Randomized Controlled Study of the Effectiveness of Stepped-Care Sleep Therapy In General Practice

NCT03532282

September 01, 2020

1. PURPOSE OF THE STUDY

a. Brief Summary

This project aims to fill in the science-to-service gap between proven efficacy of cognitive behavioral therapy for insomnia (CBTi) and future large scale implementation. We have developed and propose to test a primary-care-friendly stepped-care CBTi model (STEPPED CARE) that offers an easy to use Decision Checklist for matching delivery of CBTi to individual patient characteristics so that patients will begin treatment with the appropriate delivery mode (online or therapist-lead) and will be allowed to transition from online to therapist-lead delivery if they do not sufficiently benefit form the online only treatment.

b. Objectives

The investigators hope to learn the relative merit of the STEPPED CARE approach and an ONLINE ONLY approach with respect to reduction of insomnia severity and use of hypnotic medication, as well as future implementation potential. Results will yield a simple and effective way for primary care providers to prescribe CBTi to middle aged and older adults.

c. Rationale for Research in Humans

The purpose of this study is to determine efficacy and effectiveness of a non-pharmacological interventions for humans with insomnia.

2. STUDY PROCEDURES

a. Procedures

Screening participants will begin participation with a phone screen (attached) or an online self-administered screening checklist. Those who are not excluded will have an informed consent visit (in person or via Zoom); if they agree, they will sign a consent form (either on paper or electronically via RedCap). They will then undergo screening, using

structured clinical interviews for sleep disorders and for mental disorder (both are attached), and questionnaires (attached). Eligible participants will be randomized.

Those randomized to ONLINE ONLY will receive a code to a commercially available online CBTi called Sleepio and will have access to the program for 12 months.

Those assigned to STEPPED CARE will in Step 1 (8 weeks) receive CBTi either as a self-help intervention, using the Sleepio program, or with a therapist. This decision will be based on a DECISION CHECKLIST that considers patients' clinical presentation based on data they provide. During the second step, those assigned to STEPPED CARE, who in step 1 received Sleepio intervention but had insufficient progress after 8 weeks, will be switched to a therapist-led treatment. Regardless of the specific path for all those assigned to STEPPED CARE the duration of treatment will be 12 months.

Randomly selected participants (25% of the sample) will additionally undergo interviews at baseline and at the end of study and queries about their experience with insomnia ans its treatment. (The interview script be uploaded once finalized and before participant enrollment.)

Participants will undergo periodic assessments during this 12 months (at baseline, and months 2, 4, 6, 9, & 12). These assessments will include study questionnaires and the use of an Actiwatch™ for two weeks.

b. Procedure Risks

The research protocol involves minimal risk. It offers effective and effective low risk intervention to all participants

c. Use of Deception in the Study

No deception is involved.

d. Use of Audio and Video Recordings

To enhance accessibility, patients receiving therapist-lead CBTi will be able to choose to receive therapy session remotely via a secure videoconferencing, rather than in person.

e. Alternative Procedures or Courses of Treatment

Alternative to online and in-person CBTi is the use of hypnotic medications. However, this alternative is not superior to study interventions. In fact, the American Geriatric Society states “Don’t use benzodiazepines or other sedative–hypnotics in older adults as first choice for insomnia, agitation, or delirium “. That said, we note that no standard care will be withheld at any time from participants once enrolled, regardless of treatment assignment. That is, study interventions will be added to usual care and patients will be free to seek care in the community.

f. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Patients are free to continue any therapy for insomnia on their own after they completed all study procedures; these will not be provided by the study.

g. Study Endpoint(s)

There is no plan for interim analysis.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

The prevalence of insomnia and use of prescription sleep medications increase around age 50, approximately one in three older adults (50 and older) reporting persistent difficulty maintaining sleep and one in five reporting difficulties initiating sleep. This is also a time of increased use of sleep medications. According to a 2013 report from the National Center for Health Statistics the prevalence of use of sleep medication increases three fold starting in middle age. In addition to multiple negative consequences of insomnia in the general population, among older individuals the consequences of insomnia include exacerbation of age related cognitive decline (such as slower reaction time and memory impairment), visual impairment, and greater risk for imbalance and falls. The negative impacts of hypnotic use are also greater among older than younger adults. Although the safety of sedative hypnotic medications has improved over time, significant concerns about tolerance, dependence, daytime sedation, and risk for imbalance, falls, and motor vehicle crashes persist and remain a concern for primary care physicians, particularly when treating older adults. As a result, there is effort to reduce prescribing of sedative hypnotics, particularly to older adults. The American Geriatric Society Beer Criteria for potentially inappropriate medication use in older adults recommends avoiding use of benzodiazepines for treatment of insomnia and use of non-benzodiazepine hypnotics for more than 90 days (chronic use). It is therefore particularly important to reduce the use of hypnotic medications among older adults and to provide effective alternative treatments.

