Title: Sleep Without Insomnia or The Use of Chronic Hypnotics (SWITCH)

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NCT number: NCT03687086

Document date: June 19, 2020

SWITCH STUDY PROTOCOL (06.19.2020)

APPENDIX: "Video/Telehealth Visit Addedum to SWITCH Study Protocol" is at end of document

Design

This is a 5-year multi-site randomized controlled trial that will recruit participants from UCLA Health System and VA Greater Los Angeles.

Setting: To ensure that we meet enrollment targets, the study will include both VAGLA and UCLA Health System. At least 1,200 unique patients at VAGLA have the targeted hypnotics listed in their medical records for at least 3 months within the past 6 months, and 9,100 unique patients at UCLA Health System who receive primary or medicine subspecialty care in the northwest Los Angeles UCLA Health System outpatient clinics have the targeted medications listed within 12 months.

Inclusion/Exclusion criteria:

Inclusion criteria:

- Age > 55 years
- Use of lorazepam, alprazolam, temazepam, clonazepam and/or zolpidem for current or prior insomnia symptoms 2 or more nights per week for at least 3 months
- Current or prior insomnia symptoms
- Available to attend weekly in-person or video sessions over 9 weeks

Exclusion criteria:

High risk for complications in outpatient hypnotic discontinuation program:

- Seizure disorder
- Supratherapeutic or high baseline hypnotic dose (> diazepam-equivalent of 8 mg/night). Note that for individuals on > 1 of the targeted hypnotics, the total baseline hypnotic dose in diazepam-equivalents will be calculated and if > 8 mg/night, individual will be excluded.
- High baseline risk of complicated withdrawal; benzodiazepine intoxication or current or past symptoms of complicated benzodiazepine/alcohol withdrawal (e.g., seizure, delirium at baseline (prior to taper))
- Polydrug use (e.g., chronic high dose opioids)
- Unable to keep study medications in secure location
- Evidence of prescription fraud (e.g., multiple prescriptions for same drug filled at UCLA and non-UCLA pharmacies, diversion)

Discontinuation of hypnotic not appropriate:

- Study-targeted hypnotic used to treat another clinical condition (e.g., panic disorder)

Poor candidate for CBTI:

- Presence of bipolar disorder
- Cognitive impairment (e.g., Mini-Mental State Examination < 24)
- Sleep/wake difficulty is better explained by another sleep disorder such as restless legs syndrome, narcolepsy, insufficient sleep syndrome, or circadian rhythm sleep-wake disorders
- Untreated sleep-disordered breathing (apnea-hypopnea index >= 30)
- Moderate sleep apnea (apnea-hypopnea index between 15-29.99) and daytime sleepiness (Epworth Sleepiness Scale score >10)
- Medically/psychiatrically unstable (e.g., planned major surgery during the study period; psychosis, suicidal, active alcohol/substance abuse based on history and medical records)
- Unstable housing situation

Recruitment
Recruitment will include a three-step screening process.

Step 1 (identification of participants): We will identify participants aged > 55 years who have current prescriptions for lorazepam, temazepam, alprazolam, clonazepam, and/or zolpidem (see "Hypnotics types" section below) for > 3 months. The sources we will use to identify these patients include: medication lists from electronic health records, and recruitment flyers.

A recruitment flyer with a cover memo to UCLA Health System providers will be distributed to providers in primary care, mental health, and sleep medicine clinics. The memo describes the study and basic eligibility criteria and asks the provider to share the flyer with appropriate patients. The flyer contains the study telephone number, so interested patients can call for more information. Recruitment flyers also will be posted in approved areas of outpatient clinic waiting areas (as directed by clinic manager/administrator).

A recruitment letter and opt-out card will be mailed to patients identified from the electronic health record. Only authorized research staff will have access to the names of patients who will receive the mailing. Patients will be asked to return the opt-out card in a postage-paid envelope within 7 days of the letter mail date to indicate whether they wish to be called by our research staff. The letter will explain that research staff will call the patient if the opt-out card is not returned within the 7-day timeframe. The letter will also list the research office telephone number so patients can call to ask questions or indicate their willingness to participate.

Study physicians (e.g., Zeidler, Fung) will directly recruit potential participants in clinics that evaluate patients for sleep and geriatrics (e.g. sleep clinic, pulmonary clinic, geriatrics clinics). Potential participant's privacy will be maintained by discussing the study within the context of a confidential clinic visit and only having participant information shared with relevant study staff after participant agrees to initiate screen process. All data obtained from participant during the recruitment process will be stored in locked filing cabinets.

Step 2 (screening for current or prior insomnia and current hypnotic use
Telephone screening:
Study staff will telephone potential participants who were sent the recruitment letter but did not return the "opt out" card. Staff will leave 1 telephone message. Individuals who do not return our call will be considered as "not interested" in participating.

During this telephone call, the study will be explained and oral consent for screening will be obtained from individuals who express interest in the study (see Telephone Screening Script). Eligibility criteria will be assessed with a structured screening questionnaire (see Telephone Screening Questionnaire). The screening questionnaire will include items to assess the following: 1) current insomnia symptoms, 2) hypnotic use, 3) chronicity of use and number of days per week hypnotic is used, 3) major health events (e.g., surgery) within the past month (individuals with a recent major event will be re-contacted 3 months later), 4) housing situation (e.g. homelessness), 5) access to transportation to the medical center, 6) perceived physical, emotional or substance use being a barrier to participating in the study sessions. Patients who contact the study as receiving the recruitment flyer will also be administered the screening questionnaire. Following completion of the telephone screening questionnaire, eligible and interested individuals will be scheduled for an initial in-person meeting to obtain written informed consent. An email address or mobile number will be requested at the end of the screening visit, which

will be used for study-related appointment reminder emails/calls/texts, if the patient agrees to the reminder emails/calls/texts (preferred method will be documented).

Individuals will be given the choice of having their study visits at UCLA or at either the VA West Los Angeles campus or the VA Sepulveda campus. This option allows individuals to choose the location that is most convenient for them. Individuals who express interest in a VA site will be informed that this choice entails following the VA Research and Development and VA IRB protocol, including signing VA forms, storage of their research data on VA servers and offices, and management of their study medications by VA staff. Individuals who choose to be seen at UCLA will follow the procedures described below. Those who choose to be seen at the VA will be enrolled in the VA study, and will no longer be considered UCLA study participants. Participants seen at the VA will sign a VA consent form and a VA HIPAA Authorization. In addition, they will be asked to sign a UCLA HIPAA Authorization for Research so VA study staff can assess their UCLA medical records to document medications and diagnoses.

In-person screening
Patients recruited directly by study staff in clinic will have the option to complete the screening process in-person with a member of the study team. Patients deemed eligible for participation will be offered to complete the in-person consenting process immediately following the in-person screening (see *in-person consent visit* below for additional information).

