention effects in important secondary outcomes (pain severity, depression, fatigue), exploratory mediation analyses will assess whether observed effects are explained by intervention-control differences in improvements in insomnia severity, employing statistical methods for evaluating mediation effects [61,62]. Our data analyses will also include examination of outcome differences in participants residing in U.S. Health Resources and Services Administration (HRSA) professional shortage areas.

For our economic analyses, we will first evaluate whether either arm is economically dominant (i.e. providing better outcomes at lower costs or improving either outcomes or costs while having no effect on the other outcome). If neither arm is dominant, we will estimate the incremental cost per quality adjusted life years (QALYs) gained from the healthcare sector perspective over the study follow-up period (i.e. 1 year time horizon). We will account for sampling uncertainty by using nonparametric bootstrapping techniques.

Our cost estimates will capture both patient healthcare utilization costs and intervention costs as previously described. We will analyze costs and outcomes for two months to fourteen months after enrollment. We will censor the first two months after randomization to align with changes in healthcare use and outcomes that can be reasonably attributable to CBT−I. Receipt of the full six sessions of treatment is expected to take approximately 60 days. The post-treatment assessment of change in quality of life will be performed at the time of treatment completion. We do not expect changes to healthcare utilization attributable to CBT-I to manifest within the first two months. However, we will measure the costs of delivering the intervention (e.g. interventionist time) during to first 60 days and attribute these costs to the intervention group.

2.9.2. Evaluation of statistical power

We used PASS software (http://www.ncss.com/software/pass/) to estimate the least detectable difference for a repeated measures design with two follow-up observations per participant, assuming autocorrelation of 0.5 and a compound symmetry covariance structure. Estimates of means and standard deviations for primary and secondary outcomes were from control group data for participants with ISI ≥ 11 and Pain Severity ≥5 at baseline from the completed Lifestyles trial [22]. Estimates of the number of participants who will have post-treatment and 12-month outcome data available (N = 128 per arm) is also based on the Lifestyles trial. The estimate of sample size available for analyses of 12-month healthcare costs is based on the percent of Lifestyles participants with ISI ≥ 11 and Pain Severity ≥5 at baseline who remained enrolled at GH over a two-year follow-up period (93.3%), informing measurement of healthcare costs in the current study using KPW EHR data. As shown in Table 3, the trial is designed to detect a difference in ISI insomnia severity of 1.5, representing an effect

Table 3
Detectable difference, effect size and power estimates for the proposed N for pair-wise comparisons.

	Control mean	S.D.	Detectable difference: intervention vs. control	Effect size	Power, two-sided test with alpha = 0.05
Primary outcome:					
Insomnia Severity Index	11.9	4.8	1.46	0.30	80% (N = 128 per arm)
Secondary outcomes					
BPI pain severity	5.4	1.6	0.49	0.31	80% (N = 128 per arm)
PHQ-8 Depression	11.7	6.8	2.07	0.30	80% (N = 128 per arm)
Fatigue	13.8	6.0	1.83	0.31	80% (N = 128 per arm)
12-mo ambulatory costs	$23,832	$16,148	$4932	0.31	80% (N = 128 per arm)

