Multicomponent Behavioral Sleep Intervention for Insomnia in Older Adults with Mild Cognitive Impairment

PI: Miranda V. McPhillips

NCT04364191

IRB PROTOCOL#: 832826

Date of Document: March 15, 2023

Institutional Review Board
3600 Civic Center Blvd., 9th Floor
Philadelphia, PA 19104
Phone: 215-573-2540
(Federalwide Assurance # 00004028)

DATE: 15-Mar-2023
TO: Miranda V Mcphillips
CC: Foo, Stephanie
Delahanty, Michelle

RE:
IRB PROTOCOL#: 832826
PROTOCOL TITLE: Multicomponent Behavioral Sleep Intervention for Insomnia in Older Adults with Mild Cognitive Impairment

SPONSOR: NO SPONSOR NUMBER
REVIEW BOARD: IRB #8

IRB AMENDMENT: NOTICE OF APPROVAL

Dear Dr. Mcphillips,

The documents noted below, for the above-referenced protocol, were reviewed by the Institutional Review Board using the expedited procedure set forth in 45 CFR 46.110 and approved on 14-Mar-2023.

Consistent with the regulations set forth in 45 CFR 46.109(f), continuing review of this research is not required. IRB approval of this protocol will not expire and continuing review applications should not be submitted. However, you are still required to submit modifications and reportable events to the IRB for review.

The documents included with the application noted below are approved:

-HSERA modification submission (confirmation # dicaaaje) submitted 3/1/2023

ONGOING REQUIREMENTS:

- You must obtain IRB review and approval under 45 CFR 46 if you make any changes to the protocol, consent form, or any other study documents subject to IRB review requirements. Implementation of any changes cannot occur until IRB approval has been given.
- Reportable event, such as serious adverse events, deviations, potential unanticipated problems, and reports of non-compliance must be reported

to the IRB in accordance with Penn IRB SOP RR 404.

- When enrolling subjects at a site covered by the University of Pennsylvania's IRB, a copy of the IRB approved informed consent form with the IRB approved from/to stamp must be used unless a waiver of written documentation of consent has been granted.

COMMITTEE APPROVALS: You are responsible for assuring and maintaining other relevant committee approvals. This human subjects research protocol should not commence until all relevant committee approvals have been obtained.

If your study is funded by an external agency, please retain this letter as documentation of the IRB's determination regarding your proposal.

If you have any questions about the information in this letter, please contact the IRB administrative staff. A full listing of staff members and contact information can be found on our website: http://www.irb.upenn.edu

***This letter constitutes official University of Pennsylvania IRB correspondence. ***

Modification

Basic Info

Confirmation Number:	**dicaaaje**
Protocol Number:	**832826**
Created By:	**MCPHILLIPS, MIRANDA V**
Principal Investigator:	**MCPHILLIPS, MIRANDA V**
Protocol Title:	**Multicomponent Behavioral Sleep Intervention for Insomnia in Older Adults with Mild Cognitive Impairment**
Short Title:	**MBSI-I in MCI**
Protocol Description:	**This pilot randomized controlled trial will test a brief (4 week), tablet-based, personalized, multicomponent behavioral sleep intervention for insomnia (MBSI-I) in older adults with MCI, compared to a sleep education control. Study assessments will be performed at pre-treatment (baseline), post-treatment (four weeks) and at 12 weeks post treatment follow-up.**
Submission Type:	**Social and Biological Sciences**
Application Type:	**EXPEDITED Category 2 and Category 4**

PennERA Protocol Status

Approved

Resubmission*
No

Are you submitting a Modification to this protocol?*

Yes

Current Status of Study

Study Status

Closed to subject enrollment (remains active)

If study is currently in progress, please enter the following

Number of subjects enrolled at Penn since the study was initiated

27

Actual enrollment at participating centers

0

If study is closed to further enrollment, please enter the following

Number of subjects in therapy or intervention

13

Number of subjects in long-term follow-up only

0

IRB Determination
If the change represents more than minimal risk to subjects, it must be reviewed and approved by the IRB at a convened meeting. For a modification to be considered more than minimal risk, the proposed change would increase the risk of discomfort or decrease benefit. The IRB must review and approve the proposed change at a convened meeting before the change can be implemented unless the change is necessary to eliminate an immediate hazard to the research participants. In the case of a change implemented to eliminate an immediate hazard to participants, the IRB will review the change to determine that it is consistent with ensuring the participant′s continued welfare. Examples: Convened Board Increase in target enrollment for investigator initiated research or potential Phase I research Expanding inclusion or removing exclusion criteria where the new population may be at increased risk Revised risk information with active participants Minor risk revisions that may affect a subject′s willingness to continue to participate Expedited Review Increase in target enrollment at Penn where overall enrollment target is not exceeded or potentially sponsored research Expanding inclusion or removing exclusion where the new population has the same expected risk as the previous, based on similarities of condition Revised risk information with subjects in long-term follow-up Minor risk revisions with no subjects enrolled to date
Expedited Review

Modification Summary
Please describe any required modification to the protocol. If you are using this form to submit an exception or report a deviation, enter 'N/A' in the box below.
We initially planned to power the study on two primary outcomes, sleep latency and health related quality of life and required a sample size of 40. However, given that this is a pilot study, Covid-19 and other time constraints, we decided to power the study on our main primary outcome of sleep latency. Our new sample size requirement is 27. We would like to change our analysis plan. For continuous outcomes, both mixed-effects model and GEE approach provide population average estimates. Even though we proposed to use mixed-effects models with random slopes and random intercepts in our original proposal, we feel that we may run into issues with model convergence and model estimation especially for model with random slope due to smaller sample size. Since GEE with exchangeable covariance matrix is less likely to suffer from model convergence issue, we decided to change from mixed-model to GEE. The estimates from mixed-model with only random-intercept and GEE with exchangeable covariance matrix should be very similar and both of these models. For categorical outcomes, since mixed-model provides subject level estimate and GEE provides population averaged estimates changing from one to another would be answering two different questions. But our outcome is continuous and both approaches will provide population averaged estimate, using either mixed-effects model or GEE is appropriate.

Risk / Benefit
Does this amendment alter the Risk/Benefit profile of the study?
No

Change in Consent
Has there been a change in the consent documents?
No

If YES, please choose from the options below regarding re-consenting

Deviations

Are you reporting a deviation to this protocol?*

No

Exceptions

Are you reporting an exception to this protocol?*

No

Protocol Details

Resubmission*
Yes

Hospital Sites
Will any research activities and/or services be conducted at a Penn Medicine affiliated hospital site?
No

Study Personnel

Principal Investigator

Name:	**MCPHILLIPS, MIRANDA V**
Dept / School / Div:	**602 - Biobehavioral and Health Sciences**
Campus Address Mail Code	
Address:	**149 ROSE LANE**
City State Zip:	**SPRINGFIELD PA 19064-0000**
Phone:	**484-631-5397**
Fax:	**-**
Pager:	
Email:	**mvarr@nursing.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed :	

Study Contacts

Name:	**FOO, STEPHANIE**
Dept / School / Div:	**602 - Biobehavioral and Health Sciences**
Campus Address Mail Code	
Address:	
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	**sfoo@upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**02/16/2024**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Name:	**DELAHANTY, MICHELLE**
Dept / School / Div:	**602 - Biobehavioral and Health Sciences**
Campus Address Mail Code	
Address:	
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**02/11/2024**
Name of course completed :	**Penn CR: Full Onboarding: Good Clinical Practice: An Introduction to ICH GCP Guidelines (2HRS)**