In-person consent visit
At the consent visit, potential participants will be shown the wrist actigraph and WatchPat monitoring equipment to ensure that they become familiar and comfortable with this equipment. Capacity to give informed consent will be evaluated with a brief questionnaire (Evaluation to Sign a Consent Form for Research) that asks the participant to recount major procedures and risks of the study. Participants who are unable to provide informed consent will be excluded; proxy consent will not be pursued. Participants who are able to provide informed consent will be asked to sign the written informed consent form and HIPAA authorization and will be provided with copies. A licensed study physician or nurse practitioner will perform the consent procedure.

-Preparation for consent visit:

- Patients who request a copy of the consent and HIPAA authorization form prior to the consent visit will be sent copies of these documents via email, delivery (US Postal Service, FedEx, etc.), fax, or text, based upon patient preference. The address or number will be stored in the project database, REDCap.
- Prior to the consent visit, the study staff will review the UCLA electronic health record for study exclusion criteria and if the patient is ineligible, the patient will be contacted, and the in-person visit will be cancelled to avoid unnecessary in-person contact. We will not cancel consent visits for patients who indicate to our staff that the information obtained from the electronic health record is inaccurate.

<u>Step 3 (in-person baseline assessment to determine remaining eligibility criteria:</u> The purpose of the in-person visit will be to further explain the study, obtain written informed consent and begin the baseline assessment. After participants have provided written informed consent (in-person Visit 1), they will complete a baseline assessment that consists of 2 visits (each 45-60 minutes) to the study site.

- Questionnaires included in the baseline assessment:
  - Self-Administered Comorbidity Questionnaire, plus additional questions
  - Insomnia Severity Index (ISI)
  - Pittsburgh Sleep Quality Index (PSQI)
  - Dysfunctional Beliefs and Attitudes about Sleep – 16 item (DBAS-16)
  - Morningness Eveningness Questionnaire (MEQ)
  - Disturbing Dream/Nightmare Severity Index (DDNSI)
  - Restless Leg Syndrome questionnaire (RLS)
  - STOP-Bang questionnaire
  - Epworth Sleepiness Scale (ESS)
  - Brief Pain Inventory (BPI)
  - WHO Quality of Life -BREF (WHOQOL-BREF)
  - Mini-International Neuropsychiatric Interview (MINI) only for participants who have a history of bipolar disorder.
  - Primary Care Post Traumatic Stress Disorder (PC-PTSD)
  - Generalized Anxiety Disorder (GAD-7)
  - Patient Health Questionnaire-Depression Module (PHQ-9)
  - World Health Organization Alcohol, Smoking, and Substance Involvement Screening Test (WHO-ASSIST)
  - Trails A & B tests
  - Digit Symbol Substitution and Symbol Copy
  - Mini-Mental State Examination (MMSE)
  - One-leg standing balance
  - Benzodiazepine Dependence Questionnaire (BDEP)
  - Clinical Institute Withdrawal Assessment Scale – Benzodiazepines (CIWA-B)
  - Credibility/expectancy questionnaire (CEQ)
  - Demographic questions
  - Fall event question
  - International Classification of Sleep Disorders 3 diagnostic criteria for insomnia questions
  - Nighttime urinary symptoms questions

- Blood pressure, pulse and respiration will be measured
- A wrist actigraph will be given to participants to wear at home for 1 week
- A sleep diary and a medication log will be given to participants to complete while wearing the actigraph.
- Screening for sleep apnea – all participants will be administered the STOP-Bang questionnaire to screen for symptoms of sleep apnea. If a participant scores > 4 on the STOP-Bang and does not have documentation of a previous sleep study in the medical record, s/he will be sent home with a portable sleep apnea screening device (WatchPAT) to wear for one night and to return the next day. The WatchPAT is an FDA approved device and is used clinically for in-home screening for sleep apnea. Participants will be instructed how to attach the sensors and will wear the device for one night. The PI or one of the MD co-investigators will talk with the participant about the results of the test. The results will be shared with the participant's healthcare provider if requested by the participant.
- Hypnotic medication log - Using a structured hypnotic abstraction form (see Hypnotic Abstraction Form), we will review the UCLA electronic record to obtain data about hypnotic prescriptions. We will also query the California Controlled Substance Utilization Review and Evaluation System (CURES) database to obtain data about non-UCLA hypnotic prescriptions.

Eligibility determination for randomization
The final determination of eligibility will take place during a weekly meeting of the investigators. At least one physician (Fung or Alessi) and at least one sleep psychologist (e.g., Martin) will participate at these meetings. During this "pre-randomization review" meeting, individuals who no longer meet the hypnotic criteria at the baseline assessment will be excluded. Individuals adherent to sleep-disordered breathing therapy and restless legs syndrome (RLS) therapy or with insomnia symptoms incompletely explained by RLS will be considered for intervention, as would be done in clinical practice. Individuals with insomnia symptoms due to circadian rhythm sleep disorders or inadequate opportunity for sleep will be excluded.

Participants with an apnea-hypopnea index $\geq$ 30 (from WatchPAT test) will not be eligible for randomization. Participants with an apnea-hypopnea index between 15 and 30 (moderate sleep apnea) and with daytime sleepiness (Epworth Sleepiness Scale score > 10) will also not be eligible for randomization. Participants with an apnea-hypopnea index between 15 and 30 and no daytime sleepiness will be eligible for randomization. We will inform participants with an apnea-hypopnea index > 15 that they may have sleep apnea and, with their permission, will inform their primary care, or other appropriate, provider.

A review of the participant's medical record will be completed to assess for unstable medical or psychiatric conditions (e.g., new chemotherapy) that would make it difficult to maintain the participant's engagement in the study. These individuals would also not be appropriate for CBTI under usual care conditions. Individuals excluded for unstable conditions will be reassessed 3 months later for eligibility, which is the process that would occur in a clinical setting. We will include individuals with stable psychiatric or medical conditions such as chronic pain or depression. Finally, we will notify the participant's hypnotic prescriber at UCLA Health System (via encrypted email) about our intention to taper and discontinue the patient's hypnotic in case there are undocumented clinical indications other than insomnia (see Email to Prescribers). If the prescribing physician does not agree with tapering the medication, the individual will not be randomized. Participants determined to be ineligible for the study will be notified by mail (see Participant Ineligibility Letter)**.**

Randomization
Individuals who complete the baseline assessment and meet all inclusion/exclusion criteria will be randomly assigned to one of the two intervention groups: MTcap (N=28) or SGT+CBTI (N=28). Both interventions are described below. Randomization procedures will follow the CONSORT criteria for randomized trials. Stratified randomization will be used to ensure that both groups are balanced in baseline hypnotic drug type half-life (i.e., temazepam/zolpidem; alprazolam/lorazepam; clonazepam) and gender. The study statistician will generate the stratified randomization sequence. A set of envelopes containing the group assignment will be generated and stored in a secure file drawer accessible only authorized staff. Once final eligibility is determined, the data manager will open the next envelope in sequence within the appropriate stratum.

