

**Augmenting Benzodiazepine Receptor Agonist Deprescribing with
Yoga and Acupuncture Among Older Adults: A Single Arm
Feasibility Trial of 30 Patients
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PRÉCIS

Augmenting Benzodiazepine Receptor Agonist Deprescribing with Yoga and Acupuncture Among Older Adults: A Single Arm Feasibility Trial of 30 Patient Objectives

Specific Aim 1. Feasibility of study enrollment: Assess our ability to enroll 30 older adults taking BRZA including screening, and recruitment. Hypotheses: Within an 8-month period we will refine enrollment procedures from outpatient clinics. Anticipated results: Develop efficient and replicable procedures to enroll the target population.

Specific Aim 2. Feasibility of study treatments: Evaluate fidelity, adherence, and acceptability of 12-week BRZA deprescribing augmented with acupuncture and yoga treatments. Hypotheses: Treatment conditions will have high fidelity ($\geq 90\%$ assessed by fidelity checklists), adherence ($\geq 80\%$ attendance to offered treatment sessions), and acceptability (≥ 15 out of 20 rating scoring by participants for acceptability, appropriateness, and feasibility of intervention). Anticipated Results: 1) Revise and finalize manualized treatment protocols for BRZA deprescribing, acupuncture, and yoga. 2) Measure participant adherence and acceptability of study treatments.

Specific Aim 3: Feasibility of study outcome assessments: Assess the feasibility of outcome assessments at baseline, 4, 8, and 12 weeks (primary outcome: BRZA dose reduction, secondary outcomes: insomnia and anxiety). Hypotheses: Data collection is successful including extraction of BRZA dose from medical records, and high survey completion rate with low perceived burden by participants. Anticipated Results: Optimize data collection procedures for randomized multi-site clinical trial.

Design and Outcomes

This study consists of a single arm clinical feasibility study to augment protocol-driven BRZA deprescribing augmented with combined acupuncture and yoga. Adults who are 65 years or older that are taking BRZA will be recruited. Deprescribing will be provided at weekly visits with a psychiatric nurse practitioner at the Osher Center for Integrative Health at Vanderbilt University Medical Center (VUMC). Participants will receive acupuncture and yoga from a staff acupuncturist and yoga instruction from a yoga instructor at the Osher Center. Feasibility of study enrollment will occur through the study enrollment period. Feasibility of study treatments will be evaluated during and after study treatment delivery. Feasibility of study outcome assessments will occur at baseline, 4, 8, and 12 weeks. Throughout the research process, we will engage with a Stakeholder Advisory Panel consisting of patients (older adults with experience receiving BRZA, yoga and/or acupuncture) and clinicians (geriatricians, psychiatrists, and pharmacists with experience in BRZA deprescribing and addiction medicine).

Interventions and Duration

- A. Intervention: Participants will enroll into 12-week protocol drive deprescribing treatment augmented with yoga and acupuncture.
- a. Protocol-driven deprescribing: Participants will be scheduled for weekly 30-minute visits with a psychiatric nurse practitioner provider. Psychiatric nurse practitioners are well-trained to deliver BRZA deprescribing protocols. The provider will use the Benzodiazepine & Z-Drug Deprescribing Algorithm. The algorithm consists of the following steps:
 - Engage patients by discussing potential risks, benefits, withdrawal plan, symptoms, and duration
 - Recommend deprescribing
 - Slow taper and then stop BZRA (e.g. 25% reduction every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days). Providers will also offer behavioral sleeping advice.
 - Monitor every 1 week for duration of tapering for withdrawal symptoms and potential benefits.
 - b. Participants will also be scheduled for acupuncture and yoga instruction with an effort the schedule at the same time back-to-back at the Osher Center.
 - i. Acupuncture: Participants will receive the standardized acupuncture treatment protocol one-on-one. Visits with acupuncturist will be about 30 minutes.
 - ii. Yoga: Participants will receive the standardized yoga treatment protocol one-on-one. Visits will be about 30 minutes with the yoga instructor. Participants will be taught a yoga practice and provided with a handout for home practice. Participants will be encouraged to practice daily at home.
- B. Duration: Participants will be enrolled into a 12-week intervention and an additional 4 weeks to complete follow-up assessments for a total of 16 weeks of study participation.

Sample Size and Population

A total of 30 adults 65 years or older with use of BRZAs will be enrolled in this study.

1. STUDY OBJECTIVES

1.1 Primary Objective

Specific Aim 1. Feasibility of study enrollment: Assess our ability to enroll 60 older adults taking BRZA including screening, recruitment, and randomization.

Hypotheses: Within an 8-month period we will refine enrollment procedures from outpatient clinics. Anticipated results: Develop efficient and replicable procedures to enroll the target population.

Specific Aim 2. Feasibility of study treatments: Evaluate fidelity, adherence, and acceptability of 12-week BRZA deprescribing augmented with acupuncture and yoga treatments. Hypotheses: Treatment conditions will have high fidelity ($\geq 90\%$ assessed

by fidelity checklists), adherence ($\geq 80\%$ attendance to offered treatment sessions), and acceptability (≥ 15 out of 20 rating scoring by participants for acceptability, appropriateness, and feasibility of intervention). Anticipated Results: 1) Revise and finalize manualized treatment protocols for BRZA deprescribing, acupuncture, and yoga. 2) Measure participant adherence and acceptability of study treatments.