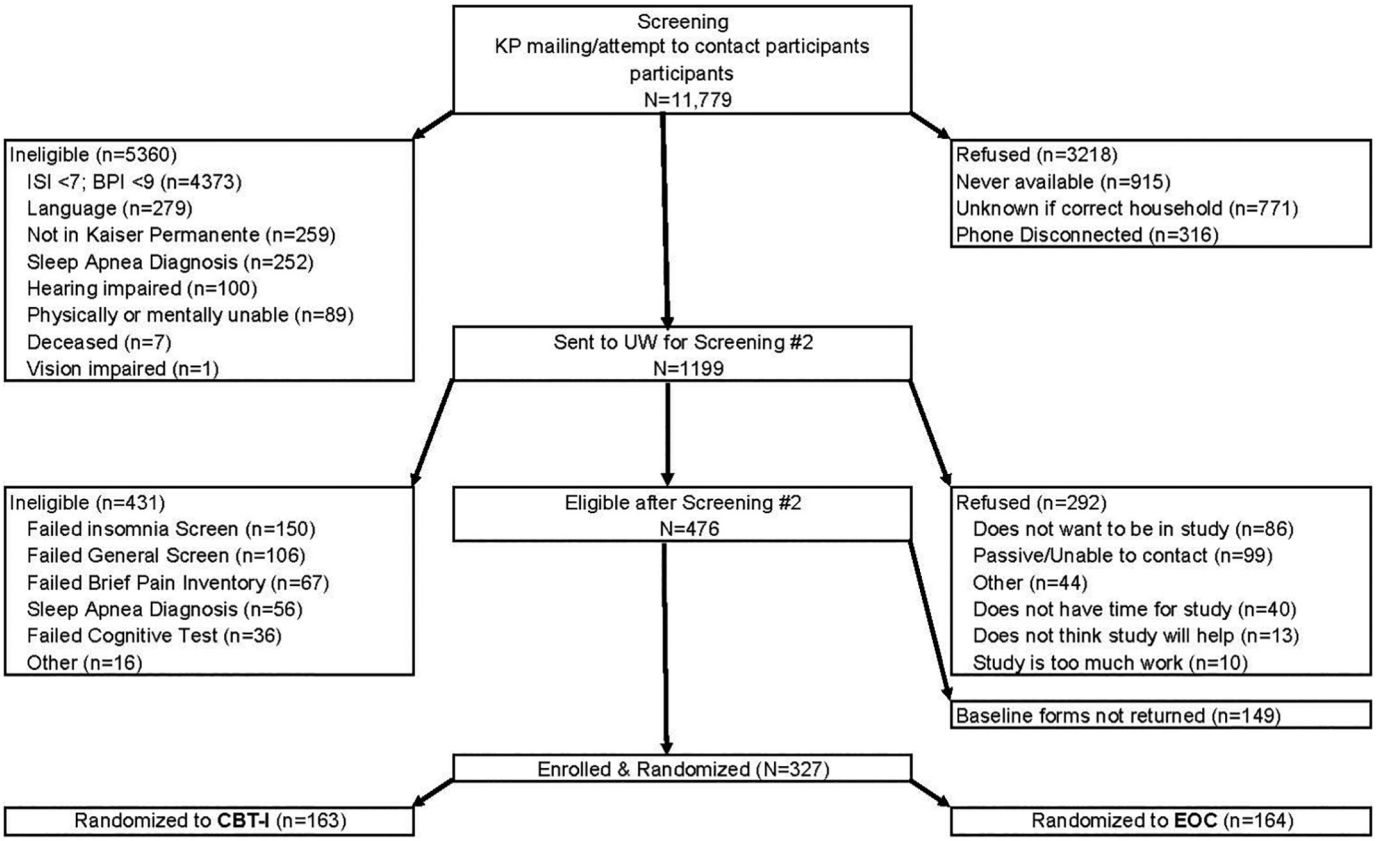

Fig. 2. Consort flow diagram for enrollment of potentially eligible participants.

size of 0.31. We also note that a clinically important group difference is generally much smaller than a clinically important difference for an individual patient. Outcome analyses will report both mean differences and responder analyses [63].

This trial is also powered to detect similar effect sizes for patient-reported secondary outcomes and a 21% reduction in healthcare costs (effect size 0.31). Table 3 shows detectable differences for PHQ-8 and BPI Pain Severity, but similar effect sizes will be detectable for other outcomes (e.g., fatigue).

3. Enrollment results

3.1. Screening survey response

KPWRHI survey research staff contacted 11,779 potentially eligible KPW enrollees, among whom 5360 were ineligible (Fig. 2). The most common reason for ineligibility was not meeting study severity criteria for the ISI and/or BPI (N = 4373). Contact information for 1199 potentially eligible participants was sent to UW for second screening. Among those completing the second screening, 476 (39.7%) met study severity criteria with an ISI score ≥ 11 and BPI ≥ 9 plus other eligibility requirements and were invited to participate in the study.

Baseline assessment was initiated for 476 persons, of whom 327 were enrolled in the trial when they returned all assessment and consent materials, and scheduled an initial telephone intervention session with an OATS sleep coach. The efficient telephone-based two-stage screening, enrollment, intervention and follow-up processes permitted randomization of 21% more persons than originally planned (327 enrolled in 2 years versus 270 in 3 years planned) (Fig. 3).

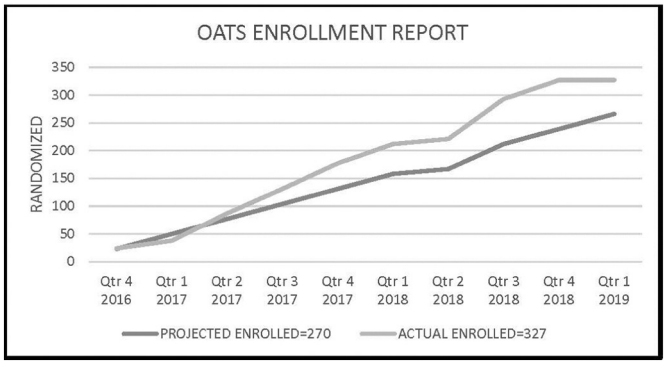

Fig. 3. Pace of enrollment (planned versus actual) into the OsteoArthritis and Therapy for Sleep (OATS) clinical trial.