Interventions
Both interventions will involve 8 sessions provided by a trained cognitive behavioral therapy for insomnia (CBTI) interventionist. The intervention period is expected to last approximately 9 weeks (but may be extended as described below). Both interventions include a tapering protocol for benzodiazepine use, behavioral therapy for insomnia, plus weekly assessment for withdrawal symptoms (see table below).

Week	Session	Basic Components Groups A & B	Time
1	1	Education + sleeping medication taper + side-effect monitoring	60 minutes
2	2	Education + sleeping medication taper + side-effect monitoring	60 minutes
3	3	Education + sleeping medication taper + side-effect monitoring	60 minutes
4	4	Education + sleeping medication taper + side-effect monitoring	60 minutes
5	5	Education + sleeping medication taper + side-effect monitoring	60 minutes
6	6	Education + sleeping medication taper + side-effect monitoring	60 minutes
7		Side-effect monitoring only	20 minutes
8	7	Education + sleeping medication taper + side-effect monitoring	60 minutes
9 Beginning of week		Side-effect monitoring only	20 minutes
9 End of week	8	Education + sleeping medication taper + side-effect monitoring	60 minutes

During week 7 and at the beginning of week 9 of the intervention, participants will only receive the withdrawal symptom assessment. The actual content and structure of the behavioral therapy and tapering protocol will differ between the two groups, although the dose reduction schedule will be the same for the two groups (described below). Intervention sessions will take place in designated, private research rooms/offices at UCLA or at off-campus sites (VA West Los Angeles and Sepulveda campuses). All interventionist sessions (unless participant declined audio-recording during the informed consent process) will be audio-recorded and a random subset will be rated using a structured rating sheet to ensure fidelity to the treatment protocol. The interventionist will also maintain a session-by-session list of information covered and recommendations made. “Progress notes” will be maintained by the interventionist and reviewed during weekly “intervention meetings.” These processes will ensure fidelity over the course of the study and avoid the risk of contamination across study arms.

Measures collected during intervention:

A urine sample will be collected from participants at the first intervention session. The urine sample will be tested by a licensed, accredited clinical laboratory (e.g., UCLA clinical lab) for benzodiazepines and zolpidem to confirm the participant’s use/nonuse of these hypnotics.

The following measures will be collected weekly throughout the intervention for participants in both study groups.

Clinical Institute Withdrawal Assessment Scale - Benzodiazepines (CIWA-B): This 22-item instrument includes patient symptoms and clinical observations (e.g., tremor) to assess and monitor the type and severity of symptoms of benzodiazepine withdrawal.

Vital signs: These physical examination measurements will be taken weekly: blood pressure, pulse, and respiratory rate.

Insomnia Severity Index (ISI): The ISI is a 7-item instrument that measures perceived severity of insomnia symptoms (total score ranges from 0 to 28).

Epworth Sleepiness Scale (ESS): This 8-item questionnaire assesses general level of daytime sleepiness.

Daily sleep and habits diary: Participants will use the diary to record bedtime, wake time, total sleep time, time to fall asleep, time awake at night, number of awakenings, napping, exercise, caffeine/alcohol/tobacco use. Participants in the MTcap group only will also record their perceived hypnotic dose taken and their daytime function and sleep quality.

MTcap (Masked Taper plus cognitive behavioral therapy-augmented program):

a. **Hypnotic taper protocol:** Participants will receive encapsulated hypnotics in a blister taper pack prepared by a compounding pharmacy. Participants will be informed that gradual dose reduction will occur during the program, but they will be blinded to the actual dose they receive each day. The planned rate of reduction of hypnotic will be about 25% per week. The final taper pack will consist of 4 placebo capsules (nights 1-4) and 3 empty blisters (nights 5-7). This planned rate of taper would yield a taper length similar to those reported in other studies, where the average length of taper was 49 days (range 6.5 to 84 days).

b. **Cognitive behavioral therapy for insomnia-augmented program**: The 8 sessions will incorporate the key components of CBTI (sleep restriction, stimulus control, cognitive restructuring, targeted sleep hygiene) and CBT targeting hypnotic withdrawal. Using the masked doses as a CBT tool, we will add exercises and concepts designed to address and alter expectations for hypnotics. A daily sleep/perceived hypnotic dose diary will be used as a tool for challenging expectancies about hypnotics, refining treatment recommendations, and adjusting the weekly plan. At the last session, the interventionist will inform MTcap participants of the actual doses that they were taking over the 9-week intervention. Participants will be given the taper schedule that the SGT+CBTI group followed unless there was a plateau in the tapering, in which case participants will be shown a revised taper schedule. The interventionist will tell participants the dose that they are currently taking and will review the last week's sleep diary to compare what participants thought they were taking with the actual dose. A study physician will also be available if the participant has specific medical or pharmacological questions about the taper.

SGT+CBTI:

a. **Hypnotic taper protocol**: Participants will receive hypnotics in a traditional medication container prepared by a contracted compounding pharmacy. Participants will also receive a printed taper schedule (see attached Taper Schedule) that reduces the hypnotic using the same schedule as the MTcap group. Each participant will be given a pill cutter so they can cut pills in half or into quarters as directed. A printed taper schedule is routinely used in clinical practice to assist patients in reducing hypnotic use. An exception to this protocol will occur if the prescribed medication is temazepam. This medication only comes in capsule form, so it cannot be cut into halves or quarters. Consequently, the participant will receive two difference strengths of temazepam (e.g., 15mg and 7.5mg) in two separately labeled bottles. Rather than cutting the higher strength capsule in half,

participants will take the lower strength capsule. This is the taper method that is used clinically for temazepam.

b. **Cognitive behavioral therapy for insomnia**: Participants will receive standard CBTI (i.e., stimulus control, sleep restriction, targeting maladaptive beliefs about sleep, sleep hygiene, and relaxation techniques), and will not be provided with the extra exercises and tools that the MTcap group will receive. The sleep diary that participants will complete will be slightly different from the MTcap sleep diary.

Modified taper plans

We have identified specific situations when the taper plan may need to be modified:
a) Withdrawal symptoms/extended taper required:
The taper may be extended up to a maximum of 16 weeks if the participant has withdrawal symptoms or cannot tolerate the scheduled taper, based upon changes in several of the CIWA-B items and vital signs, along with the patient's, interventionist's, and study physicians' judgments. In the MTcap group, an extended taper may be achieved by giving a duplicate 7-day blister pack (e.g., plateauing the doses until the participant is ready to move to the next blister pack). In the SGT+CBTI group, participants will be instructed to repeat a particular week in the printed taper schedule. Participants will continue to be monitored with weekly CIWA-B, vital signs, and the interventionist will review and reinforce key content of the intervention.