Other Investigator

Name:	**HODGSON, NANCY A**
Dept / School / Div:	**602 - Biobehavioral and Health Sciences**
Campus Address Mail Code	
Address:	**418 Curie Blvd.**
City State Zip:	**Philadelphia PA 19104-4217**
Phone:	**215-898-8413**
Fax:	**-**
Pager:	
Email:	**hodgsonn@nursing.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**12/15/2023**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Responsible Org (Department/School/Division):

602 - Biobehavioral and Health Sciences

Key Study Personnel

Name:	**WARD, JACK**
Department/School/Division:	**DM-Geriatrics**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**CONI, JANI J**
Department/School/Division:	**DM-Geriatrics**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**09/13/2024**
Name of course completed:	**Penn CR: Full Onboarding: Good Clinical Practice: An Introduction to ICH GCP Guidelines (2HRS)**

Name:	**GOONERATNE, NALAKA**
Department/School/Division:	**DM-Geriatrics**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**POR Recertification Quiz - Full Board Review - SOM**
GCP Training Completed:	**Yes**
Training Expiration Date:	**01/21/2024**
Name of course completed:	**Good Clinical Practice (GCP) for the Experienced Investigator - OCR**

Name:	**CHANDAKA, ASHA**
Department/School/Division:	**DM-Geriatrics**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**09/12/2024**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Name:	**PACK, ALLAN I**
Department/School/Division:	**DM-Sleep Medicine**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**POR Recertification Quiz - Full Board Review - SOM**
GCP Training Completed:	**Yes**
Training Expiration Date:	**05/19/2025**
Name of course completed:	**CITI Good Clinical Practice (GCP) - OCR**

Disclosure of Significant Financial Interests*
Does any person who is responsible for the design, conduct, or reporting of this research protocol have a **FINANCIAL INTEREST**?
No

Penn Intellectual Property*
To the best of the Principal Investigator's knowledge, does this protocol involve the testing, development or evaluation of a drug, device, product, or other type of intellectual property (IP) that is owned by or assigned to the University of Pennsylvania?
No

Certification
I have reviewed the *Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials* and the *Financial Disclosure Policy for Research and Sponsored Projects* with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

Study Instruments

Discuss the particulars of the research instruments, questionnaires and other evaluation instruments in detail. Provide validation documentation and or procedures to be used to validate instruments. For well know and generally accepted test instruments the detail here can be brief. More detail may be required for a novel or new instrument. For ethnographic studies identify any study instruments to be used (i.e. for deception studies) and describe in detail where, when and how the study will be conducted and who or what are the subjects of study. Note: For more information on how to conduct ethical and valid ethnographic research, follow the link For oral histories or interviews provide the general framework for questioning and means of data collection. If interviews or groups settings are to be audio taped or video taped describe in detail the conditions under which it will take place. Include a copy of any novel or new test instruments with the IRB submission.

Sleep Measures: Consensus Sleep Diary (electronic version). We will derive sleep latency, wake after sleep onset, sleep efficiency, total sleep time, and daytime napping; Actigraphy will be used objectively assess various variables such as leep latency, wake after sleep onset, sleep efficiency, total sleep time, and daytime inactivity; Insomnia Severity Index (ISI),a widely used measure of insomnia; Pittsburgh Sleep Quality Index (PSQI), a widely used measure of sleep quality; Epworth Sleepiness Scale, a widely used measure of daytime sleepiness; Pre-sleep Arousal Index, this measure has been shown to change with relaxation and mindfulness training based on prior work performed by Dr. Gooneratne; Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16), a validated instrument to assess maladaptive beliefs regarding sleep that exacerbate insomnia, and has been shown to improve with insomnia treatment; the 16-item version will be used as it has more favorable psychometric properties than the 30-item or 10-item versions. Quality of Life: RAND Medical Outcomes Study Short Form-36 (SF-36), one of the most widely used health-related quality of life measures, frequently used to measure HRQOL in older adults. It is a multidomain that measures physical and mental components of HRQOL with eight subscales. The 8 subscales contribute to two resulting component summaries: a mental component summary (MCS) and a physical component summary (PCS). Both PCS and MCS scores range from 0 to 100, representing worst to best health. Higher scores indicate better HRQOL. Global Activity: Pleasant Events Schedule; participants will rate how often they do certain activities and how much they enjoy it. Results will guide the tailoring of the intervention. Physical Activity: Objective PA, characterized by mean level of physical activity (counts/minute), will be measured by Actigraphy. Subjective PA will be obtained from the Physical Activity Scale for the Elderly (PASE). Cognition: Telephone interview for Cognitive Status (TICS). TICS is a standardized test of cognitive function that can be administered over the phone or in person. Participants are given a TICS Total Score which is associated with one of four impairment ranges: Unimpaired, Ambiguous, Mildly Impaired, and Moderately to Severely Impaired. TICS-M scores of 28-36, based off ranges and optimal cutpoints determined in various studies, will determine eligible participants. (Graff-Radford wt al., 2006; Cook et al., 2009; Zietemann et al., 2017; Knopman et al., 2010). Social Activity: Participation in social activity will be recorded in the tablet. Systemic inflammatory biomarkers, including cytokines (IL-6, IL-1ß, TNF-) and C-reactive protein (CRP), will be assessed at baseline, post-intervention and 3 month post intervention follow up. These will be assayed using dried blood spots (DBS). DBS provides an easy to obtain, transport, and analyze blood source. (Ostler MW, Porter JH, Buton OM. Dried blood spot collection of health biomarkers to maximize participation in population studies. Journal of Visualized Experiments, 83, 50973.) Participants will be instructed to use a Lancet to prick their finger and drop five drops of blood onto filter paper. They will keep the filter paper with blood spots lying flat and uncovered at room temperature to 24-48 hours to let the blood spots dry before putting in a biohazard bag with a dissicant. After 48 hours and until sample pick up, they will place in the refrigerator. After pickup, the blood sample will be labeled, transported, and stored in a -80°C freezer until ready to be analyzed. All four biomarkers will be stored at Laboratory of Innovative and Translational Nursing Research and then assayed at CHOP Translational Core Laboratory utilizing a matrix independent platform (Mesoscale Discovery, Rockville MD). Other information includes age, race, education, life style (tobacco and alcohol use, BMI), depression (15-item GDS-SF 132,133 has been validated as an assessment of depression, with a yes/no format that facilitates use), medication use (antidepressant, benzodiazepine, sleep medication), and self-reported medical conditions. This information will be collected via questionnaires.

Group Modifications
Describe necessary changes that will or have been made to the study instruments for different groups.
No modifications will be made.

Method for Assigning Subjects to Groups
Describe how subjects will be randomized to groups.
The proposed study is a randomized controlled non-crossover pilot study in which 27 participants will be allocated in a 1:1 ratio to the MBSI-I intervention arm or an education only control arm for a treatment period of four weeks. Assignment by 1:1 simple randomization will occur via the Randomization module in REDCap. A randomization table will be designed and uploaded to the REDCap system, to reflect 1:1 simple randomization.