CBTi is an effective skill-based psychotherapy for insomnia. The American College of Physicians (ACP) issued new practice guidelines stating that “Cognitive behavior therapy should be the initial treatment option in persons with chronic insomnia.” CBTi improves sleep among middle aged and older adults without comorbidities, among patients with psychiatric and medical comorbidities, and among patients with hypnotic dependence. Importantly, CBTi has more durable benefits than hypnotic medications among midlife and older adults. CBTi can reduce the use of sleep medication for two reasons: (a) it can be offered as an alternative to hypnotics as an initial treatment option; and (b) it can facilitate reduction or discontinuation of sleep medications for those already taking them. Reduction/discontinuation of hypnotic use during CBTi can be indirect (i.e., some patients spontaneously reduce their use as they acquire new skills) or direct (i.e., therapist assisted), particularly when the CBTi protocol includes a specific module to address medication taper/discontinuation.

There is a major gap between the current state of the science and actual clinical practice: Limited access to CBTi is a major barrier to its wide-scale use as a first line treatment insomnia and ergo to the implementation of the ACP guidelines. Current models of therapist-led delivery are a major limiting factor in treatment access, largely due to the low number of trained providers relative to those needing treatment (largely due to the low number of trained providers relative to those needing treatment). Pilot studies have examined alternatives to traditional therapist-led delivery methods, such as abbreviated CBTi and delivery using telehealth among older adults; it is unlikely that, even if the results from these pilot tests are proven effective in large-scale trials, they alone can meet the demand for insomnia treatment in primary care. Another approach to increasing access to CBTi is to thoughtfully utilize consumer directed CBTi products, such as online programs. Such products offer patients a convenient way to receive treatment that addresses several barriers to therapist led-CBTi, including geographic, mobility, scheduling constraints, reduced waiting time for therapy, reduced stigma and embarrassment in seeking help, flexibility in accessing self-paced treatment, and efficient use of resource within the healthcare system. However, online CBTi programs have limitations. They are less effective than in-person treatment, with effect size for reduction in insomnia severity being half of the effect size following in-person therapy (Cohen d = 1.2 vs 2.3). In addition, online CBTi programs have high dropout rates (low engagement) that may contribute to lower efficacy. Current online CBTi programs are not the best choice when the goal is to reduce frequent use of hypnotic medications because they do not include modules to support the often difficult process of discontinuing these medications. (Although, through improving sleep, online CBTi can lead to hypnotic discontinuation among some users, effect sizes are smaller than therapist-led CBTi.) Online CBTi programs also do not include modules to address circadian rhythm factors, such as those present among individuals with unusual sleep schedules. Individuals who, based on past research on CBTi are at increased risk for dropping out from therapist-led CBTi are likely at even greater risk for dropping out from or online CBTi programs, since they lack flexibility in tailoring the intervention to support adherence.

STEPPED-CARE CBTi has strong potential for overcoming the shortcomings of an online only approach, while maintaining the scalability advantages offered by an online CBTi.

b. Findings from Past Animal Experiments

Not applicable.

4. NVESTIGATIONAL DEVICES

Investigational Device 1	
Name:	Sleepio
Description:	Sleepio is an online consumer program. There is no device involved. However, participants can get a free app to have access to some aspects of the program on their personal device if they so choose.

5. PARTICIPANT POPULATION

a. Planned Enrollment

This is a single site study. We hope to randomize 240 middle aged and older adult patients with insomnia disorder

b. Age, Gender, and Ethnic Background

Age: 50 and older
Gender: all
ethnicity: all

c. Vulnerable Populations

Recruitment will NOT target potentially vulnerable populations; but they will not be excluded.

d. Stanford Populations

Recruitment will NOT target laboratory personnel, employees, and/or students; but they will not be excluded

e. Healthy Volunteers

Healthy volunteers will not be included.

f. Recruitment Details

Patients will be recruited from primary care clinics that are part of the Stanford Health care system. Patients will be identified as potentially eligible through a search of electronic health records. The search will be based on age, insomnia diagnosis or use of sedative hypnotics, and the absence of a diagnosis of dementia or the need for an interpreter; all of which can easily be extracted from the electronic medical records. Those identified will be invited to participate, using a Myhealth message (scripts for SHC clinics and for SHA are attached). The SHC MyHealth message will be sent on behalf of individual primary care clinic providers/directors and the protocol director who have given their explicit permission for us to do so.