If the participant is found to have mild symptoms of withdrawal based on select items from the CIWA-B or on mild changes in vital signs, the study physician (e.g., Drs. Fung or Alessi) will be informed and the physician and the participant may decide to plateau the taper until the participant is ready to continue with the dose taper. If participants are found to have moderate, severe, or very severe scores on select items in the CIWA-B, moderate or severe vital sign changes, or have worsening severe insomnia, the study physician will be informed and she will discuss the patient's symptoms with a staff psychiatrist to determine whether changes to the taper schedule are needed (including increasing or plateauing the dose) and whether the patient needs additional clinical evaluation. If the patient needs immediate clinical evaluation, the participant will be escorted to the outpatient clinic or for life-threatening emergencies at our facility, we will call 911.

b) Hypnotic dosed as "prn" at baseline: Taper schedules for participants who used their hypnotic "as needed" at baseline will be adjusted so that the starting week's total weekly hypnotic dose does not exceed the participants' total weekly baseline hypnotic dose.
For the MTcap group, the capsules on the predetermined drug-free days will be filled with an inert filler substance. The participants will still be instructed to take the capsule on a scheduled based nightly, not as needed. The use of inert capsules will ensure that the participant is not exposed to the drug more frequently than the baseline exposure. An increase in adherence to the taper protocol is one rationale for using capsules filled with inert filler substance rather than instructing participants not to take any capsule at all (i.e., similar to oral contraceptive inert pills that are provided in the monthly oral contraceptive pill pack). Another rationale for using insert capsules is related to our study's objective, which aims to develop an intervention for reducing placebo effects, such as the effects related to the conditioned response of taking the drug and attributing sleep and daytime function—which are known to vary from day to day—to the act of taking the pill.
For the SGT+CBTI (supervised gradual taper + CBTI) group, the paper taper schedule will indicate which days of the week the participant should and should not take the hypnotic. For example, Mondays, Wednesdays, Fridays, and Saturdays may be deemed drug days, while Tuesdays,

Thursdays, and Sundays may be deemed drug-free days. The gradual tapering of drug doses on the drug days will occur over the two-month period. The drug-free days will be clearly marked on the taper schedule. A progressive increase in the number of drug-free days will occur during the taper.

c) More than 1 hypnotic at baseline: Participants who use >1 of the target hypnotics will be tapered off the targeted hypnotics simultaneously using two different blister packs.

Protocols for preparation of hypnotics

MTcap group: The blister packs containing the hypnotic will be prepared by a contracted compounding pharmacy experienced in preparing medications for research purposes. Dr. Fung or Dr. Alessi will use California tamper resistant prescription forms for controlled substances to write a prescription for of the appropriate hypnotic that will cover the entire intervention period. The prescriptions will be sent via encrypted email or fax to the pharmacy. The compounding pharmacy will prepare the blister packs for the intervention period (e.g., 8 weeks, but could be longer if the participant needs a prolonged taper) and send them via overnight mail or courier to the UCLA Research Pharmacy. If necessary, the medications will be picked up by research staff and transported to the Research Pharmacy. The research pharmacist will label the blister packs per UCLA protocols. The medication information will be entered into CareConnect (not as an active order) as "[medication name] study material Week [enter #] ".

SGT+CBTI group: Dr. Fung or Dr. Alessi will write prescriptions for the appropriate hypnotic that will cover the entire intervention period. The prescriptions will be sent via encrypted email or fax to the pharmacy. The compounding pharmacy will prepare a 30-day supply of the appropriate medication for the participant. The medication will be dispensed in a regular prescription bottle and labeled by the pharmacy. At the end of the month, a second 30-day supply of medication will be prepared and dispensed. The medication will be sent via overnight mail or courier to the UCLA Research Pharmacy. If necessary, the medications will be picked up by research staff and transported to the Research Pharmacy. The medication information will be entered into CareConnect (not as an active order) as "[medication name] study material Week [enter#]".

Protocols for distribution of hypnotics

A chain of custody will be established and documented. Only authorized members of the research team will be permitted to have contact with the medications. A delegation log will be maintained. For both groups, a member of the research team will pick-up the medication bottle or blister packs from the UCLA Research Pharmacy upon arrival of the participant to the UCLA site and give it to the participant at the appropriate intervention session (for the SGT+CBTI group, at the initial session; for the MTcap group, at each intervention session). In the rare case that a participant reschedules the appointment after the medication has been dispensed, the medication will be temporarily stored in a safe. In the rare case that a patient withdraws from the study after the medications have been dispensed from the research pharmacy, the medication will be disposed of following US Drug Enforcement Agency Public Controlled Substance Safe Disposal protocol (e.g., in a DEA authorized collection bin, with two witnesses signing the chain of custody log).

For participants seen at off-campus sites, a research team member will transport the medication via personal car from the UCLA Research Pharmacy to the off-campus site. The medication will be placed in a locked bag and stored in the trunk during transport. The medication will be stored in a locked safe at the off-campus location until the participant receives it at the first session. If the participant does not come to the appointment, the medication will be returned to the safe.

Care coordination at end of intervention period

Participants in the MTcap group will be told the benzodiazepine/z-drug dose that they are taking when they complete the intervention (or if they withdraw before the 9-week intervention period). The primary care providers of participants in both groups will be informed of the final medication regimen, so patients can continue to be monitored for withdrawal, if necessary.

Follow-up assessments

We will encourage participants to complete assessments even if they elect not to complete the intervention. All follow-up assessments will be conducted by research staff who are blinded to group assignment.

Post-treatment assessment

The post-treatment assessment will begin on the same day that the participant completes session 8 of either intervention. At the end of session 8, a participant will be provided with an actigraph to wear at home for 1 week and a sleep and medication diary to complete. When the participant returns the actigraph and diary after 1 week, he/she will be administered selected questionnaires included in the baseline assessment. In addition, a urine sample will be collected to confirm participants' self-report of hypnotic discontinuation. The CURES database will also be queried to obtain data about prescriptions for controlled medications. Participants will also be given a six-month fall log to record any falls they experience during the period between the post-assessment and the six-month follow-up assessment.

Six-month follow-up

The six-month assessment will occur six-months after session 8 is completed (or was scheduled to be completed if a participant drops out of the intervention). This assessment will include 2 visits to the study site. The measures collected will be identical to the post-treatment assessment. At visit 1, the participant will receive an actigraph to wear at home for 1 week, a sleep and medication diary to complete, and selected questionnaires will be administered. At visit 2, the participant will return the actigraph, diary, six-month fall log and will complete additional questionnaires and provide a urine sample. The CURES database will also be queried to obtain data about prescriptions for controlled medications.