Specific Aim 3: Feasibility of study outcome assessments: Assess the feasibility of outcome assessments at baseline, 4, 8, and 12 weeks (primary outcome: BRZA dose reduction, secondary outcomes: insomnia and anxiety). Hypotheses: Data collection is successful including extraction of BRZA dose from medical records, and high survey completion rate with low perceived burden by participants. Anticipated Results: Optimize data collection procedures for multi-site clinical trial.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

BRZA including benzodiazepines and other z-drug hypnotics such as zolpidem, zopiclone, and zaleplon are associated with unacceptable health risks for older adults. Common reasons for older adults to be prescribed BRZA include insomnia and anxiety despite lack of evidence for long-term clinical efficacy.¹ Guidelines advise BRZA deprescribing using a slow tapering strategy. Barriers to BRZA deprescribing include rebound symptoms of insomnia and anxiety. Regionally, the Southern United States has the highest rates of BRZA prescription including our area of middle Tennessee.²

2.2 Study Rationale

Over 28 million older adults in the United States use complementary health and integrative therapies, with nearly one out of three reporting perceived benefits for sleep and stress.³ The Osher Center for Integrative Health at VUMC is the major academic integrative health clinic in the mid-South and one of the busiest in the U.S. with over 18,000 ambulatory visits a year. The most common conditions treated at the Osher Center are similar to other academic integrative health clinics: chronic pain, anxiety, fatigue and/or sleep problems.⁴ About 25% of patients who visit the Osher Center are 65 years or older. Many patients receive multiple integrative modalities simultaneously such as acupuncture and yoga. While common in clinical practice, research evidence for combining integrative therapies is lacking.⁵

3. STUDY DESIGN

This study consists of a single arm clinical study among 30 older adults taking BRZA to assess the feasibility of protocol-driven BRZA deprescribing augmented with combined acupuncture and yoga. Adults who are 65 years or older that are taking BRZA will be recruited. Deprescribing will be provided at weekly visits with a psychiatric nurse practitioner at the Osher Center for Integrative Health at Vanderbilt University Medical Center (VUMC). Participants will receive acupuncture and yoga from a staff acupuncturist and yoga instruction from a yoga instructor at the Osher Center. Feasibility of study enrollment will occur through the study enrollment period. Feasibility of study treatments

will be evaluated during and after study treatment delivery. Feasibility of study outcome assessments will occur at baseline, 4, 8, and 12 weeks. Throughout the research process, we will engage with a Stakeholder Advisory Panel consisting of patients (older adults with experience receiving BRZA, yoga and/or acupuncture) and clinicians (geriatricians, psychiatrists, and pharmacists with experience in BRZA deprescribing and addiction medicine).

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

All participants enrolled will meet the inclusion and exclusion criteria of the study as stated below. We will not exclude patients on the basis of gender, race, ethnicity, or religious preferences and practices.

4.1 Inclusion Criteria

- Use of BRZA at least 4 times in the last one month.
- Age 65 years or older
- English speaking
- Ability to understand study procedures and to comply with them for the entire length of the study.

4.2 Exclusion Criteria

- Cognitive impairment (Mini-Mental Screening Examination ≤ 24)
- Drinking more than 3 alcoholic beverages per day.
- Substance abuse disorder
- Uncontrolled psychiatric disorders, such as major depression or psychosis
- Inability or unwillingness of individual or legal guardian/representative to give written informed consent.

4.3 Study Enrollment Procedures

Recruitment and Referral Sources: We will primarily focus on recruitment through the Vanderbilt Health System with focus on the adult outpatient primary care clinics.

Pre-screening: We will compile a list of universal names for BZRA medications. This list will be used to query adults 65 years and older from primary care clinics at Vanderbilt University Medical Center that have been prescribed a BRZA medication. Data extraction at VUMC occurs with permission of the Vanderbilt Committee on Opioid Monitoring and Stewardship (VCOMS). VCOMS is charged with overseeing VUMC's opioid and controlled substance prescribing data as well as monitoring

prescribing practices mandated by federal and state laws. To evaluate the prescribing practices of controlled substances including BRZA medications.

Screening and Study Sample Selection: We will contact individuals with positive pre-screening at clinic visits through mailed letters, web-based portal, and/or phone. We will include patients taking BRZA for insomnia and anxiety.

Enrollment Procedures: Individuals interested in participation will go through primary phone screening by research staff to determine eligibility based on criteria listed above. If eligible, research staff will explain the research protocol, answer questions, and discuss informed consent. Potential subjects interested in participation will be scheduled for a research visit with research staff for secondary screening. Secondary screening will consist of a direct interview to confirm eligibility including administration of Mini-Mental Screening Examination. After secondary screening, eligible and willing individuals will complete informed consent and baseline testing at the same research visit. We will document number of individuals screened, approached to participate, reasons for declining, number successfully enrolled, and average time between screening and enrollment.

5. STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

Participants will enroll into either 12-week of integrated BRZA deprescribing, acupuncture, and yoga.

Setting: BRZA deprescribing by a psychiatric nurse practitioner will occur at the Osher Center for Integrative Health either in person at the clinic or via telehealth based on participant preference. The acupuncture and yoga will be provided at the Osher Center for Integrative health at VUMC. Interventions will be delivered in already dedicated private rooms at OCIH for delivery of these services.

Interventions:

(1) BRZA deprescribing: Participants will be scheduled for weekly 30 minute visits with a psychiatric nurse practitioner provider. Psychiatric nurse practitioners are well-trained to deliver BRZA deprescribing protocols. The provider will use the Benzodiazepine & Z-Drug Deprescribing Algorithm.⁶ The algorithm consists of the following steps:

- Engage patients by discussing potential risks, benefits, withdrawal plan, symptoms, and duration
- Recommend deprescribing
- Slow taper and then stop BZRA (e.g. 25% reduction every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days). Providers will also offer behavioral sleeping advice.
- Monitor every 1 week for duration of tapering for withdrawal symptoms and potential benefits.

At weekly visits with participants, the psychiatric nurse practitioner will assess participants for withdrawal symptoms. We will use the Clinical Institute Withdrawal Assessment – Benzodiazepine (CIWA-B) to evaluate severity of withdrawal symptoms.⁷ This instrument consists of 17 items that are patient-reported and 5 items that are clinician reported with cumulative scores indicating mild to very severe withdrawal symptoms (total scores range: 0-80).

As a medical visit, documentation of the visit will occur in the electronic health record and patients' billed for this medical encounter.

(2) Acupuncture: The acupuncture protocol was developed based on principles of Traditional Chinese Medicine (TCM), our own clinical experience and published trials, with incorporation of points that treat pain, anxiety and fatigue. It serves as a guide for the acupuncturist to administer the acupuncture procedure. Acupuncture visits will be aligned with already existing standard clinical procedures and necessary documentation in the electronic health record. The initial visit will involve an assessment including: 1) History, 2) Tongue diagnosis, and 3) Pulse diagnosis. Patients will then receive acupuncture detailed below for each visit.