Administration of Surveys and/or Process
Describe the approximate time and frequency for administering surveys and/or evaluations. For surveys, questionnaires and evaluations presented to groups and in settings such as high schools, focus group sessions or community treatment centers explain how the process will be administered and who will oversee the process. For instance, discuss the potential issues of having teachers and other school personnel administer instruments to minors who are students especially if the content is sensitive in nature. Describe the procedure for audio and videotaping individual interviews and/or focus groups and the storage of the tapes. For instance, if audio tape recording is to be used in a classroom setting, describe how this will be managed if individuals in the class are not participating in the study. Explain if the research involves the review of records (including public databases or registries) with identifiable private information. If so, describe the type of information gathered from the records and if identifiers will be collected and retained with the data after it is retrieved. Describe the kinds of identifiers to be obtained, (i.e. names, social security numbers) and how long the identifiers will be retained and justification for use.
Baseline (pre-treatment) assessments, collected at Visit 1, subjective sleep measures and measures of health related quality of life, physical activity, cognition, social activity, and blood samples. Intervention: A 4-week intervention (see intervention description below) will be provided to participants randomized to the intervention group. Sleep diaries will be completed and Actigraphs worn for all four weeks of treatment, in both groups. Post-intervention and Follow-up data collection (visit 2 week 5; visit 3 week 16): All baseline assessments will be repeated immediately post- intervention and at three months post-intervention follow-up (sleep measures and measures of health related quality of life, physical activity, cognition, social activity, and blood samples; one week sleep diary + actigraphy). Data on demographics and other information (age, race, education, life style (tobacco and alcohol use, BMI), depression, medication use (antidepressant, benzodiazepine, sleep medication), and self-reported medical conditions will be assessed by questionnaires at baseline, post-intervention and follow-up. All source documents (questionnaires) will be collected directly from the patient using the secure web portal that will be developed for this study. This data will be stored in the electronic clinical trials software application, REDCap. This application is compliant with FDA guidelines for clinical trials software (e.g. data encryption, electronic signatures, and internal audit trail capabilities). The application and data are stored on HIPAA compliant servers. The REDCap application also can manage study logistics to ensure timely scheduling of study visits, supports double-data entry procedures, and robust data analysis features to monitor study participant recruitment and retention rates. Physiologic data, such as the accelerometer data, will be uploaded, in a de-identified form (no personal identifiers except for an identification number), to the Actiware software on a password protected laptop on a protected server. Data collected from the tablet will be collected in de-identified form, transmitted to the same University of Pennsylvania servers, where it will be stored and backed-up. Sleep diaries will be completed by the participants via tablet using MyCap, a feature of REDCap. No audio or video recordings will be made.

Data Management
Describe how and who manages confidential data, including how and where it will be stored and analyzed. For instance, describe if paper or electronic report forms will be used, how corrections to the report form will be made, how data will be entered into any database, and the person(s) responsible for creating and maintaining the research database. Describe the use of pseudonyms, code numbers and how listing of such identifiers will be kept separate from the research data.
We will apply strict procedures to maintain confidentiality and will adhere to 2003 HIPAA Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule). Each individual participant will be given a unique study identification number in REDCap. Information linking the

identification number to the participant will be stored on the HIPAA compliant servers (see more below regarding REDCap). REDCap project access will only be granted to the research team who had been approved by this IRB. All project records not included in REDCap will reflect only the ID number of each participant. Thus, research study participants names will not appear on any forms, and instead participants will use a unique identification number. The REDCap (Research Electronic Data Capture) system will be used as a central resource for quantitative data processing and management. REDCap is a web application and back-end database model designed to support data capture for research studies. The University of Pennsylvania has licensed its own version of REDCap that is housed on our own password-protected servers located within a data center inside the Penn firewall and therefore afforded the same network protections as other sensitive clinical systems. REDCap was developed specifically around HIPAA-security guidelines with features such as data encryption. It provides an intuitive interface for data entry with data validation, audit trails for tracking data manipulation and export procedures, automated export procedures for seamless data downloads to common statistical packages, including SAS, and procedures for importing data from external sources. We will use standard operating procedures to guide all data management activities, such as the naming and identification of variables, data cleaning and handling of missing data. All data obtained from self-report measures will be entered directly into the REDCap database on encrypted laptop computers as collected to reduce data collection time, increase accuracy, and prevent data loss. Data entry screens will be designed to incorporate range checks and concurrent checks to minimize errors. Missing fields will not be allowed. We will be using the Ditti application, rather than the mPhenomic platform. The new application is easier to use for older adults. The application does not collect personal identifiable information. Each user is assigned a randomized user ID that is only linked to the participant in REDCap. The app does not collect or provide any medical data. The only data collected from the app includes randomly generated ID for each ID, tap timestamps, and timestamps of when the app was opened. Again, there is no PHI or any way to link the participant to the data from the application.

Radiation Exposure*

Are research subjects receiving any radiation exposure solely because they are enrolled in this protocol? (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.)?IF YES, the protocol must be approved by the RRSC (Radiation Research Safety Committee). Consult EHRS web site: www.ehrs.upenn.edu/protocols/radiohuman.html for more information.If you have questions, email jjesik@ehrs.upenn.edu or kavyap@upenn.eduIf your protocol includes Nuclear Medicine Procedures, the protocol must be reviewed by the Nuclear Med Operations Committee: https://redcap.link/NMOPS

No

Human Source Material*

Does this research include collection or use of human source material (i.e., human blood, blood products, tissues or body fluids)? IF YES, consult the EHRS web site: www.ehrs.upenn.edu/programs/bio/bbpathogens.html for information on OSHA Bloodborne Pathogens requirements (training, vaccination, work practices and Exposure Control Plan). If you have questions, call 215-898-4453.

Yes

Image Guided Biopsies*

Does the research involve imaging guided biopsy? IF YES, please contact the Clinical Imaging Core. See https://www.med.upenn.edu/cbi for more details. Any questions should be directed to the Director of Research Operations, Dept of Radiology, Kathleen Thomas.

No

Computerized Tomography (CT) Studies*

Does the protocol involve CT scans that are not considered standard of care and are being performed for research purposes?IF YES, complete the CACTIS Committee Application: https://is.gd/CACTIS and consult CACTIS website: http://www.uphs.upenn.edu/radiology/research/labs/cactis/ for application requirements.

No

CAMRIS and MRI Studies*

Is an MRI scan being performed for research only and NOT considered standard of care (example: specific scanner, parameters or solely for the purposes of research)?NOTE: Research/non-standard use of MRI may include but is not limited to any of the following: Situations in which MRI results may impact subjects current clinical care plan or treatment decisions, such as:The study requires a

customized report with specifics regarding the study protocol (i.e., specific measurements or details); Introduction of a device of any kind during the MRI that is not used during a 'standard of care' type scan.Your MRI is not consistent with standard care time points for MRI imaging.Your MRI is not paid for by insurance.IF YES, consult CAMRIS website: https://www.med.upenn.edu/camris/application-and-faq.html for application requirements and required institutional consent form language.
No

Cancer Related research not being conducted by an NCI cooperative group*
Does this protocol involve cancer-related studies in any of the following categories? Therapeutic, Prevention, Supportive Care, Screening, Early Detection, or Diagnostic, Epidemiologic, Observational, Outcome, Ancillary or Correlative. For a description of these categories, see http://www.ctsrmc.org/submitting_a_protocol.php NCI Cooperative Groups are as follows:Alliance for Clinical Trials in OncologyNCI Clinical Trials Group (Canadian Cancer Society) (NCCTG)Children's Oncology Group (COG)NRG Oncology GroupECOG-ACRIN Cancer Research GroupSouthwest Oncology Group (SWOG) IF YES, the protocol must be submitted to the Cancer Center's Clinical Trials Scientific Review Committee for scientific review and approval prior to obtaining IRB approval. Consult the CTSRMC website: www.ctsrmc.org for application requirements
No