Incentives for study participation

Participants will receive up to $150 for participation in the study. All enrolled participants will receive $25 for completing the baseline assessment. Participants who are randomized will receive $25 for the 2 hypnotic withdrawal assessments, and $50 for the post-treatment assessment and $50 for the 6-Assessment. Participants will receive payment even if they do not complete all components of an assessment. However, they will not be paid if they do not return the WatchPat or actigraph. Participants who go to UCLA Westwood for a study visit, will be given vouchers for parking fees associated with the UCLA Parking Structure ($12/day).

Follow-up for Missed Appointments

Participants who miss a study appointment will be telephoned by research staff on the day of the missed appointment. If the participant does not return the call within 10 days of the missed appointment, a letter will be sent that encourages the participant to contact the research office (see Missed Appointment Letter). If a participant has not returned an actigraph or Watch-PAT device, the letter will also include a paragraph about the importance of returning the device and a reminder that the participant may be charged for any unreturned sleep devices (see Missed Appointment Letter). If the participant does not return the device after 10 days from the date of the first letter, a second letter

will be sent reminding participants that they may be charged for any unreturned sleep monitoring devices (see Failure to Return Device Letter).

Benefits and Risks

Potential direct benefits: Participants will learn techniques that could help them discontinue hypnotics and improve their sleep. It is possible that participants in this study may experience improved sleep quality following the intervention programs. Participants may also experience a reduction in the health risks associated with chronic hypnotic use (i.e., cognitive impairment, falls).

Potential benefits to society: Hypnotic discontinuation is of critical importance to older adults. Clinical guidelines and professional groups recommend that older patients not be prescribed benzodiazepines and z-drugs, and in the context of insomnia, effective non-pharmacological treatments for insomnia are available. This study has the potential to boost hypnotic discontinuation rates. In addition, the study may provide new insight into the placebo effect. The ultimate goal of this line of research is to implement a program that can reduce hypnotic use long-term in older patients with current or past insomnia.

Potential risks/discomforts:

Benzodiazepine withdrawal symptoms: Symptoms are not common with withdrawal of low doses of benzodiazepines, but could include dizziness, anxiety, depression, and insomnia. The proposed intervention has a similar risk level to behavioral/ pharmacological strategies recommended by healthcare providers to adults as part of routine clinical care. Based on our pilot data and our team's collective clinical experience with low-dose hypnotic discontinuation, withdrawal symptoms that warrant protocol changes are uncommon. To reduce the risk of severe withdrawal symptoms, adults at high risk of complicated withdrawal or on high benzodiazepine doses (based on comorbidities, current prescriptions, and answers to assessment questions) will not be randomized to receive the intervention. Participants will be monitored weekly with the Clinical Institute Withdrawal Assessment-Benzodiazepine [CIWA-B] instrument and with weekly vital signs. If the participant is found to have mild symptoms of withdrawal based on select items from the CIWA-B or on mild changes in vital signs, a study physician (e.g., Drs. Fung or Alessi) and the participant may decide to plateau the taper until the participant is ready to continue with the dose taper. If participants are found to have moderate, severe, or very severe scores on select items in the CIWA-B, moderate or severe vital sign changes, or have worsening severe insomnia, the study physicians will discuss the patient's symptoms with a staff psychiatrist to determine whether changes to the taper schedule are needed (including increasing or plateauing the dose) and whether the patient needs additional clinical evaluation. If the patient needs immediate clinical evaluation, the participant will be escorted to the outpatient clinic or for life-threatening emergencies at our facility, we will call 911.

Confusion about duplicate hypnotic prescriptions: Participants may not understand that the hypnotic provided by the study (in blister packs or medication bottle) replaces the hypnotic that they were previously taking. This could result in participants taking both prescriptions at the same time, which would result in a higher dose than prescribed, and possible side-effects (e.g., daytime sleepiness, dizziness). To avoid confusion about duplicate hypnotic prescriptions, participants in both groups will be asked to bring all their medications to the first intervention session. The interventionist will identify the hypnotic that will be tapered and will place the bottle in a zip-locked plastic bag with a secure plastic tie. A label will be affixed to the outside of the plastic bag that states, "Do not take this medication during the 9-week SWITCH study unless instructed by the study staff." The interventionist

will explain that the participant will receive the same hypnotic either in a new medication bottle or in the blister packs and should put the old prescription in the plastic bag in a safe location.

Increased daytime sleepiness: Adjustments to the participant's sleep habits may result in some initial daytime sleepiness. Daytime sleepiness will be monitored during each weekly in-person intervention assessment with the Epworth Sleepiness Scale, and participants with increased daytime sleepiness will be counseled on the possibility of impaired cognition and increased fall and motor vehicle crash risk. If excessive daytime sleepiness is thought to be due to study-related sleep restriction (as opposed to, for example, a newly-prescribed medication from the individual's physician), the prescribed sleep schedule will be adjusted.

Mental discomfort: The minor risks associated with completion of the questionnaires include tediousness, fatigue, and/or mental discomfort answering the items. Participants could also find wearing the actigraph and WatchPAT device to be annoying or uncomfortable. To reduce the risk of mental discomfort among participants, research staff will be trained to recognize discomfort in participants, and they will be trained to remind participants of the voluntary nature of the research and the option for participants to decline participation in any portion of the research project.

Falling during one-leg balance test: Participants could lose balance and fall during the one-leg balance test. To reduce the risk of falling during the one-leg balance test, research staff will place a gait belt around participants. For participants who use mobility aids, two research staff will perform the testing and additional steps such as placing a walker around the participant may also be employed.

Sleep disruption: It is possible that the one night of sleep apnea screening could disrupt sleep since participants would not be used to sleeping with sensors on their fingers and wrist. However, home sleep apnea testing is performed routinely in clinical practice and older adults are able to sleep for sufficient amount of time to make the test valid.

Skin irritation: The sensors worn for one night as part of the WatchPAT device the actigraph wrist band worn for 7 days may cause skin irritation or an allergy. We have extensive experience using wrist actigraphy and the WatchPat system, and have chosen these devices because they are well-tolerated by participants. They are also substantially less burdensome than other objective methods of recording sleep (i.e., requiring the participant to spend a night in a sleep laboratory). Research staff will carefully review with participants potential skin problems associated with wearing the wrist actigraph and the WatchPat sensors. Participants will be told to remove the device if they have any significant discomfort or any evidence of skin injury. Participants will have access to a research staff person, in case they have questions or concerns about the equipment. In addition, the company which makes the WatchPAT device has a 24-hour advice line that also provides troubleshooting support. Our monitoring devices are checked regularly to insure safe and proper operation. Dr. Fung (PI) will be notified immediately of any significant discomfort experienced by study participants.