Points Selection

1) Core points for insomnia:

- Bilateral: Anmian (EX-HN22), Shenmen (HT7), Sanyinjiao (Sp6), Neiguan (PC6)
- Midline: Baihui (GV20), Shenting (GV24), Yingtang (EX-HN3)
- Unilateral: Shenmen (Auricular), Sympathetic (Auricular)

2) As focal pain, generalized ache, anxiety/depression and fatigue are common in subjects of chronic insomnia, supplemental points (3-5) can be added chosen from the table below.

3) The table of the points is meant to serve as a guide, but if the acupuncturist wishes to use an additional point not described in the table based on their clinical judgment for that specific patient case, additional points can be used, but must be sufficiently documented

4) Limit the total of points to 8-16.

Needle types

- 1) Seirin Needles : (Manufactured in Japan, Distributed by Wabbo Company, Lake Elsinore CA, or Lhasa OMS, Weymouth, MA)
- 2) Pine Acupuncture Needles (Manufactured in South Korea, Distributed by Wabbo Company, Lake Elsinore CA)

Needle sizes

Auricular Points: 0.16mm x 15mm-30mm

Body Points: 0.16mm--0.25mm x 30mm-40mm

Acupuncture Administration

- a. Assist patient to lie comfortably on a table.

- b. Wipe the needling points with alcohol.
- c. Insert needle to appropriate depth with brief stimulation to achieve “De Qi” sensation (De Qi is optional).
- d. Set timer for 30 minutes.
- e. Document acupuncture procedure in electronic health record as per procedure.
- f. Check patient in 15 minutes for comfort.
- g. Remove needles and wipe any blood with a gauze or cotton tipped applicator.
- h. Assist patient to slowly get up from the examination table.
- i. Complete documentation using the case report form in electronic health record as per procedure.

Acupuncture will be provided at no charge to patients.

(3) Yoga: This yoga protocol was developed based on principles of yoga therapy in the Viniyoga tradition. The goal of the protocol is to teach older adults a yoga practice to be practiced at home that reduces anxiety and improves sleep. The yoga practice will be taught individually by a yoga therapist at the Osher Center for Integrative Health at Vanderbilt University Medical Center certified by the International Association of Yoga Therapists. Participants will receive a progressive and gradual practice over 12 weeks to the individual’s capacity. Participants will be encouraged to practice daily in the evening. The length of the home yoga practice will be 10-15 minutes. In-person classes with yoga instructors will be 30 minutes.

5.2 Concomitant Interventions

5.3.1 Allowed Interventions

All subjects will continue with routine treatment of medical conditions including all medications. Changes in medications will be at the discretion of usual healthcare providers. Any changes in medications or other concomitant interventions initiated during the study period will be documented.

5.3.2 Required Interventions

No additional interventions are required except for those proposed for in study protocol.

5.3.3 Prohibited Interventions

Participants receiving the intervention will be asked to not participate in other treatments or programs at OCIH exception those in the study protocol. Any other integrative concomitant interventions initiated during the study period will be documented.

5.4 Adherence Assessment

Adherence will be assessed as part of Specific Aim 2 specified below.

6. STUDY PROCEDURES

6.1 Schedule of Evaluations

Assessment	Recruitment (Day-180 to Day -14)	Enrollment and Research Visit 1 (Day 0)	Tx Visit W1	Tx Visit W2	Tx Visit W3	Tx Visit W4	Research visit 2 (W5)	Tx Visit W5	Tx Visit W6	Tx Visit W7	Tx Visit W8	Research visit 3 (W9)	Tx Visit W9	Tx Visit W10	Tx Visit W11	Tx Visit W12	Research visit 4 (W13)	Focus groups
Specific Aim 1: Feasibility of Study Enrollment																		
Pre-screening	X																	
Screening		X																
Informed Consent		X																
Specific Aim 2: Feasibility of Study Treatments																		
Fidelity			X	X	X	X		X	X	X	X		X	X	X	X	X	
Adherence			X	X	X	X		X	X	X	X		X	X	X	X		
Acceptability																	X	X
Specific Aim 3: Data Collection Assessment																		
Primary: BRZA dose		X					X					X					X	
Secondary: Insomnia, anxiety		X					X					X					X	

6.2 Description of Evaluations

6.2.1 Enrollment

Pre-Screening: As specified above in study enrollment, prescreening will be performed with permission of the Vanderbilt Committee on Opioid Monitoring and Stewardship (VCOMS) that will provide a list of potential participants that meet the inclusion criteria of BRZA use and older than 65 years of age.

Screening: Individuals interested in participation will go through primary phone screening by research staff to determine eligibility based on criteria listed above. If eligible, research staff will explain the research protocol, answer questions, and discuss informed consent. Potential subjects interested in participation will be scheduled for visit with research staff to confirm eligibility.

Consenting Procedure: After screening, participants eligible and willing to participate will given a written informed consent by the research staff. The informed consent forms ask patients to participate in a 12-week intervention study to receive study interventions weekly, three additional research visits and one focus group. Details of all study procedures will be provided, including purpose of the studies, interventions including frequency of visits and time commitment, assessments, risks and benefits, and voluntary nature of the program. Any changes to research procedures or intervention will prompt revision of the consent form, with subsequent review and approval from Vanderbilt IRB. A digital copy of the signed consent will be stored in a REDCap database.

6.2.2 Baseline evaluation

Enrollment: Enrollment into the study will be defined by patient having met all screening criteria and signed informed consent.

Baseline Assessments: For participants who have successfully been screened for eligibility and are enrolled into the study, baseline assessments will be performed to measure study outcomes.

- BRZA dose: We will extract data from the electronic health record regarding the unit dose drug strength and number of pills dispensed. We will supplement with EHR data regarding BRZA use with patient interviews.
- Questionnaires : PROMIS Anxiety Scale, PROMIS Sleep Disturbance
- Other Current Medications
- Concomitant Interventions
- Prior use of integrative modalities
- Expectations of treatment

6.2.3 Blinding: As a pilot study, research assistants and investigators will not be blind to treatment assignments. The study statistician will be blinded to treatment assignments.

6.2.4 Follow-up Visits

Once a week for 12 weeks at the Osher Center for Integrative Health

- Fidelity and adherence to acupuncture treatments
- Fidelity and adherence to yoga treatments
- BRZA dose: Patient self-report at weekly treatment visits including pill counts.