HIPAA / Protected Health Information
Does the research proposal involve accessing (viewing / using), collecting, or disclosing of protected health information (PHI) directly from participants or their medical or dental record for research purposes?
Yes

CHPS Resources*
Does the research involve CHPS resources?
No

HUP Inpatient Nursing Resources
Does this research include an inpatient admission at HUP?
No

If the answer is YES, indicate which items is is provided with this submission:

Modified research informed consent document that incorporates HIPAA requirements

Use of UPHS services*
Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures , whether considered routine care or strictly for research purposes? (UPHS includes all Penn hospitals and clinical practices, including the Clinical Care Associates network of community practices). Examples of UPHS services/tests/procedures includes the Clinical Translational Research Center (CTRC), laboratory tests, use of the pathology lab, cardiovascular imaging tests or radiology imaging tests (whether being billed via the Service Center or through UPHS), other diagnostic tests & procedures and associated professional services, etc.
No

Veteran's Affairs (VA) Patients or Subjects
Does your study involve data from Veteran's Affairs (VA) patients or subjects?
No

If yes, was this approved by the Philadelphia VA?

No

Out of State Research
Will any Penn personnel conduct any research activities outside of the State of Pennsylvania?
No

Research involving Virtua Health
Will any Penn personnel conduct any research activities at a Virtua Health site location, OR in

collaboration with Virtua Health System personnel, OR using any Virtua Health System resources (e.g., medical records)?
No

Primary Focus*
Clinical Trial (prospectively assigning subjects to health-related interventions to evaluate outcomes)

Protocol Interventions

x	**Sociobehavioral (i.e. cognitive or behavioral therapy)**
	Drug
	Device - therapeutic
	Device - diagnostic (assessing a device for sensitivity or specificity in disease diagnosis)
	Surgical
	Diagnostic test/procedure (research-related diagnostic test or procedure)
	Obtaining human tissue for basic research or biospecimen bank
	Survey instrument
	None of the above

The following documents are currently attached to this item:

There are no documents attached for this item.

Sponsors

Business Administrator

Name:	**LIU, CHIU-FANG**
Dept / School / Div:	**631 - Office of Nursing Research**
Phone:	**215-898-8413**
Fax:	**-**
Pager:	
Email:	**chiufang@nursing.upenn.edu**

Department budget code

000 - 000 - 0 - 000000 - 0000 - 0000 - 0000

Funding Sponsors

Funding sponsors billing address
If you have selected a commercial or industry sponsor, please provide the appropriate address and contact information for the Sponsor for the purposes of billing for IRB review fees (initial review, continuing review and convened modification fees apply here). If the Sponsor is not industry/ commercial, this information is not necessary to provide with your application.

Funding sponsors gift
Is this research being funded by a philanthropic gift?

Regulatory Sponsor

IND Sponsor

none

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Industry Sponsor

None

Project Funding*
Is this project funded by or associated with a grant or contract?
Yes

Selected Proposals

Proposal No	Title
10067882-01	**Multicomponent Behavioral Sleep Intervention for Insomnia in Older Adults with Mild Cognitive Impa**

Sponsor Funding
Is this study funded by an industry sponsor?
No

Status of contract

The following documents are currently attached to this item:

There are no documents attached for this item.

Multi-Center Research

Penn as lead
1. Is this a multi-center study where Penn is serving as the Lead Site or the Penn PI is serving as the Lead Investigator?
No

Management of Information for Multi-Center Research

Penn irb of record
2. Is this a multi-center study where the Penn IRB will be asked to serve as the IRB of Record for other external study sites?
No

Other Sites

No other sites

Protocol

Abstract
Insomnia symptoms in older adults with mild cognitive impairment represent a significant public health burden in terms of impaired quality of life, risks from untreated insomnia, and risks from pharmaceutical insomnia treatment. To address the limitations in the most effective non-pharmacological treatments for insomnia in older adults with mild cognitive impairment, a randomized pilot study will be conducted to test a brief (4 week), tablet-based, personalized, multicomponent behavioral sleep intervention for insomnia, compared to a sleep education control, in this at-risk group.

The findings of the proposed project will inform future, larger scale clinical trials and may provide a novel and innovative way for older adults with mild cognitive impairment to achieve better sleep and health-related quality of life outcomes.

Objectives

Overall objectives
1) Determine the preliminary immediate (one month) and sustained efficacy (3 months) of MBSI-I compared to sleep education on sleep related outcomes. 2) Determine the preliminary immediate (one month) and sustained efficacy (3 months) of MBSI-I compared to sleep education on health related quality of life. 3) Exploratory Aim: To explore the mechanisms by which MBSI-I affects sleep and health related quality of life

Primary outcome variable(s)
Sleep latency: measured at baseline, immediately post intervention (4 weeks) and 3 months post-intervention (16 weeks). Sleep latency will be derived from subjective sleep diaries and referes to the time it takes a person to fall asleep, starting from the first intention to sleep. Health-related quality of life, measured at baseline, immediately post intervention (4 weeks) and 3 months post-intervention (16 weeks). Health related quality of life is a multi-dimensional concept that includes domains related to physical, mental, emotional and social functioning. We will use the RAND Medical Outcomes Study Short Form-36 (SF-36), one of the most widely used health-related quality of life measures frequently used to measure HRQOL in older adults. It is a multidomain that measures physical and mental components of HRQOL with eight subscales. The 8 subscales contribute to two resulting component summaries, a mental component summary (MCS) and a physical component summary (PCS). Both PCS and MCS scores range from 0 to 100, representing worst to best health. Higher scores indicate better HRQOL.

Secondary outcome variable(s)
Additional sleep outcomes include wake after sleep onset, total sleep time, sleep efficiency, sleep quality and insomnia symptoms, measured with Actigraphy, sleep diary and other validated sleep questionnaires. These variables are measured at baseline, immediately post intervention (4 weeks) and 3 months post-intervention (16 weeks). We will explore the mechanisms by which the intervention affects sleep and health related quality of life measures via standardized questionnaires and inflammatory biomarkers.

Background
Healthy sleep is critical for optimizing health related quality of life, including physical, social, emotional, and cognitive domains while untreated sleep disturbances can result in physical, psychological, social, and economical impairments. Insomnia is the most common sleep disturbance in older adults and is characterized by difficulty initiating or maintaining sleep, awakening too early, and next day consequences such as difficulty concentrating. Epidemiological studies of older adults have reported insomnia prevalence of 10-40%;8 yet, less than 15% of patients with insomnia consult a healthcare provider or receive treatment. Furthermore, it is estimated that 7% to 20% of older adults have mild cognitive impairment (MCI) and 60% of people with MCI have some sleep disturbances. MCI is a degenerative condition characterized by cognitive decline; insomnia symptoms are bidirectionally linked to cognitive decline. Insomnia is often managed with pharmacologic agents which can be associated with adverse medical complications; memory impairments make treating insomnia even more challenging. Cognitive behavioral therapy is the most widely used nonpharmacological treatment for insomnia and although efficacious in older adults has potential challenges in people with MCI. Thus, it is critical to develop and test interventions that are brief and accessible to improve insomnia in this growing at-risk population.

Study Design

Phase*
Phase I

Design
The proposed study is a randomized controlled non-crossover pilot study in which 40 subjects will be allocated in a 1 to 1 ratio to the MBSI-I intervention arm or an education only control arm for a

treatment period of four weeks. All study consents and education regarding the intervention will take place via telephone and video-conferencing calls. Questionnaires will be completed via REDCap.