Confidentiality and privacy breach: There is risk of breach of privacy via unintentional disclosure of Protected Health Information, which could lead to embarrassment and fraud, which in turn could have negative financial impact on participants. To ensure confidentiality of the research data collected, all participants will have a unique identification number assigned that is not based on any identifying information. This identification number will be used for all computer databases, which will be stored behind a UCLA network server, as well as for hard copy data collection forms. Access to these databases and hard copy forms will be limited to the study's approved research staff and will not be transmitted. Research hypnotic tracking logs (that use subject identification numbers) will be maintained to ensure that all of the hypnotics that are prepared, dispensed, and disposed (if unused) are accounted for at all times. These hypnotic tracking logs will be shared with the VA research

pharmacy (via a shared folder located behind a firewall). Consent forms and hard copies of data forms will be stored in locked file cabinets in locked offices with access limited to approved research staff. Electronic lists of names and contact information will be kept separate from other data in limited access folders on the UCLA secure server.

We will rent a United States Post Office Box, where participants may mail study documents if they are unable to drop off the document to our research office or meet our research staff to hand deliver the documents. Our research staff will transport the study documents directly from the US P.O. Box to the research office.

Risk/Benefit analysis

The risks of the study are no greater than the risks associated with current clinical protocols for discontinuation of a hypnotic. In fact, monitoring for side-effects will be more structured during the study than in clinical practice. Considering the study's potential to assist participants in reducing/ discontinuing hypnotic use, the risk/benefit balance appears acceptable

Primary data analysis plan and power analyses

We will use an intention-to-treat approach for all analyses. We plan to randomize 188 individuals (including both UCLA and VA sites), of whom we expect 13% to drop out (i.e., fail to complete study assessments) by 6-months, yielding N=164 participants with complete data (~ 82 per group). *We base this drop-out on our completed study (Alessi VA Merit 08-295)*. We will include terms for stratification characteristics in all of the models. All analyses below assume α=0.05, power=0.80, and two-sided hypothesis tests. Effect sizes are in the measure's natural units and Cohen's *d* (large=.8; medium=.5; small=.2).

- ***H1: Dysfunctional Beliefs and Attitudes About Sleep – Medication Scale ratings will improve with MTcap compared to SGT+CBTI post-treatment and at 6 months follow-up***: **Analysis:** We will fit a 2 (group) by 3 (time) mixed model analysis of variance (ANOVA) model. Interaction terms will be used to assess the change in DBAS medication item (from baseline→post-treatment, baseline→6 months) for MTcap vs. SGT+CBTI group. **Power Analysis:** Based upon our prior research, we estimate the correlation of DBAS scores from baseline to 6-months will be *r*=0.55 (95% CI=0.42-0.65) and the standard deviation will be 2.1. Assuming n=82 per group, the study could detect an effect of 0.9 units on the DBAS-16 scale (Cohen's *d*=0.43). If the baseline to follow-up correlation is *r*=0.42 (95% lower confidence limit [LCL]), the detectable effect size is 1.0 unit on the DBAS-16 scale (Cohen's *d*=.47).
- ***H2a: Participants who receive MTcap will have increased likelihood of hypnotic discontinuation post-treatment and at 6 months follow-up compared with those who receive SGT+CBTI*****:** The logistic regression models' dependent variable will be hypnotic discontinuation (yes=1/no=0 at post-treatment and 6-month follow-up) and the primary predictor of interest will be treatment group assignment (MTcap vs. SGT+CBTI). **Power Analysis:** We estimate that the SGT+CBTI group will have 60% discontinuation (based on prior studies = 59% to 63%, and our CBTI clinic's quality improvement data = 58% see "Technical Preliminary Studies"). We posit that a discontinuation percentage for the MTcap would need to be 80% (i.e., 20% greater) to be clinically meaningful. With an analytic sample size of n=82 per group, the study could detect a 20% difference in hypnotic discontinuation rate between groups (SGT+CBTI 60% vs. MTcap 80%). If the discontinuation rate of SGT+CBTI exceeds 60%, the study can detect even smaller differences (e.g., 17.8% difference if SGT+CBTI discontinuation rate is 70%). Even if the discontinuation percentage for the SGT+CBTI group is 50%, the study could detect a 21.3% difference (SGT+CBTI 50% vs. MTcap 71.3%). In our feasibility study, masked tapering resulted in 100% hypnotic discontinuation at post-treatment.
- ***H2b: Participants who receive MTcap will use less hypnotic post-treatment and at 6 months follow-up compared with those who receive SGT+CBTI***: **Analysis:** Two outcomes will be

assessed: frequency (i.e., days used, 0 to 7) and quantity (i.e., average daily dose in diazepam milligram equivalents). For each outcome, we will fit a 2 (group) by 3 (time) mixed model analysis of variance (ANOVA). Interaction terms will be used to assess the change in the outcome (from baseline→post-treatment, baseline→6 months) for MTcap vs. SGT+CBTI. **Power Analysis:** For these calculations, we use statistics from our recent study, which found a baseline to 6-month correlation of *r*=0.83 (95% CI=0.77-0.88) and a standard deviation of 1.94 for a similar outcome measure—"days used of medications commonly used for insomnia" (days used, 0 to 7 days). Assuming *r*=0.83 and n=82 per group, we could detect a treatment effect of 0.5 (*d*=0.26) (i.e. a discontinuation rate of half a day more for MTcap vs. SGT+CBTI group). Assuming *r*=0.77 (i.e., using the LCL), we could detect a treatment effect of 0.6 days (*d*=0.31). If we disregard these prior data, power calculations still show that we could detect a treatment effect of Cohen's *d*=.44 with n=82 per group. For quantity of use, power calculations indicate that we could detect a treatment effect of *d*=0.44 with n=82 per group.

- ***H3: Insomnia Severity Index scores will be lower with MTcap compared to SGT+CBTI at 6 months follow-up***. **Analysis:** Similar to H2, we will fit a mixed model ANOVA, and an interaction term will assess the change in ISI from baseline to 6 months for MTcap vs. SGT+CBTI. **Power Analysis:** Based on prior research, we found the standard deviation (SD) and "baseline-to-6 month follow-up" correlation of ISI scores to be SD=5.3 and *r*=0.39 (95% CI=0.24-0.52), respectively. Assuming *r*=0.39 with a sample size of n=82 per group, the study could detect an effect of 2.56 units on the ISI (or a Cohen's *d*=0.48). Assuming *r*=0.24 (i.e., using the LCL), we could detect an effect of 2.86 units on the ISI (or a Cohen's *d*=0.54). These power analyses suggest that the study could detect effects that are medium sized (i.e., *d*=0.48, *d*=0.54).

Exploratory data analysis plan: Using latent class analysis to identify group memberships based upon PHQ-9, GPM, ISI, and ESS measured at baseline, we will examine whether latent group membership moderates the strength of the treatment effect (i.e., examine if the MTcap treatment effect is stronger for particular latent class groups). To explore changes in cognition and balance, we will test whether MTcap improves Digit Symbol Substitution, MMSE, Trails A & B, & One-leg balance post-treatment and at 6-month follow-up, using mixed model ANOVA methods described above.