At 4, 8 weeks, and 12 weeks

- Questionnaires: PROMIS Anxiety Scale, PROMIS Sleep Disturbance

- Changes in any other medications
- Concomitant Interventions

6.2.5 Completion/Finally Evaluation

After completion of the study

- BRZA dose: After all study participants complete the study we will retroactively extract data from the electronic health record regarding the unit dose drug strength and number of pills dispensed at designated time points (Baseline, 4, 8, and 12 weeks).
- Focus groups: 5-10 participants will be grouped after completion of the treatments qualitatively assess acceptability. We will offer three focus groups during the study period.
- Questionnaires: PROMIS Anxiety Scale, PROMIS Sleep Disturbance
- Changes in any medications
- Concomitant Interventions
- Expectations of treatment

Subjects who discontinue the study intervention early will require no specific evaluations. The reason for discontinuation will be documented. If research subjects no longer want to participate in the research study, we will terminate the patients from the study. Patients terminated from the study will be advised to continue medical treatment with their regular medical providers. Patients not participating in the study will have BRZA dose extraction from the electronic health record, but no other monitoring, follow-up, or questionnaires.

7. SAFETY ASSESSMENTS

This research protocol employs BRZA deprescribing, acupuncture, and yoga among older adults that involves low risk to human subjects. Subjects will be frequently asked about symptoms relating to adverse events or discomfort. While expected to be very rare, possible serious adverse events related to each treatment interventions are describe below in addition to non-serious adverse events.

(1) Acupuncture:

Serious Adverse Events:

- Pneumothorax (collapsed lung)
- Infection at the needle insertion site
- Allergic reaction to needles or materials used
- Nerve damage
- Hematoma (formation of a large blood clot)

Non-serious Adverse Events:

- Pain or discomfort at the needle insertion site
- Minor bleeding or bruising
- Dizziness or lightheadedness
- Fatigue
- Emotional release or mood changes

(2) Slow Breathing:

Serious Adverse Events:

- Hyperventilation-induced respiratory alkalosis
- Fainting due to low blood pressure

Non-serious Adverse Events:

- Dizziness or lightheadedness
- Mild headache
- Nausea
- Shortness of breath or feeling of suffocation (initially)
- Muscle cramps or spasms

Benzodiazepine Deprescribing:

Serious Adverse Events:

- Seizures
- Delirium
- Severe rebound anxiety or insomnia
- Suicidal thoughts or behaviors
- Psychosis

Non-serious Adverse Events:

- Mild to moderate withdrawal symptoms, such as anxiety, irritability, or insomnia
- Headaches
- Nausea or gastrointestinal discomfort
- Muscle aches or stiffness
- Changes in appetite or weight

There may be risks and side effects that are currently unknown and/or unanticipated. Because these risks are unlikely given previous studies of these treatments, and most are inherent risks within the general population and not solely due to study procedures, the potential benefits of this study to the individual and society reasonably outweigh the risks.

7.1 Specification of Safety Parameters

We will monitor for all adverse events during the study. The Data Safety and Monitoring officer will monitor and review adverse events. This will include verification that, when indicated, these events have been reported to the appropriate agencies (e.g. IRB) and that such reports have been made in a timely manner. The Officer (TBN) will be a medical physician. Dr. Birdee will also review information on the completeness of data and the rate of patient accrual relative to the protocol timeliness.

We will use the Clinical Institute Withdrawal Assessment – Benzodiazepine (CIWA-B) to evaluate severity of BRZA withdrawal symptoms.⁷ This instrument consists of 17 items that are patient-reported and 5 items that are clinician reported with cumulative scores indicating mild to very severe withdrawal symptoms (total scores range: 0-80). The psychiatric nurse practitioners will assess participants using this instrument at their scheduled visits. We will monitor participants for urgent care, emergency department, and hospital admissions for adverse events related to the study. Moderate and severe withdrawal symptoms or serious adverse events will prompt reporting to the Data Safety Monitoring Committee.

7.2 Adverse Events and Serious Adverse Events

Definition - An adverse event (AE) is any untoward medical occurrence in a subject temporally associated with participation in the clinical study or with use of the experimental agent being studied. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.) or any combination of these.

A Serious Adverse Event (SAE) is any adverse event that results in one or more of the following outcomes:

- Death
- A life-threatening event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- Important medical event based upon appropriate medical judgment

Research staff and treatment providers will document and report solicited AEs. Unsolicited events will be captured through observation by research staff. Research staff will document unsolicited events and report AEs according to data safety monitoring plan. Events will be documented in the RedCap data entry system including date and time of event which will avoid double capture.

Adverse Reporting: The Independent Monitor will monitor and review adverse events, and toxicities and events that may be related to the intervention.

- a) Non-serious adverse events will be reviewed on a monthly basis by the Independent Monitor. The Officer will be notified of serious adverse events within 24 hours of occurrence and reviewed within 48 hours.
- b) Unexpected fatal or life-threatening AEs related to the intervention will be reported to the Grant Administrators (USDen) within 7 days. Other serious and unexpected AEs related to the intervention will be reported to the Grant Administrators within 15 days.
- c) Anticipated or unrelated SAEs will be handled in a less urgent manner but will be reported to the Independent Monitor, IRB, Grant Administrators, and other oversight organizations in accordance with their requirements. In the annual AE summary, the Data Safety Monitor will state that they have reviewed all AE reports.

7.4 Reporting Procedures

Adverse events will be documented by research staff in RedCap. Research staff will notify Dr. Birdee of non-serious adverse events within 24 hours. Dr. Birdee will present all non-serious adverse events to the Data Safety Officer for monthly review. Research staff will notify Dr. Birdee of serious adverse events immediately. Dr. Birdee will notify the Independent Monitor within 24 hours of occurrence, who will review the event within 48 hours. If upon review the SAE is determined to be related to the intervention, Dr. Birdee will report the occurrence to the Grant Administrators in 7 days for unexpected fatal or life threatening AEs and 15 days for other serious and unexpected AEs. After being informed, Dr. Birdee will verify the severity of all AEs. Dr. Birdee will initially assess if the AE is related to the study interventions as definitely, probably, possibly or unrelated. The Independent Monitor will review and confirm the relatedness and severity of AEs. AEs reports will be distributed to the Independent Monitor electronically via email.