Study duration
The new, updated study protocol will be conducted over a two year period; the first few months have been devoted to establishing study databases, study operating procedures (SOP) and other logistic study initiation steps related to the Covid-19 protocol changes. Subject recruitment will begin in month four and continue during year 2, concluding in month 10 of year 3 (a total of two and a half years of subject recruitment, which is adequate to enroll 27 subjects). The final 3 months of year 3 will be devoted to data analysis and manuscript writing. The project will begin once we have IRB approval. Participants will be in the study for a total of 17 weeks, including baseline visit, intervention, post-intervention and three month follow-up.

Resources necessary for human research protection
Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Please allow adequate time for the researchers to conduct and complete the research. Please confirm that there are adequate facilities for the research.
The study team includes Dr. McPhillips, PhD, RN, faculty at the University of Pennsylvania, School of Nursing and her mentoring team: 1) Primary mentor: Dr. Nancy A. Hodgson, PhD, RN, FAAN (NH) is a Professor in the Department of Biobehavioral Health and the Anthony Buividas Endowed Term Chair in Gerontology at the Penn School of Nursing. She is an expert in clinical trials and the development and translation of biobehavioral sleep interventions to ease symptom burden for cognitively frail older adults and the study of the physiologic mechanism underlying the effect of behavioral interventions to reduce symptom distress. 2) Co-mentor: Dr. Nalaka S. Gooneratne, M.D, M.Sc. (NG) is an Associate Professor at the Penn School of Medicine, Division of Geriatric Medicine and the Center for Sleep and Respiratory Neurobiology, Associate Director of the Masters in Translational Research program, and Director of the mHealth mobile app development service. He is an expert in geriatric sleep research and mobile device technology. 3) Co-mentor: Dr. Allan Pack, MBChB, PhD, FRCP (AP) is a Professor of Medicine at Penn, Director of the Center for Sleep and Circadian Neurobiology (CSCN), and Chief of the Division of Sleep Medicine. Dr. Pack is a leader in the field of sleep medicine and has a primary focus on sleep, chronobiology and biomarker research. All investigators have a certificate of completion for required education on the protection of human research participants and meet the NIH criteria for continued training in responsible conduct of research. Dr. McPhillips will oversee all research related activities. Stephanie Foo and Michelle Delahanty are part-time clinical research coordinators and Jack Ward is a part-time research assistant. All staff members have been approved in the previous modification and will work under Dr. McPhillips' supervision. Staff will be responsible for developing and executing procedures and processes of study implementation including day-to-day operations (e.g. meeting coordination, meeting minutes), preparing Data/Safety monitoring reports, ongoing reports, database development, recruitment and retention, payments, data collection, and budget oversight. They will work closely with the PI to ensure that data collection is conducted on schedule. Any research staff that will be directly involved in data collection will have one on one training sessions with Dr. McPhillips. Dr. McPhillips has a research office at Ralston House, with locked cabinets for storing secure data. The Penn School of Nursing has a secure research server for online data storage. We also have a secure research laptop for data collection. We are confident we have appropriate space and resources for conducting this study.

Characteristics of the Study Population

Target population
Older adults with insomnia and mild cognitive impairment

Subjects enrolled by Penn Researchers
40

Subjects enrolled by Collaborating Researchers
0

Accrual
ACCESS TO THE POPULATION We plan to recruit 27 participants from three sources: 1) Division of Geriatric Medicine Division Ralston House clinic: There are currently 2,864 active patients, with 40% having mild cognitive impairment (MCI), yielding a potential 1,145 patients with MCI. We will use EPIC to generate a list of eligible participants coming in for clinic visits each week. Staff will introduce patients to the study team for further screening. This first method of recruitment is on hold due to Covid-19. 2) PennSeek search of MCI and insomnia yielded 870 potential participants. After obtaining permission to contact from their provider and completing a telephone screening call, consent and research visits will be set up via telephone or video-conferencing call. 3) Recruitment will also include contacting participants from a recruitment database (I.e., subject registry), which contains names of over 1000 individuals who participated in or were not eligible for study team members' previous or on-going studies and have indicated a willingness to be contacted for future studies. Participant information will be accessed via REDCap, and participants will be contacted by phone to determine interest and eligibility for this study. ANALYSIS: Power calculation was done using PASS v21. We initially planned to power the study on two primary outcomes, sleep latency and health related quality of life and required a sample size of 40. However, given that this is a pilot study, Covid-19 and other time constraints, we decided to power the study on our main primary outcome of sleep latency. Thus, the study is powered to detect time averaged difference of two groups in a repeated measures design for the primary, continuous outcome of sleep latency using the generalized estimating equation (GEE) approach. To estimate the necessary sample size, we assumed equal allocation between the treatment and control groups. The minimum time averaged difference in sleep latency between the two groups we were interested in detecting was set at 4.5 minutes with a standard deviation of 4. We expect an even larger effect size, given the work of Cassidy-Eagle et al.42 Assuming a baseline correlation r = 0.80 between multiple observations from the same subject over time and anticipating 20% attrition, we require 27 total participants in the study to achieve 80% power.

Key inclusion criteria
Must meet inclusion criteria of: 1) age 55 and older; 2) mild cognitive impairment: Telephone Interview for Cognitive Status (TICS) Total score with a range of 28-36 3) have subjective sleep diary evidence of insomnia, with an average sleep latency greater than 30 min or wakefulness after sleep onset of greater than 60 min during the one week pre-treatment assessment; 4) live in the community; 5) speak English as primary language (most of the study questionnaires only have validated English-language versions).

Key exclusion criteria
Exclusion Criteria include 1) Presence of moderate to severe cognitive impairment defined as TICS 28; 2) Visual or manual dexterity impairment that prevents them from pressing yes/no buttons, or selecting a number at 24 point font. 3) Current sedative-hypnotic or other sleep aid use on a regular or as needed schedule within the prior three months; 4) The presence of an acute medical or psychiatric condition (such as acute congestive heart failure at high likelihood of imminent hospitalization) which, in the judgement of the research team, would interfere with the subjects ability to realistically follow the study protocol

Vulnerable Populations

	Children Form
	Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form
	Fetuses and/or Neonates Form
	Prisoners Form
	Other
x	**None of the above populations are included in the research study**

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
N/A

Participant recruitment
Please describe the plan to equitably identify and recruit a diverse group of participants that is reflective of the population under study. If this is a multicenter protocol, the recruitment plan should describe the local (Penn) site's plan. Describe:how potential participants may be identified (review of medical records, Slicer Dicer, DAC reports including referrals from physician offices and clinics);who may approach potential participants;methods to achieve sample diversity and inclusiveness;what information may be presented to or discussed with them; andthe context and setting in which recruitment will happen.
We plan to recruit 27 participants from three sources: 1) Division of Geriatric Medicine Division Ralston House clinic, 2) PennSeek, 3) Recruitment Database. 1) Division of Geriatric Medicine Division Ralston House clinic: We will use EPIC to generate a list of eligible participants coming in for clinic visits each week. Staff will introduce patients to the study team for further screening. This method of recruitment is on-hold due to Covid-19. 2) PennSeek: After obtaining permission to contact potential participants from their provider, we will contact them for a telephone screening call. 3) Recruitment will also include contacting participants from a recruitment database (I.e., subject registry), which contains names of over 1000 individuals who participated in or were not eligible for study team members' previous or on-going studies and have indicated a willingness to be contacted for future studies. Participant information will be accessed via REDCap, and participants will be contacted by phone to determine interest and eligibility for this study.