The MyHealth message for SHA will be sent on behalf of Dr. Bohan, Chief Medical Officer, University Healthcare Alliance, and the Protocol director, who has given us permission to do so.

Patients without an active MyHealth account will be sent a letter via mail. This letter will have the identical content as the attached MyHealth scripts on a departmental letter head.

The attached script includes a link to a contact form which is also attached, and a study website

Those who respond to the invitation will be phone screened.

In addition, patients may contact us by responding to IRB approved advertisements, through brochures, flyers, and electronic media. Patients who contact the study team directly will be considered for inclusion, even if they do not receive care at the Stanford health care system.

g. Eligibility Criteria

i. Inclusion Criteria

- Age>=50
- Meets criteria for insomnia disorder
- Residing in California
- Has primary care provider in California

ii. Exclusion Criteria

- Cannot be consented in English without an interpreter
- Does not have a reliable telephone service
- Lack physical or mental capacity to participate in treatment. Examples include, but are not limited to, thought disorder and Cognitive impairment (mini mental status exam score < 25).
- Presence of alcohol use disorder or drug use disorder, excluding sedative hypnotic or anxiolytic (taken for sleep), with current withdrawal symptoms or if severe (per DSM-5);
- Use of substances that cause sleep disturbances (e.g., stimulants, prednisone)
- Family member that resides in same household as another study participant
- Inability to use and cannot get help from a trusted other for using the internet daily.
- The study physician determines their participation is not medically advised for any reason.
- Does not currently receive CBTi

h. Screening Procedures

Participants will begin screen with a telephone screen or a self-administered online screening checklist (both uploaded). Those not excluded will undergo two structured clinical interviews conducted by trained research personnel: 1) the Duke Structured Interview for Sleep Disorders (DSISD) for ascertaining insomnia and documenting other sleep disorder diagnoses; 2) the widely used Structured Clinical Interview for DSM Disorders (SCID), MINI version to assess severe unstable comorbid psychiatric conditions that might better explain the insomnia symptoms; 3) the Folstein Mini-Mental Status Exam (MMSE). These questionnaires and interviews are attached. 4) For consented participants, who the study physician identified as medically complex (e.g., taking more than 10 prescription medications), we will request medical clearance from their PCP; (for those receiving care outside we will use the attached letter.)

i. Participation in Multiple Protocols

Participants will be asked if they are currently participating in another study. When a potential participant reports participating in another study where there is a potential for

the two studies to compromise patient safety or the integrity of data collected in either of the two studies, we will contact the protocol director of the other study to discuss how to best resolve the situation. (An example of such a situation is when a patient participates in a study that requires them to receive another treatment for insomnia.)

j. Planned Duration of the Study

We expect the study will last 5 years, with a 4 year active recruitment period. A participant will be in the study for approximately 14 months after being randomized.

6. RISKS

Treatment-related risks:
1) Transient increase in daytime sleepiness/tiredness might be experienced as a result of an initial restriction of time in bed during the implementation of stimulus control and sleep restriction protocols, which are part of CBTi. Some patients experience increase in anxiety in response to the recommendation to decrease time in bed. Initial increase in daytime sleepiness has been documented when time in bed is severely restricted but there are no known estimates of the frequency of daytime sleepiness as a side effect of the more conservative time in bed restriction protocol we will be using in this study. There are no available estimates regarding the frequency of increased anxiety in response to the recommendation to restrict time in bed.
2) Gradual taper of hypnotic medications might involve mild transient worsening of sleep, anxiety about sleep, and/or daytime sleepiness.

Risks associated with other procedures involved in the study as part of the data collection and measurement involve minimal risk. These include (a) the potential for loss of privacy and confidentiality; (b) legal limits to the confidentiality of information obtained if risk of harm to self or others, including children, is disclosed (in our experience, this has been very rare); (c) experiencing distress from being asked to focus on sensitive issues such as depression (In our years of conducting research with hundreds of patient we found this to be rare); (d) some participants may consider the study measures time-consuming, inconvenient, or otherwise disruptive of their usual routines; and (e) some patients might not like wearing a wrist band or experience minor skin irritation when wearing the actigraph on their wrist.

7. BENEFITS

All participants will receive cognitive behavioral therapy for insomnia free of charge.

The STEPPED CARE option we propose to test has the potential to improve sleep, reduce use of hypnotic medications, promote safety, and offer convenient access to treatment for midlife and older adults, while using resources efficiently.

8. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.