7.5 Followup for Adverse Events

AEs will be monitored by the Independent Monitor and Dr. Birdee for recurrences, resolution, and ongoing toxicities that may be related to the intervention. Documentation and reporting for follow-up AEs will occur according to reporting procedures described in Section 7.4. The duration for follow-up will be for the length of the study period while patients are enrolled in the study. If

non-serious adverse events are related to the interventions such as yoga or acupuncture, then the protocol will be modified to avoid adverse events. If the frequency of non-serious adverse events is higher than anticipated or alters the benefit risk ratio, the study investigators after conferring with Independent Monitor, will also modify treatment protocol. Two or more specific adverse events among subjects will prompt modification of the treatment interventions.

7.6 Safety Monitoring

This Human Subjects research study will undergo independent monitoring from the Independent Monitor, which is described in detail in the Data Safety Monitoring Plan (DSMP) under the guidelines provided by the STUDY SPONSER. The Independent Monitor will meet with the PI prior to enrollment of subjects into studies.

8. INTERVENTION DISCONTINUATION

The intervention will be discontinued for a participant if: 1) the intervention is associated with an adverse effect for a specific subject i.e. subject does not tolerate the intervention, 2) the subject no longer is interested or willing to receive the intervention or participate in the study, or 3) the subject's healthcare provider no longer recommends that the patient receive the intervention for medical reasons. The Independent Monitor and the principal investigator will review cases upon occurrence for discontinuation of intervention.

This study will be stopped prior to its completion if: 1) the interventions are associated with adverse effects that call into question the safety of the intervention, or 2) difficulty in study recruitment or retention will significantly impact the ability to evaluate the study endpoints, or 3) any new information becomes available during the trial that necessitates stopping the trial; or 4) other situations occur that might warrant stopping the trial.

Participants will be followed with their permission if the study is discontinued. The duration of follow-up will be length of the proposed study. We will continue to document adverse events, medications, and vital signs during the follow-up period. Temporary discontinuation of the treatment may occur if the participants are absent due to travel/vacation, illness including hospitalization, non-compliance, or difficulties with transportation to sessions. Treatment will continue upon return to regularly scheduled sessions. We will continue to document adverse events and medications during temporary discontinuation.

Subjects may withdraw from the study at any time. Investigators may end the participation of the subject if they no longer qualify, have a serious adverse event, or upon request of the Independent Monitor. To withdraw from the study, subjects will notify Dr. Birdee. At that time, patients will no longer take part in any interventions and no further research data will be collected.

9. STATISTICAL CONSIDERATIONS

9.1 General Design Issues

As the goal of the project is to evaluate feasibility the analyses will be primarily descriptive.

9.2 Sample Size

The goal of this proposal, as specified in the Funding Opportunity Announcement for NCCIH Multi-Site Feasibility Clinical Trials of Mind and Body Interventions, is not to have sufficient power to either measure preliminary effects of study treatments on primary outcomes. We selected our sample size based NCCIH's recommendations to consider "participant flow, budgetary constraints, and number of participants needed to reasonably evaluate goals." A sample size of 30 per each treatment group is considered sufficient to assess feasibility.

9.3. Blinding

As a pilot study, research assistants and investigators will not be blind to treatments.

9.4 Definition of Populations

All analyses will be performed as intention-to-treat. Our intent-to-treat population will include all participants who meet study criteria and are enrolled into the study regardless of receipt of treatments or follow-up assessments.

9.5 Interim Analyses and Stopping Rules

As a feasibility study, we will be conducting interim analyses of outcomes. We will monitor subject accrual, adherence to interventions, and safety during the study period. Dr. Birdee will present data on subject accrual with research staff and the Independent Monitor.

SAE's related to the intervention will suspend enrollment and/or the study intervention until a safety review is convened (either routine or ad hoc) by Independent Monitor to determine whether the study intervention should continue per protocol, proceed with caution, be further investigated, discontinued, or be modified and then proceed. If non-serious adverse events are related to breathing practice, then the breathing protocol will be modified to avoid adverse events. If the frequency of non-serious adverse events is higher than anticipated or alters the benefit risk ratio as determined by the Independent Monitor and the principal investigator, the study investigators will also modify the treatment protocol. Two or more specific adverse events among subjects will prompt modification of the treatment protocol.

9.5 Outcomes

9.5.1. Specific Aim 1. Feasibility of Study Enrollment:

Assessment: We will assess recruitment by documenting the number individuals screened, the number approached to participate, reasons for declining, the number successfully enrolled, and the average time between screening and enrollment. Screening interviews will be conducted via phone calls and in-person visits. We will document the number of withdrawn, lost to follow-up, and complete the study. We will document reasons for withdrawal. Completion of the study will be defined as the number of patients that completed a baseline measurement and completed the 12-week assessments.

Data Analysis: We will describe categories in percentages for reasons individuals decline to participate. We will calculate the percentage of individuals approached to participate who enroll and percentage of those enrolled who complete baseline, 4-, 8-, and 12-week outcome assessments.

We hypothesize that among participants approached and are eligible, 25% will enroll into the study. We estimate that 50% of individuals will meet eligibility criteria at secondary screening, and 25% of eligible individuals will consent. We anticipate 80% completion rate for the study. To achieve recruitment, we anticipate secondary screening on 288 adults, of whom 144 will be eligible and 36 will consent.

9.5.2. Specific Aim 2. Feasibility of Study Treatments:

Fidelity assessment: We will assess fidelity of integrative treatments by having a clinical acupuncturist and yoga therapist not involved in the study observe integrative sessions. Observers will use a fidelity checklist to randomly assess 10 acupuncture and yoga sessions respectively across all study participants. The research team will modify fidelity measures (fidelity checklists) used in prior acupuncture and yoga trials for this proposal. During yoga sessions, yoga therapists will also rate participants' performance using observation rating forms with 4 items using a Likert scale (0-5): 1. willingness of participant in practice, 2. level of engagement, 3. quality of practice, and 4. documentation and rationale for any modifications to protocol.