Recruitment Materials
Is the research team using any recruitment materials? These may include but are not limited to: phone call scripts, radio/video scripts, flyers/brochures, internet postings, email, letters to potential participants, letters to patient physicians, My Penn Medicine (MPM), other direct messaging, etc. For guidance regarding recruitment materials, please review the IRB's guidance on Participant Recruitment Materials online:https://irb.upenn.edu/recruitment
No

Use of Penn Media & Social Media Services
Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

Participants will be compensated for their time completing all research related activities, with a maximum compensation of $200. The compensation will be in the form of gift card, and broken down into three payments: 1) Payment 1: $50 at the end of Visit 1 (day 1; week 1) 2) Payment 2: $100 at the end of Visit 2 (post-intervention; week 5) 3) Payment 3: $50 at the end of Visit 3 (12 weeks post intervention; week 16)

Study Procedures

Suicidal Ideation and Behavior

Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)? Centeral nervous system(CNS) effect: the ability of a test article to enter into and potentially interact with the central nervoous system (brain and spinal cord). Clinical Investigation: Any experiment that involves a test article and one or more human subjects that either is subject to requirements for prior submission to the Food and Drug Adminstration (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to the requirements for prior submission to the FDA under these sections of the act, but, the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

No

Procedures

Study Procedures: A) Subjects: The target study population is older adults with mild cognitive impairment who have insomnia. B) Recruitment and Screening: We will recruit 27 eligible participants from three sources: 1) Division of Geriatric Medicine Division Ralston House clinic (on hold due to Covid), 2) PennSeek, and 3) Recruitment Database. After consent, subjects will be screened for key inclusion criteria. First, they must answer yes to one of the insomnia screening questions and score within the a 28-36 range on the TICS. Participants will be asked if it takes them longer than 30 minutes to fall asleep on most nights and/or if they are awake for more than 60 minutes during the nighttime period. Next, they will receive (either by mail or contactless delivery to their door) actigraph device and a tablet to complete a sleep diary for a period of one week. Once insomnia inclusion criteria are confirmed from the actigraph and diary data, we will contact participants by phone to schedule Visit 1 via videoconference. C) Randomization: All retained participants will be randomly allocated (1:1) to either intervention or control arm. D) Baseline (pre-treatment) assessments, collected at Visit 1, include sleep measures and measures of health related quality of life, physical activity, cognition, social activity, and blood samples. E) Intervention: A 4-week intervention (see intervention description below) will be provided to subjects randomized to the intervention group. Sleep diaries will be completed and actigraph device worn for all four weeks of treatment, in both groups. F) Post-intervention and Follow-up data collection (visit 2 week 5; visit 3 week 16): All baseline assessments will be repeated immediately post- intervention and at three months post-intervention follow-up (sleep measures and measures of health related quality of life, physical activity, cognition, social activity, and blood samples; one week sleep diary + actigraphy). G) Demographics: Data on demographics and other information (see measurement section) will be assessed by questionnaires at baseline, post-intervention and follow-up. Intervention: The intervention will include a meaningful activity protocol during the day and Assistive Relaxation Therapy at night. The personalized meaningful activity protocol will be developed based on the individuals factors contributing to insomnia, typical daily circadian profile, functional status, and preference for activity. The individuals typical circadian profile will be calculated from the one-week baseline accelerometer data using algorithms previously developed by Dr. Gooneratne (co-mentor) and research team. The intervention will be broken into: 1) Sleep Hygiene Education, including content on routine, stimulus control principles, food/drink/substance intake (caffeine, alcohol, etc.), activity, naps, etc; 2) Meaningful Activity Modules a) Physical Activity, including content from the Go4Life Campaign (NIA) on endurance, strength, balance, and flexibility b) Cognitive Activity including various cognitively stimulating games and exercises such as cross-word puzzles and c) Social engagement including identifying social support persons, group activities in the area and using technology to stay connected; 3) Assistive Relaxation Therapy (ART), a breath-based relaxation application that is coupled with a physical anchoring task. After reviewing baseline assessments to determine etiological risk factors contributing to the insomnia, each participant and the PI will construct their meaningful activity plan. Thus, study participants in the intervention arm will receive (1) tablet computer with Ditti application (for ART) and REDCap application, sleep education material, and meaningful activity modules; (2) Actigraph wrist watch device. They will be instructed how to use the tablet and encouraged to use the tablet. They will be asked to complete the daily sleep diary on the tablet, use the activity modules daily as pre-determined times personalized to the participant, use ART when they get in bed and if they awake during the night to help them with their insomnia symptoms for a four-week period. They will be asked to wear the actiwatch on the non-dominant wrist to monitor sleep/wake patterns. Participants will have weekly to biweekly phone consultation with the study interventionist to receive guidance and adjustment on activity plans. Based on previous research,

physical, social, or cognitive activity has shown significant improvement in sleep in 2-4 weeks and ART therapy has improved sleep latency in just two weeks. Thus, we feel confident that a 4 week intervention period is sufficient and justified. As per NIH guidelines, we are providing additional details related to the intervention relevant for assessing Human Subjects Safety. The following components which will be used for the four-week intervention period. Tablet computer connected by wireless cellular phone data. Tablet-enabled sleep diary: The Sleep Diary will be administered via the REDCap, utilizing the MyCap feature. Sleep Education Information: Sleep education/sleep hygiene information will be loaded to the tablet; participants will also receive a print copy. Meaningful Activity Modules: There will be three modules related to physical, social and cognitive stimulating activity. These will be loaded to the tablet; participants will also receive a print copy. Assisted Relaxation Therapy (ART) will be loaded onto the tablet via Ditti application. We will ask the study participant to engage in an anchoring task (finger tap) on the tablet screen at the exhalation point of the breathing cycle while they are lying in bed trying to sleep. Study participants will be asked to use the ART intervention every night as they are trying to fall asleep, or when they wake up at night. They will use it every night for four weeks. For ART intervention to work, it must be used on a nightly basis when in bed. It will be administered via the tablet. These technologies do not constitute a medical device as per FDA guidance related to mobile device technologies. Actiwatch Spectrum Plus: Each participant will be given an Actiwatch Spectrum Plus (Koninklijke Philips, N.V.), a piezoelectric accelerometer worn on the non-dominant wrist. Movement data are sampled at a rate of 32 Hz, and activity counts are recorded in 60-second epochs. Additionally, the watch has Silicon photodiode light sensors, and a button that enables participants to signal when they first try to fall asleep and when they get out of bed in the morning. The button can also be used to signal naps. Periods of activity and inactivity are analyzed in order to estimate sleep/wake status. Computer programs are used to derive levels of activity/inactivity, rhythm parameters and daytime naps. Wrist actigraphy monitoring has been shown to be a reliable way to objectively monitor sleep-wake cycles. Control arm: The control arm will consist of sleep education materials. They will be asked to complete the tablet-enabled sleep diary and wear an actigraph device on the non-dominant wrist. See attached for protocol table.