APPENDIX: VIDEO/TELEHEALTH VISIT ADDENDUM TO SWITCH STUDY

Video/telehealth Standard Practices

- Throughout the modified protocol, MyChart/CareConnect Video will be the preferred platform that will be used. In the event that this platform fails, we will follow current UCLA Health System guidance and use currently approved patient-facing platforms. If no video platforms work, we will use telephone only. If telephones do not work, we will reschedule the visits as needed.

- We will use standard video/telehealth practices including verifying identity, privacy, location, emergency contact information, in case of emergency.

Inclusion/Exclusion criteria:

Inclusion criteria: same as previously approved protocol with one addition. The participant must be:

- "Available to attend weekly in-person **or video** sessions over 9 weeks"

Exclusion criteria: No changes

Recruitment

Step 1 (identification of participants): No changes

Step 2 (screening for current or prior insomnia and current hypnotic use

Telephone screening:

No changes except--Following completion of the telephone screening questionnaire, eligible and interested individuals will be scheduled for an initial meeting to obtain written informed consent. An email address or mobile number will be requested at the end of the screening visit.

Patient preference for social/physical distancing

Following completion of the screening questionnaire, eligible and interested patients will be asked whether they prefer "Always In-Person" visits (**AIP**) versus "Sometimes In-Person" visits (**SIP**, which will entail picking-up/dropping-off of study material/equipment in-person versus "Never In-Person" visits (**NIP**, all study materials transported via mail/delivery services). Individuals who opt for AIP will follow the approved in-person protocol.

AIP=Patient prefers Always In-Person contact with study team

SIP=Patient prefers Sometimes-In-Person contact with study team. Specifically, video visits for assessments and intervention, but is willing to pick up and drop off study material

NIP=Patient prefers Never In-Person contact with study team. All contact is remote/virtual.

Step 3: Consent visit

Video consent option for SIP and NIP

Patients will be offered a video visit as an alternative to an in-person consent visit. A UCLA Health System approved video visit platform (e.g., Care Connect Video Visit) will be used. The same procedures used for the in-person consent visit will be used for the video visit.

The same staff that conduct the in-person consent visit will conduct the video visit.

- Preparation for consent appointment:
  - Auto-generated appointment reminder in CareConnect will be sent for CareConnect video visit.
  - Research staff will email/text instructions for the appointment, appointment date/time, copy of enrollment/consent documents (e.g., informed consent form, UCLA HIPAA form, participant list of rights, etc.).

- Research staff will deliver (mail/courier/delivery service) a cover sheet describing the contents of the delivery, enrollment/consent documents, self-addressed, postage paid return envelope, paper disposable ruler (needed for assessment visit to obtain neck circumference)

- Return of study materials
  - Patients who electronically sign enrollment/consent documents (e.g., informed consent form, HIPAA forms) will email the signed forms back to the research staff. We will follow UCLA Health System Compliance and IT guidance and will only use approved electronic signature software, if and when they become available.
  - Patients who sign hard copies of the consent and HIPAA forms will mail the signed forms back in the return envelope.

<u>Step 4 Baseline assessment to determine remaining eligibility criteria:</u> After participants have provided written informed consent, they will complete a baseline assessment that consists of 2 visits (each 45-60 minutes).

Baseline Visit Procedures

1) Version for SIP participants

- At the beginning of the Baseline 1 visit, staff will instruct participant that they need a blank piece of paper and pen. The research assistant will administer questionnaires in original protocol, except Trails and Digit Symbol/Symbol Copy, which will be moved to Baseline 2 visit. The RA will show the responses to questionnaires.
- Research staff will document the responses in electronic format or hard copy and store the copies in the approved research servers or office spaces.
- At the end of the Baseline 1 visit, the research staff will arrange for in-person pick-up of materials **Pick-Up** of Baseline materials:
  - A wrist actigraph will be given to participants to wear at home for 1 week
  - A sleep diary will be given to participants to complete while wearing the actigraph
  - If a participant scores > 4 on the STOP-Bang and does not have documentation of a previous sleep study in the medical record, s/he will be sent home with an Food and Drug Administration-approved portable sleep apnea screening device (e.g., WatchPAT, NoxT3, Alice NightOne) to wear for one night. The sleep study will be interpreted by a board-certified sleep medicine physician on the research team (e.g., Dr. Fung, Dr. Zeidler). The participant will return the device the next day to the research office.
  - Hypnotic medication log - Using a structured hypnotic abstraction form (see Hypnotic Abstraction Form), we will review the UCLA medical record to obtain data about hypnotic prescriptions. We will also query the California Controlled Substance Utilization Review and Evaluation System (CURES) database to obtain data about prescriptions of controlled substances.
  - Paper copies of the Trails, Digit Symbol/Symbol Copy will be included in the packet to be used at the video Baseline 2 visit
  - Other baseline assessment forms/instructions
  - “Return Delivery” packaging to be used when returning materials to research office

2) Version for NIP participants

- At the beginning of the Baseline 1 visit, staff will instruct participant that they need a blank piece of paper and pen. The research assistant will administer questionnaires in original protocol, except Trails and Digit Symbol/Symbol Copy, which will be moved to Baseline 2 visit. The RA will show the responses to the questionnaires video or by sharing desktop.
- At the end of the video appointment, the research staff will arrange for delivery of study materials. **Delivery** of Baseline materials:
  - A wrist actigraph

- Sleep diary
- Trails and Digit Symbol/Symbol Copy to be used at video Baseline 2 visit
- If STOP-BANG > 4, then portable sleep apnea screening device (e.g., WatchPAT, NoxT3, Alice NightOne)
- Hypnotic medication log
- Other baseline assessment forms/instructions
- Postage-paid, pre-addressed, insured delivery packaging ("Return Delivery" packaging)

In both the SIP and NIP patients, the One-leg Balance will be omitted due to the need for physical contact to safely perform this test.

MINI: As needed video MINI appointment: If a MINI is needed, a separate video MINI visit with a staff trained in administering the MINI will be arranged and preparatory emails will be sent to the participant.

Eligibility determination for randomization
No change

Randomization
No change

Interventions
No change to content of sessions

Preparatory emails to schedule each video intervention session (automated email and emails from interventionist to patient confirming video appointments—the list of emails may be combined in one email and during the intervention, changes to video appointments will be made either by corresponding with the participant or via email)

Getting Materials/Medications to Randomized Participants:

1) Version for SIP Participants
    - Pick Up of materials prior to session 1:
        - Notebook of content for weeks 1 to 9 (last week's content omitted)
        - Diaries for all weeks
        - Blood pressure cuff (if participant does not have one)
        - CIWA, ISI, ESS questionnaires (in sealed envelopes, labeled for each session)
        - Medications for MTcap: 3 week supply plus 3 weeks PRN plateau
        - Medications for SGT: 1 bottle (no change) plus Paper Taper Schedule and pill cutter in a sealed envelope to be opened at Session 1 (no change to content of taper schedule)
        - Extra copies of forms/instructions
        - Postage-paid, self-addressed return envelopes
    - Pick Up of meds at Day 14
        - Medications for MTcap: 3 week supply plus 3 weeks PRN plateau
    - Pick Up of meds at Day 28
        - Medications for MTcap: Remaining 2 weeks supply plus 2 weeks PRN plateau
        - Box for returning materials at the end of sessions
    - Delivery of final session content material will be timed to occur with "session 8 content"
2) Version for NIP Participants
    - Similar to SIP schedule above, except that delivery of materials/medications will occur in lieu of in-person pick up.