Fidelity analyses and modifications of study treatments: Based on fidelity checklists, we predict minor variations in the administration of the integrative treatment interventions of acupuncture and yoga. If the fidelity is less than 90%, integrative providers will individually undergo further training with one-to-one tutorials and subsequent observation and re-evaluation of fidelity (in a "teach-to-goal" process).

Adherence Assessment: The psychiatric nurse practitioner, acupuncturist, and yoga therapist will document participants' attendance and duration of sessions. For yoga, participants will be asked to

report characteristics of home yoga practice on a weekly basis (frequency of practice, duration of practice, and time of day).

Adherence Analysis: We will calculate percent attendance as the frequency of participant treatment visits over the total number of possible treatment visits (N=12). We will categorize the level participant attendance as high ($\geq 80\%$), moderate (60-79%), and low ($<60\%$). We will calculate the average weekly frequency of home yoga practice. We will categorize home practice as high (≥ 5), moderate (3-4), and low (<3) weekly frequency.

Acceptability Assessment: After completion of treatment interventions, participants in both treatment arms will rate the acceptability (Acceptability of Intervention Measure), appropriateness (Intervention Appropriateness Measure) and feasibility (Feasibility of Intervention Measure) using three validated instruments respectively.⁸ Each instrument consists of 4 items with scale values ranging from 1 to 5. Responses are averaged for each instrument with higher scores indicating greater acceptability, appropriateness, or feasibility (range 1-20).

In addition, after completion of treatment interventions, participants will be recruited for focus group of 5-10 participants by treatment group to qualitatively assess acceptability. We will offer three focus groups per treatment arm (up to 6 groups). Focus groups will be conducted in collaboration with the Vanderbilt University Qualitative Research Core (QRC). Focus groups will follow a semi-structured script and be facilitated by a stakeholder patient and QRC staff. Focus groups will ask participants a series of open-ended questions focusing on acceptability, attitudes, convenience, and barriers to treatment interventions and study procedures. Focus groups will be audio recorded and transcribed using approved transcription software.

Acceptability Analysis: Participants scores for acceptability, appropriateness and feasibility will be calculated for median with 95% confidence intervals. A median score ≥ 15 will be considered high for acceptability, appropriateness, and feasibility of intervention. The QRC will perform coding and analysis of the focus group transcripts. Focus group data will be supported and analyzed by the QRC in the following steps: 1) Transcription of audio recordings, 2) Coding system development and reliability testing, and 3) Development of a conceptual framework that incorporates existing theory and newly generated material from focus groups.

9.5.3. Specific Aim 3: Data Collection Assessment: Assess the feasibility of outcomes (Primary outcome: BRZA dose reduction, secondary outcomes: insomnia and anxiety) at baseline, 4, 8, and 12 weeks.

Primary outcome - BRZA dose reduction: Prescription doses of BRZA will be extracted from the EHR. Data extraction at VUMC occurs with permission of the Vanderbilt Committee on Opioid Monitoring and Stewardship (VCOMS). The principal investigator presented the project to VCOMS on 4/16/2023 for approval of extraction. Data extraction for outcome assessments will occur after completion of the study for all participants. We will then query the EHR regarding BRZA doses at baseline, 4, 8, and 12 weeks.

Secondary outcome assessments: These questionnaires will be administered on tablets during visits.

Insomnia: We will use the PROMIS Sleep Disturbance computerized adaptive testing (CAT) that has been validated among adults.⁹ This 27-item instrument assesses difficulties staying and falling sleeping.

Anxiety: We will use the PROMIS Anxiety (CAT) that has been validated among adults.¹⁰

Data Collection Analyses: We will estimate feasibility of data collection for study measures by calculating proportion participants from whom we collect primary and secondary outcomes. Data quality will be monitored through the study by assessing for missing data, outliers, and incorrect data entry.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Research will administer a laptop or tablet to collect data through REDCap. Subjects may opt to complete questionnaires online at home. Other data collected regarding enrollment and feasibility of treatment will be entered directly into REDCap.

To protect confidentiality, all data will be stored in a locked file cabinet located in the secured office of the research coordinator. All computers and data files will be password protected. All data processed will be in aggregate form and data collection forms will only be labeled with subject's unique identification number.

10.2 Data Management

The principal investigator will be responsible for data management.

10.3 Quality Assurance

10.3.1 Training

All research staff will have completed the online Collaborative Institutional Training Initiative Training (CITI) prior to participation in research activities. Staff will participate in ongoing monthly workshops offered by the Vanderbilt Human Subjects Protection Program Responsible Conduct of Research-related principles and practices offered through the Human Research Protection Program. Dr. Birdee will directly oversee training of research staff in regards to conducting to the planned research.

10.3.2 Metrics

Dr. Birdee and Dr. Pennings will monitor data collection to assure quality control. Data will be entered into REDCAP, which is a web-based application to support data capture for research studies, allowing assessment of data collection quality including timely and complete data entry. Dr. Birdee will provide monthly updates to the Independent Monitor and research mentors regarding patient recruitment and enrollment.

10.3.4 Protocol Deviations

Protocol deviations will be captured through direct observation by research staff regarding patient recruitment and enrollment, intervention administration, adherence, and safety monitoring. Protocol deviations will be reviewed by the principal investigator and discussed with the research team and as needed with the Independent Monitor.

10.3.5 Monitoring

Dr. Birdee will monitor for protocol compliance, data quality, and review of documentation to assure protocol compliance. This will include review of inclusion/exclusion criteria to insure eligibility (during recruitment), informed consents (upon enrollment, adverse event reporting (upon occurrence), and data collection in REDCap (monthly basis).

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol and the informed consent documents and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for oversight of the study.

11.2 Informed Consent Forms

A signed consent form will be obtained from each participant. For participants who cannot consent for themselves, such as those with a legal guardian (e.g. person with power of attorney), this individual must sign the consent form. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be given to each participant or legal guardian and this fact will be documented in the participant's record.

11.3 Participant Confidentiality

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a locked file cabinet. All computer entry and networking programs will be done

using PIDs only. Information will not be released without written permission of the participant, except as necessary for monitoring by IRB, NIH, and the OHRP.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NIH, or other government agencies as part of their duties to ensure that research participants are protected.