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception? Deception could be considered any direct misinformation presented to the subject or omission of key information pertaining to the design or nature of the project.
No

International Research
Are you conducting research outside of the United States?
No

Analysis Plan
Power Analysis for Sample Size described previously under "Accrual". Descriptive statistics will be used to characterize the sample, with measures of central tendency and variation for continuous measures, and frequencies and percentages for dichotomous and categorical variables. Descriptive estimates will be generated for all participants at each of the observed time points, and by intervention group within each time point. Distributional assumptions and outliers will be assessed via graphical approaches. Baseline characteristics between groups will be compared appropriate two sample -test or non-parametric Wilcoxon Rank Sum test for continuous variables and Chi-square test for categorical variables. Primary analysis will be carried out under the intent to treat (ITT) framework. To evaluate the difference between groups in our primary outcome, we will utilize the GEE model with time, group, and group by time as the primary predictors. A simple exchangeable correlation structure will be used to model the correlation between multiple observations from the same subject. Given that GEE is less likely to suffer from model convergence, we changed our initial approach from mixed-model to GEE. GEE analysis does not require complete data over time and all available data from all subjects will be used in estimation. We have assumed 20% missingness in our sample size estimation. For missingness more than 20% we will explore imputing missing values when feasible. Given the real time data transmission and ability to call participants and remind them to complete sleep diary, we do not anticipate a great deal of missing data. We will report end of study effect sizes along with p-values and parameter estimates. We will construct reference cell contrasts to evaluate change relative to baseline

and consecutive time comparisons will be conducted by profile contrasts. It is reasonable to assume due to our sample size GEE models may fail to converge. In such situations we will obtain difference in score between two time points and conduct two sample t-test or Wilcoxon Rank Sum test for two groups comparisons. We will adjust our type I error rate to adjust for multiple comparison under this scenario.

The following documents are currently attached to this item:

There are no documents attached for this item.

Data confidentiality

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

x **Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**

x **Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.**

x **Wherever feasible, identifiers will be removed from study-related information.**

A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

x **Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.**

Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

Subject Confidentiality

We will apply strict procedures to maintain confidentiality and will adhere to 2003 HIPAA Standards for Privacy of Individually Identifiable Health Information (the Privacy Rule). Each individual participant will be given a unique study identification number in REDCap. Information linking the identification number to the participant will be stored on the HIPAA compliant servers (see more below regarding REDCap). REDCap project access will only be granted to the research team who had been approved by this IRB. All project records not included in REDCap will reflect only the ID number of each participant. Thus, research study participants names will not appear on any forms, and instead participants will use a unique identification number. To ensure HIPAA compliancy, the Ditti application on the tablet will be password protected and users will be given a non-identifiable username. This participant username will be used (along with a password) by the subject to log onto the application; they will not use their e-mail or other personal identifier as the username. The Ditti application or tablet will not store any personal health information or a participants name, birthdate, sex, home address, or other personal information; it will only record tap events (time-stamped). Recorded data will be encrypted using standard protocols at rest and in transfer, leaving no point at which the raw data will be openly readable until accessed by the research team. The linkage between participant ID and participant name can only be determined from the participants link key, which will be stored in REDCap as previously described. Rigorous security protocols that restrict data access points will also be implemented, requiring research staff to securely authenticate their identity before accessing the data. Access to the study participants identities will only be available to the immediate research staff. Data from Ditti will be abstracted and entered directly into REDCap. Access to the study participants identities will only be available to the immediate research staff. The tablet app falls within the category of motivating patient behaviors, which according to the latest FDA guidance is considered within the category of enforcement discretion, therefore it does not require prior FDA review and approval. The app does not carry significant risk to research study participants (it is not implanted and does not expose the body to significant external energy for diagnostic or treatment purposes), thus it is within the category of FDA IDE device exemption. Prior research conducted by the mHealth service using similar exercise/behavioral intervention apps has been approved as an FDA IDE device exempt app. All data

will be coded with a study specific identifying number and all data will be de-identified. The identifying number will be kept on a password-protected, secure server as described previously. All study data will be transmitted using encryption, and stored on secure servers as noted previously. The majority of data will be collected electronically via the REDCap system and no data will be obtained on paper. Information will be compiled from all the participants in the study and, when published, data will be reported in aggregate form. As a result of aggregation, no individual participants will be identifiable from the written materials. Data will be saved for seven years and securely deleted after. The REDCap (Research Electronic Data Capture) system will be used as a central resource for quantitative data processing and management. REDCap is a web application and back-end database model designed to support data capture for research studies. The University of Pennsylvania has licensed its own version of REDCap that is housed on our own password-protected servers located within a data center inside the Penn firewall and therefore afforded the same network protections as other sensitive clinical systems. REDCap was developed specifically around HIPAA-security guidelines with features such as data encryption. It provides an intuitive interface for data entry with data validation, audit trails for tracking data manipulation and export procedures, automated export procedures for seamless data downloads to common statistical packages, including SAS, and procedures for importing data from external sources. We will use standard operating procedures to guide all data management activities, such as the naming and identification of variables, data cleaning and handling of missing data. All data obtained from electronic medical record review and self-report measures will be entered directly into the REDCap database on encrypted laptop computers as collected to reduce data collection time, increase accuracy, and prevent data loss. Data entry screens will be designed to incorporate range checks and concurrent checks to minimize errors. Missing fields will not be allowed. If tablets are lost or stolen, the users password can be changed on the administrative end. This will cause the account to automatically log-out and will require the new credentials to be input into the fields in order to access the Ditti user interface.

Sensitive Research Information*

Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record? [NOTE: This does not apply to: 1) research information that would not normally be included in the electronic medical record or 2) information that is in the electronic medical record as part of clinical care.]

No

Subject Privacy

Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).

Scientific environments must be safe for both the researcher and the research subjects, and also protect participant privacy, confidentiality, and autonomy. Research visits will take place via telephone or secure videoconference meeting. No meetings will be audio or video recorded.

Disclosures

Will any data or specimens from Penn participants OR other research generated work product (e.g., intellectual property) be disclosed to any individuals, entities, or vendors, etc. outside of Penn?

No

Data Protection*

x	**Name**
x	**Street address, city, county, precinct, zip code, and equivalent geocodes**
x	**All elements of dates (except year) for dates directly related to an individual and all ages over 89**
x	**Telephone and fax number**
	Electronic mail addresses
	Social security numbers
x	**Medical record numbers**
	Health plan ID numbers
	Account numbers
	Certificate/license numbers
	Vehicle identifiers and serial numbers, including license plate numbers
	Device identifiers/serial numbers
	Web addresses (URLs)
	Internet IP addresses
	Biometric identifiers, incl. finger and voice prints
	Full face photographic images and any comparable images
	Any other unique identifying number, characteristic, or code
	None

Does your research request both a waiver of HIPAA authorization for collection of patient information and involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
Yes