4. Discussion

Although CBT-I is well established as an efficacious treatment for insomnia, including in populations with co-morbid pain [8,64,65], in-person CBT-I is not widely deployable in healthcare systems because of delivery costs, lack of personnel with requisite skills particularly in rural and disadvantaged areas, patient burden including delivery site access, and barriers to referral by primary care physicians. Telephone delivery has the advantage of giving patients across a wide geographic area access to brief efficacious CBT-I from home, increasing generalizability, access to minority and underserved populations, and outreach to rural communities and persons with limited or no access to local clinics. In contrast to internet-delivered or self-help readings, telephone CBT-I also offers personal and interactive professional guidance and support important for adherence and maximizing treatment effect [66].

4.1. Strengths

The OATS trial includes a number of scientifically significant and

innovative elements. First, through use of a telephone-delivered assessment and intervention protocol, we were able to provide outreach to participants from medically underserved populations across the state of Washington.

Second, we used a two-stage screening procedure over a three-week interval to identify patients with persistent and severe insomnia and OA pain. Our prior data suggested that CBT-I effects may be greatest and most durable in targeted patients with more severe symptoms [22]. In the current trial, we recruited individuals with moderate to severe insomnia and pain symptoms who did not improve after an initial screening (to ensure that symptoms were persistent), increasing the trial's potential for large and sustained treatment effects.

Third, the OATS trial is the largest trial of telephone-delivered CBT-I to date. Large-scale delivery models for CBT-I are needed, particularly for populations lacking access to specialty sleep clinic services, such as older adults in rural and other underserved areas. Telephone CBT-I potentially offers OA patients an effective, convenient, and relatively low-cost therapy for insomnia which can profoundly enhance quality of life.

Lastly, although other studies have examined the cost-effectiveness of in-person and on-line CBT-I interventions [67,68], the OATS trial is the first to assess costs and cost-effectiveness of telephone-delivered CBT-I in a large health care system. The OATS telephone-delivered intervention was designed to be offered in sessions that were 20–30 min in length, which is considerably shorter than standard in-person sessions in a sleep clinic. If this trial is successful and cost-effectiveness is established, telephone CBT-I has similar potential for national dissemination to reduce the substantial personal and economic burdens of OA-related insomnia and related symptoms on patients and society.

4.2. Limitations

Study limitations are acknowledged. The OATS trial includes enrollment from only a single health care organization in Washington State, and as such, study participants and findings may not be representative of those from other systems or geographic locations. However, our study design allowed us to include older adults across Washington State, including those in both rural and urban communities, and persons residing in health care professional shortage areas. We also included persons in the trial with a variety of common age-related medical morbidities, as well as persons taking medications for pain or sleep disturbance, further increasing generalizability of study findings. Participants did not undergo formal evaluation for primary sleep disorders, so we will be unable to examine whether treatment effects are consistent for participants with these conditions that may have been undiagnosed at the time of study entry. In studies of this type, it is not possible to mask interventionists to treatment assignment. However, all outcomes were collected by research staff blinded to treatment assignment. Lastly, sleep and pain outcomes are based on self-report, which for purposes of clinical practice and potential treatment scalability are the most relevant efficacy indicators. However, future studies incorporating objective monitoring, e.g., wrist actigraphy, might add value.

4.3. Future directions

If there are intervention effects in important secondary outcomes (e.g., pain severity, depression, or fatigue), the OATS trial will provide an opportunity to learn about mediators and moderators of treatment effects, adding to the limited published research available on who benefits from treatment, and through what mechanisms CBT-I works, which could help refine theoretical models of sleep and pain. If the trial is successful and cost-effectiveness is established, telephone CBT-I also has the potential for national dissemination to reduce the substantial personal and economic burdens of OA-related insomnia and related symptoms on patients and society.

5. Conclusion

In summary, the OATS trial design assessed the effectiveness of telephone-delivered CBT for insomnia relative to a telephone-delivered education only control group. The research design will allow us to evaluate intervention effects on the primary sleep outcome (insomnia severity), secondary measures as well as clinical improvement and processes of change variables, and health care utilization and costs. The telephone assessment and intervention delivery strategy allowed us to provide outreach to older adults with chronic and severe insomnia and OA pain symptoms across Washington State, including a mixture of rural, urban, and health care professional shortage areas that do not have ready access to insomnia treatment services.

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