12. Stakeholder engagement

We will engage an advisory panel of stakeholders to help with: (1) Study planning, (2) Conduct the study, (3) Analyze and disseminate results, and plan for the next phase of research.

stakeholders is outlined in the budget justification. Stakeholders will consist of older patients, patients who have received integrative therapies, geriatrician, acupuncturist, yoga therapist, ambulatory pharmacist, and psychiatrist. Stakeholders will review participant information in aggregate and/or without personal identifiers.

Conducting the study

1. Timeline: Months 2-10
2. Meeting frequency: Monthly
3. Activities
 - Review of study progress
 - Focus groups after completion of intervention.

Analyses and Dissemination

1. Timeline: Months 11-12
2. Meeting frequency: Bi-weekly
3. Activities
 - Review results to inform next steps in research
 - Share results to organizations involved with care of older patients

14. REFERENCES

1. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. *JAMA Psychiatry*. 2015;72(2):136-142. doi:10.1001/jamapsychiatry.2014.1763
2. Agarwal SD, Landon BE. Patterns in Outpatient Benzodiazepine Prescribing in the United States. *JAMA Netw Open*. 2019;2(1):e187399. doi:10.1001/jamanetworkopen.2018.7399
3. Johnson PJ, Jou J, Rhee TG, Rockwood TH, Upchurch DM. Complementary health approaches for health and wellness in midlife and older US adults. *Maturitas*. 2016;89:36-42. doi:10.1016/j.maturitas.2016.04.012
4. Wolever RQ, Goel NS, Roberts RS, et al. Integrative Medicine Patients Have High Stress, Pain, and Psychological Symptoms. *Explore N Y N*. 2015;11(4):296-303. doi:10.1016/j.explore.2015.04.003
5. Nielsen A, Teets R, Moonaz S, et al. Group Acupuncture Therapy With Yoga Therapy for Chronic Neck, Low Back, and Osteoarthritis Pain in Safety Net Setting for an Underserved Population: Design and Rationale for a Feasibility Pilot. *Glob Adv Health Med*. 2020;9:2164956120964716. doi:10.1177/2164956120964716
6. Pottie K, Thompson W, Davies S, et al. Deprescribing benzodiazepine receptor agonists: Evidence-based clinical practice guideline. *Can Fam Physician Med Fam Can*. 2018;64(5):339-351.
7. Busto UE, Sykora K, Sellers EM. A clinical scale to assess benzodiazepine withdrawal. *J Clin Psychopharmacol*. 1989;9(6):412-416.

8. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implement Sci IS*. 2017;12(1):108. doi:10.1186/s13012-017-0635-3
9. Buysse DJ, Yu L, Moul DE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. *Sleep*. 2010;33(6):781-792. doi:10.1093/sleep/33.6.781
10. Schalet BD, Pilkonis PA, Yu L, et al. Clinical validity of PROMIS Depression, Anxiety, and Anger across diverse clinical samples. *J Clin Epidemiol*. 2016;73:119-127. doi:10.1016/j.jclinepi.2015.08.036

15. SUPPLEMENTS/APPENDICES

I. Questionnaires

Demographics

	For Office Use Only: CODING COLUMN
1) Birth date:	Demog1
Month Day Year / / 19	/ / 19
2) Gender:	Demog2
1 Male	
2 Female	
3a) Race/ethnicity:	Demog3a
1 Hispanic or Latino	
2 Not Hispanic or Latino	
3b) Race:	Demog3
1 White	
2 Black or African American	
3 Asian	
4 American Indian or Alaskan Native	
5 Native Hawaiian or Other Pacific Islander	
6 More than one race (Please specify):	
7 Other (Please specify):	
4) Primary language:	Demog4
1 English	
2 Other(s) (please specify):	
5) Highest level of education:	Demog5
1 Never in high school	
2 Some high school but did not graduate	
3 High school graduate or GED	
4 Some college or 2 year degree	
5 Graduated from 4 year college	
6 More than 4-years of college	
7 Graduate degree	

6a) What category best describes your current <u>primary</u> living situation: 1 ☐ Live alone 2 ☐ Living with someone in your family or a significant other/partner 3 ☐ Living with others (ie- roommate) 6b) What best describes your current, <u>primary</u> marital status: 1 ☐ Married/significant relationship or partner 2 ☐ Widowed 3 ☐ Divorced 4 ☐ Separated 5 ☐ Single, never been married	Demog6a_____ Demog6b_____
7) What is your most recent annual household income?: 1 ☐ Less than \$15,000 2 ☐ 15,000-24,999 3 ☐ 25,000-34,999 4 ☐ 35,000-49,999 5 ☐ 50,000-74,999 6 ☐ 75,000-99,999 7 ☐ \$100,000 or more 8 ☐ Decline to answer	Demog7_____
8) What is your current employment status?: 1 ☐ Employed/self-employed full-time (>30 hrs/week) 2 ☐ Employed part-time 3 ☐ Student 4 ☐ Homemaker 5 ☐ Volunteer 6 ☐ Disabled 7 ☐ Unemployed 8 ☐ Retired	Demog8_____

Current medications

Please list the **names and doses** of all **medications (prescribed, over-the-counter, or vitamins)** you currently taking.

Name of medication/remedy/supplement	Dose and frequency	Data started (month/year)

For Office Use Only: CODING COLUMN
“1” if med listed, “0” if none listed
MedUse1_____
MedUse2_____
MedUse3_____
MedUse4_____
MedUse5_____
MedUse6_____
MedUse7_____
MedUse8 _____
MedUse9 _____
MedUse10_____
MedUse11_____
MedUse12_____

PROMIS Bank v 1.0 – Anxiety

Please complete the survey below.

Thank you!

FINAL RESULTS

T-score _____

Standard Error _____

EDANX01

In the past 7 days

I felt fearful

☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative) _____

Standard Error (Cumulative) _____

Question Position _____

EDANX02

In the past 7 days

I felt frightened

☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative) _____

Standard Error (Cumulative) _____

Question Position _____

EDANX03

In the past 7 days

It scared me when I felt nervous

☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative) _____

Standard Error (Cumulative) _____

Question Position _____

EDANX05

In the past 7 days

I felt anxious

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX07

In the past 7 days

I felt like I needed help for my anxiety

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX08

In the past 7 days

I was concerned about my mental health

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX12

In the past 7 days

I felt upset

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX13

In the past 7 days

I had a racing or pounding heart.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX16

In the past 7 days

I was anxious if my normal routine was disturbed.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX18

In the past 7 days

It had sudden feelings of panic.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX20

In the past 7 days

I was easily startled.