Measures collected during video visit intervention:

- Urine
    - SIP—a urine sample will be collected from participants between the randomization time point and the first intervention session. The urine sample will be tested for benzodiazepines and zolpidem to confirm the participant's use/nonuse of these hypnotics.
    - NIP—We will offer to mail a urine specimen collection container to the participant and to pick it up via UCLA-approved courier service to bring the specimen back to the UCLA lab in CHS that processes research specimens.
- Questionnaires: Weekly throughout the intervention for participants in both study groups the participant will complete the items and show the completed instruments to the interventionist. If necessary, the interventionist may administer the items verbally.
    - Clinical Institute Withdrawal Assessment Scale - Benzodiazepines (CIWA-B): This 22-item instrument includes patient symptoms and clinical observations (e.g., tremor) to assess and monitor the type and severity of symptoms of benzodiazepine withdrawal.
    - Vital signs: These physical examination measurements will be self-reported by participants weekly: blood pressure, pulse.
    - Insomnia Severity Index (ISI): The ISI is a 7-item instrument that measures perceived severity of insomnia symptoms (total score ranges from 0 to 28).
    - Epworth Sleepiness Scale (ESS): This 8-item questionnaire assesses general level of daytime sleepiness.
    - Daily sleep and habits diary: No change. The interventionist will look at the diary on the screen/camera.

Video visit Hypnotics Taper and CBTI-augmented program

1) MTcap (Masked Taper plus cognitive behavioral therapy-augmented program): Hypnotic taper protocol: No change to tapering rate. The interventionist will confirm with the participant at the end of each video session the blister pack that will be taken for that week. Cognitive behavioral therapy for insomnia-augmented program: No change
2) SGT+CBTI: No changes

Video Visit Extended taper plan: We have identified specific situations when the taper plan may need to be modified:

1) Withdrawal symptoms/extended taper required: In the MTcap video group, an extended taper may be achieved by instructing the participant to open the sealed envelope containing the duplicate 7-day blister pack (e.g., plateauing the doses until the participant is ready to move to the next blister pack), showing it to the interventionist and instructing the participant to take it that week. In the SGT+CBTI group, participants will be instructed to repeat a particular week in the printed taper schedule. If necessary, additional study medication will be delivered/picked up by the participant if the participant requires extended plateau or needs additional medication (e.g., participant loses medication).
2) Hypnotic dosed as "prn" at baseline: No change to approved protocol.
3) More than 1 hypnotic at baseline: No change to approved protocol.

Video Visit Protocols for preparation of hypnotics

1) MTcap group: No change. The date of pick-up/mail date will be documented in the drug accountability log.

SGT+CBTI group: No change. The date of pick-up/mail date will be documented in the drug accountability log.

Protocols for distribution of hypnotics

A chain of custody will be established and documented. Only authorized members of the research team will be permitted to have contact with the medications. A delegation log will be maintained. For both groups, a member of the research team will pick-up the medication bottle or blister packs from the UCLA Research Pharmacy. The medications will distributed according to the method described above (either pick-up or mailed versus social distancing preferences).

Care coordination at end of intervention period
No change

Follow-up assessments
The post and 6-month assessments will be conducted via video visits for SIP and NIP participants. Procedures similar to the approved in-person protocol will be followed with the following exceptions that will allow for social distancing:

Post-treatment assessment
Preparatory Emails

- (Auto-generated email): A reminder appointment email will be created and invitation for video Post 2 appointment will be sent to the patient
- (Research staff-generated email)
  - Participants will be emailed a confirmation of their Post 2 visit appointment
  - Participants will be provided instructions for preparing for the Post 2 assessment (e.g., anticipated duration, equipment/materials needed, staff contact information)

Getting Materials/Equipment to Participants

1) Version for SIP Participants will be advised to pick up Post assessment visit 1 materials (in sealed envelopes) 1 day prior to session 8 and to go to the lab to give urine sample (urine tox and urine zolpidem)
   - Diary
   - Questionnaire packet/instructions
   - Medication log
   - Fall log
   - Wrist actigraph
   - Return Box
2) Version for NIP Participants will be mailed Post materials a few days before session 8
   - Diary
   - Questionnaire packet/instructions
   - Medication log
   - Fall log
   - Wrist actigraph
   - Urine specimen container
   - Postage-paid return, insured Return Box

As with the original AIP protocol, the post-treatment assessment will begin on the same day that the participant completes session 8 of either intervention. At the end of session 8, a participant will be instructed to put on the actigraph to wear at home for 1 week and to complete the sleep and medication diary. When the participant returns the actigraph and diary after 1 week, he/she will be administered selected questionnaires included in the baseline assessment. Participants will also be instructed on the six-month fall log to record any falls they experience during the period between the

post-assessment and the six-month follow-up assessment. A courier will be sent to pick up the urine specimen and will deliver it to the UCLA lab in CHS that processes the research labs.

Six-month follow-up
Preparatory Emails

- (Auto-generated email): A reminder appointment will be created and invitation for 6-month follow-up appointment will be sent to the patient
- (Research staff-generated email)
    - Participants will be emailed a confirmation of their 6-month follow up visit appointment
    - Participants will be provided instructions for preparing for the 6-month follow up (e.g., anticipated duration, equipment/materials needed, staff contact information)

Getting Materials/Equipment to Participants

- Version for SIP Participants will be advised to pick up 6-month follow up visit 1 materials (in sealed envelopes) 1 day prior to 6-month follow up and to go to the lab to give urine sample (urine tox and urine zolpidem)
    - Diary
    - Questionnaire packet/instructions
    - Medication log
    - Wrist actigraph
    - Return Box
- Version for NIP Participants will be mailed 6-month follow up materials a few days before session 8
    - Diary
    - Questionnaire packet
    - Medication log
    - Wrist actigraph
    - Urine specimen containers
    - Postage-paid return, insured Return Box

A courier will be sent to pick up the urine specimen and will deliver it to the UCLA lab in CHS that processes the research labs.

Incentives for study participation
No changes.

Follow-up for Missed Appointments
No changes.

Benefits and Risks
no changes.

Primary data analysis plan and power analyses
No changes