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
Yes

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
Yes

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision

of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not applicable

Consent

1. Consent Process

Overview
If participant is recruited via PennSeek, their provider will give us permission to contact them. If a person is recruited through the REDCap Subject Registry, they have already indicated it is okay for a researcher to contact them and they will be contacted directly. In order to ensure that the participant truly understands what the research study entails and that his/her participation is voluntary, electronically signed informed consent (HIPAA authorization will be included in the informed consent document) will be obtained from all patients by the research team. The researcher will go over the informed consent document with each subject by phone and participants will e-sign using REDCap. Potential participants will be fully informed regarding the intensity and length of data collection required of them. The specific types and methods of data to be collected will be described in detail. The informed consent will include disclosure of the purpose and duration of the study, risks and benefits, alternatives to participating, confidentiality, and contact information for the principal investigator in case further questions arise. The participants will be made aware that the research study is voluntary, and if they choose not to be in the study or to be in the study but to stop at a later date, there will be no penalty or loss of benefits to which they are entitled. This will help to address any role conflict or coercion, so the participant does not feel he/she has to participate in the study or will otherwise lose the benefits of the University of Pennsylvania Health System. Participants will also have the opportunity to think about whether or not he/she would like to participate in the study. If a participant would like more time, they will have the opportunity to call the researcher back to set up another appointment. In order to ensure that the participant truly understands what the research study entails and that his/her participation is voluntary, participants will be asked five questions: What is the purpose of the study? What are the risks to the study? What are the benefits of the study? How to contact me, the principle investigator? How to withdraw from the study? Assessing older adults capacity to provide consent is an important step in the informed consent process. Older adults who can verbally provide 4 out of 5 answers correctly will be considered capable of providing their own consent. The researcher will again answer any questions they may have about the study. If they continue to agree to participate, then they will be asked to sign the last page of the consent form designating their consent to participate in the study. If the subject chooses to consent, he/she will be sent a signed version of their consent form; a copy will be saved in REDCap for the research team. For older adults who have given oral assent to participate in the study but cannot verbally provide 4 answers correctly (demonstrating the lack of cognitive ability to provide consent), they will not be included in this study for two reasons. First, there is no caregiver component to the intervention that would permit us to use proxy-reported informed consent and second, this study is looking at mild cognitively impairment people that should be able to give informed consent if they meet the inclusion criteria of the TICS-M.

Children and Adolescents
Not applicable

Adult Subjects Not Competent to Give Consent
All adult subjects must be competent to give informed consent.

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
No Waiver Requested

Minimal Risk*

Impact on Subject Rights and Welfare*

Waiver Essential to Research*

Additional Information to Subjects

Written Statement of Research*
No

If no written statement will be provided, please provide justificiation

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit

Potential Study Risks
We do not believe there are any major risks associated with the proposed protocol. There is minimal risk associated with finger pricks for blood samples, physical activity, and study burden. We will explain associated risk to the participants. Other potential risks to participants are fatigue from data collection, stress in response to self-report instruments or concerns related to confidentiality. In addition, the participant may experience discomfort from sleeping with the wrist watch device, but that usually subsides after the first night. If the participant cannot tolerate the watch, he/she will be instructed that removal of the watch is allowed. Participant burden, specifically fatigue, is the most likely risk related to this study. To minimize fatigue during data collection, we chose only the most relevant self-report instruments. However, given that this is an older adult population with cognitive impairment; we will offer the participant the opportunity to take breaks. It is possible that some participants may become anxious or stressed during data collection because of the questions asked, the burden of data collection, or for other personal reasons. Stress is judged to be low likelihood because the instrument questions are not highly intrusive or sensitive. However, should this occur, the participant will be asked if they would like to terminate or delay data collection. Loss of confidentiality is considered very low likelihood given the protections we will have in place and our experience in systems of protecting private information. Intervention: The study poses minimal risks to subjects beyond standard clinical care for insomnia. Sleep hygiene is a standard clinical recommendation for insomnia, and thus does not pose any additional risks to the subject beyond standard clinical care. Furthermore, the relaxation intervention component can reduce the risk of falls or daytime sleepiness associated with the standard of care treatment, conventional CBT-I. The tablet screen background is black for the sleep diary to avoid excessive light exposure at night, and the tablet screen is set to black when using the ART intervention in bed. The tablets are locked to prevent use of other applications. Plan to address risk: Finger prick via a Lancet for blood samples might result in occasional bruising, pain, or local reaction. All blood samples will be taken by the participant using precise methods provided to them. Physical Activity: In very rare occasions, the subject may fall or get injured during physical activities. These adverse events should be minimized by using personalized physical activity plans, which will be developed/designed based on the subjects personal features by the PI to be most suitable for the subject. The activity intervention will be based on an existing NIH-funded activity protocol for older adults. Any occurrence of adverse events will be immediately reported to the IRB at the University of Pennsylvania. Wrist watch discomfort: The subject may experience discomfort from sleeping with the wrist watch device, but that usually subsides after the first night. If the subject cannot tolerate the watch, he/she will be instructed that removal of the watch is allowed. Fatigue: We estimate screening and consent to take 30 minutes, quantitative data collection 20 minutes; instructions for actigraphy and sleep diary 5-10 minutes; blood samples 5 minutes. We anticipate developing the meaningful activity plan to take 30 minutes to one hour. Stress: As the PI, I will be overseeing data collection. I am a registered nurse with a masters degree specialized in the care of older adults and a PhD. Thus, I am well trained to be supportive and helpful to the participants should they become anxious or stressed in response to survey questions. If participants do become stressed, data collection will be delayed to tend to the participants emotional needs. Data collection will resume if and when the participant is ready to proceed.

Potential Study Benefits
For society in general, the study offers benefits in that it develops a new treatment option for insomnia in older adults with mild cognitive impairment, a group that has difficulty participating in traditional CBT-I and is at increased risk for side effects from pharmacotherapy for insomnia. In general, we feel that this study represents a minimal risk to participants. The treatments that they will undergo are similar to standard care for insomnia, thus pose minimal additional risk above standard medical care. It is possible that while these study results may benefit older adults in the future, participants in this study may not realize an immediate or direct benefit from participating. It is also possible that the participants gain a heightened awareness of their sleep habits and patterns after completing the sleep diary. Additionally, those randomized to the intervention group may have benefits from the intervention. As the study involves very little risk and there is significant potential for benefit, the risk / benefit ratio is favorable.

Alternatives to Participation (optional)
The alternative to participation in the study is to decline participation and continue with routine clinical care for the study participants insomnia. Refusal to participate in the study will in no way adversely affect the clinical care the study participants would otherwise receive at the University of Pennsylvania Health System.

Data and Safety Monitoring
Trial monitoring will be done by a safety monitoring committee, which includes the PI, primary mentor (Dr. Hodgson) a statistician (Subhash Aryal) and an expert in the care of older adults (Lea Ann Matura). We will evaluate the progress of the study on a monthly basis, including periodic assessments of data quality (safety and integrity) and timeliness, recruitment, accrual and retention, participant risk versus benefit, and other factors that can affect study outcome; consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial; review study performance; and discuss the resolution of problems. Furthermore, we will monitor adverse events (AEs), including serious adverse events (SAEs) and unanticipated problems (UPs). An Adverse Event is any untoward medical occurrence in a patient or clinical investigation participant and which does not necessarily have a causal relationship with this treatment. Participants will be queried regarding any changes in their health and medications at each contact. The informed consent document will list the daytime and after hours contact information for the site Principal Investigator. All AE and SAE reporting will be done in adherence with IRB guidelines; the PI will notify the IRB within 48 hours of any serious possible or potentially study-related AEs. The report will include the description of the AEs and any actions taken by the PI. SAEs in this population include, but are not limited to death, hospitalization, evidence of abuse, suicidal ideation, and medical emergencies. The PI will also keep a log of all AEs. Any deviations related to the protocol will be reported to the IRB using a deviation form immediately upon the discovery of the deviation. Given the non-invasive nature of the intervention, the team does not anticipate AEs beyond the average rate of these events in this population. The literature in the field will be continually appraised by the team. If any team member uncovers new information that would impact the safety of the participants or the ethics of our study, the PI and entire mentoring team will discuss the issues. At this time, given the low risk of the intervention, there is no plan for interim analyses or any stopping rules.

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit Assessment
We believe that the benefits far outweigh the risks to participants in this study. We feel this study is minimal risk.

General Attachments

The following documents are currently attached to this item:

There are no documents attached for this item.