Never

- ☐
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX21

In the past 7 days

I had trouble paying attention.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX24

In the past 7 days

I avoided public places or activities.

Never

- ☐
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX26

In the past 7 days

I felt fidgety.

Never

- ☐
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX27

In the past 7 days

I felt something awful would happen.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX30

In the past 7 days

I felt worried.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX33

In the past 7 days

I felt terrified.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX37

In the past 7 days

I was worried about other people's reactions to me.
Never

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX40

In the past 7 days

I found it hard to focus on anything other than my anxiety.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX41

In the past 7 days

My worried overwhelmed me.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX44

In the past 7 days

I had twitching or trembling muscles.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX46

In the past 7 days

I felt nervous

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX47

In the past 7 days

I felt indecisive.

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX48

In the past 7 days

Many situations made me worry.

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX49

In the past 7 days

I had difficulty sleeping.

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX51

In the past 7 days

I had trouble relaxing.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX53

In the past 7 days

I felt uneasy.

- ☐ Never
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX54

In the past 7 days

I felt tense.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

EDANX55

In the past 7 days

I had difficulty calming down.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

PROMIS Bank v 1.0 - Sleep Disturbance

Please complete the survey below.

Thank you!

FINAL RESULTS

T-score	
Standard Error	

Sleep105

In the past 7 days

My sleep was restful.	☐ Not at all
	☐ A little bit
	☐ Somewhat
	☐ Quite a bit
	☐ Very Much

T-score (Cumulative)	
Standard Error (Cumulative)	
Question Position	

Sleep107

In the past 7 days

My sleep was deep.	☐ Not at all
	☐ A little bit
	☐ Somewhat
	☐ Quite a bit
	☐ Very Much

T-score (Cumulative)	
Standard Error (Cumulative)	
Question Position	

Sleep115

In the past 7 days

I was satisfied with my sleep.	☐ Not at all
	☐ A little bit
	☐ Somewhat
	☐ Quite a bit
	☐ Very Much

T-score (Cumulative)	
Standard Error (Cumulative)	
Question Position	

Sleep116

In the past 7 days

My sleep was refreshing.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep109

In the past 7 days

My sleep quality was...

- ☐ Very poor
- ☐ Poor
- ☐ Fair
- ☐ Good
- ☐ Very good

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep110

In the past 7 days

I got enough sleep.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep42

In the past 7 days

It was easy for me to fall asleep.

Never

- ☐
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep45

In the past 7 days

I laid in bed for hours waiting to fall asleep.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep50

In the past 7 days

I woke up too early and could not fall back asleep.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep87

In the past 7 days

I had trouble staying asleep.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep90

In the past 7 days

I had trouble sleeping.

Never

- ☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep92

In the past 7 days

I woke up and had trouble falling back to sleep.

- ☐ Never
☐ Rarely
☐ Sometimes
☐ Often
☐ Always

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep106

In the past 7 days

My sleep was light.

- ☐ Not at all
☐ A little bit
☐ Somewhat
☐ Quite a bit
☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep108

In the past 7 days

My sleep was restless.

- ☐ Not at all
☐ A little bit
☐ Somewhat
☐ Quite a bit
☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep125

In the past 7 days

I felt lousy when I wake up.

- ☐ Not at all
☐ A little bit
☐ Somewhat
☐ Quite a bit
☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep20

In the past 7 days

I had a problem with my sleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep44

In the past 7 days

I had difficulty falling asleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep67

In the past 7 days

I worried about not being able to fall asleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep68

In the past 7 days

I felt worried at bedtime.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep69

In the past 7 days

I had trouble stopping my thoughts at bedtime.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep65

In the past 7 days

I felt physically tense at bedtime.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep71

In the past 7 days

I had trouble getting into a comfortable position to sleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep72

In the past 7 days

I tried hard to get to sleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep78

In the past 7 days

Stress disturbed my sleep.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep70

In the past 7 days

I felt sad at bedtime.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep86

In the past 7 days

I tossed and turned at night.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Sleep93

In the past 7 days

I was afraid I would not get back to sleep after waking up.

- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ Quite a bit
- ☐ Very Much

T-score (Cumulative)

Standard Error (Cumulative)

Question Position

Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), & Feasibility of Intervention Measure

Response Scale: 1 = Completely disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree, 5 = Completely agree

Scoring Instructions: Scales can be created for each measure by averaging responses. Scale values range from 1 to 5. No items need to be reverse coded.

Acceptability of Intervention Measure (AIM)

- 1) [Triple P/Implementation Strategy] meets my approval.
- 2) [Triple P/Implementation Strategy] is appealing to me.
- 3) I like [Triple P/Implementation Strategy].
- 4) I welcome [Triple P/Implementation Strategy].

Intervention Appropriateness Measure (IAM)

- 1) [Triple P/Implementation Strategy] seems fitting.
- 2) [Triple P/Implementation Strategy] seems suitable.
- 3) [Triple P/Implementation Strategy] seems applicable.
- 4) [Triple P/Implementation Strategy] seems like a good match.

Feasibility of Intervention Measure (FIM)

- 1) [Triple P/Implementation Strategy] seems implementable.
- 2) [Triple P/Implementation Strategy] seems possible.
- 3) [Triple P/Implementation Strategy] seems doable.
- 4) [Triple P/Implementation Strategy] seems easy to use.

Assessment of concomitant interventions

1. Have you started any new treatments for your health in the last 1 month? New treatments may include new medicines/supplements/herbs, procedures, or referrals to new health care providers, or other therapies.

Medications	Frequency	Data Started (month, day, year)
Procedures		
Referrals		
Other		

2. Have you started any new activities for your health in the last 1 month? New activities may include new types of exercise, participating in groups (such as group therapy, support groups, nutrition groups) or therapy (such as physical therapy, psychotherapy/psychologist), or other activities.

Exercise	Frequency	Data Started (month, day, year)
Groups		
Therapy		
Other		