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NYU School of Medicine
NYU LANGONE MEDICAL CENTER

P20 Extending Sleep to Reverse the Metabolic Syndrome in Middle-Aged Adults: Acceptability and Feasibility of a Sleep Intervention

A single site pilot study to determine the acceptability and feasibility of a twelve-week sleep extension intervention, self-management for adequate sleep intervention (SASI), in community-dwelling, middle- aged adults with the metabolic syndrome.

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Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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List of Abbreviations

AE	Adverse Event/Adverse Experience
AHI	Apnea hypopnea index
ASA24	NCI Automated Self-Administered 24-hour diet recall
AUDIT	Alcohol Use Disorders Identification Test
CAT	Computer Adaptive Testing

CBTI	Cognitive Behavioral Therapy for Insomnia
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CRC	Clinical Research Center
CRF	Case Report Form
CBRD	Center for Biospecimen Research and Development
CTSI	Clinical and Translational Science Institute
EMR	Electronic Medical Record
FBG	Fasting Blood Glucose
FFR	Federal Financial Report
GCP	Good Clinical Practice
HDL-c	High density lipoprotein cholesterol
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
ISI	Insomnia Severity Index
MetS	Metabolic Syndrome
MOP	Manual of Procedures
N	Number (typically refers to participants)
NCI	National Cancer Institute
NIH	National Institutes of Health
NINR	National Institute of Nursing Research
NYU	New York University
OHRP	Office for Human Research Protections
OSA	Obstructive sleep apnea
PI	Principal Investigator
QA	Quality Assurance
PROMIS	Patient-Reported Outcomes Measurement Information System
QC	Quality Control
RA	research assistant
REDCap	Research Electronic Data Capture

SAE	Serious Adverse Event/Serious Adverse Experience
SASI	Self-management for Adequate Sleep Intervention
SDOH	Social Determinants of Health
SOP	Standard Operating Procedure
TG	Triglycerides

Protocol Summary

Title	P20 Extending Sleep to Reverse Metabolic Syndrome in Middle-Aged Adults: Acceptability and Feasibility of a Sleep Intervention
Short Title	P20 Malone Pilot
Brief Summary	This pilot study will test the acceptability and feasibility of a sleep extension intervention in community-dwelling, short-sleeping, racially/ethnically diverse middle-aged adults with MetS. Baseline sleep habits will be assessed and used to guide individualized strategies to extend sleep. A 1-group pretest-posttest study design will test the efficacy of this 18-week study (2 weeks of baseline data collection, 1 week of study intervention planning, 12 weeks of sleep intervention delivery, final follow up 3 weeks after last day of the 12-week intervention) on sleep duration, MetS risk behaviors (reduced physical activity, increased sedentary behavior, poor diet quality), symptoms associated with MetS risk behaviors (poor affective well-being, fatigue), and self-regulation. Socio-ecological barriers and facilitators to the intervention will be identified using a quantitative and qualitative approach.
Phase	Pilot study
Objectives	Primary Objective: Test the feasibility and acceptability of a self-management for adequate sleep intervention (SASI) in community-dwelling, short-sleeping, middle-aged adults with MetS. Secondary Objective: Assess the preliminary efficacy of SASI on sleep duration, MetS risk behaviors (physical activity, sedentary behavior, diet quality), symptoms associated with MetS risk behaviors (affective well-being, fatigue) and self-regulation. Exploratory Objective: Explore the perceived barriers and facilitators of SASI (e.g., socio-ecological factors) barriers and facilitators of SASI (e.g., socio-ecological factors).
Methodology	1-group pre-test and post-test pilot study
Endpoint	Primary Endpoints: 1) Acceptability (pre-intervention and post- intervention, 2) Feasibility (recruitment rate, retention rate, protocol adherence rate). Secondary Endpoints: 1) sleep duration, 2) physical symptoms, 3) physical activity, 4) sedentary behavior, 5) diet quality, 6) affective well– being, 7) self-regulation.
Study Duration	3 years
Participant Duration	18 weeks
Duration of behavioral intervention	12 weeks
Population	Participants will be male and female, 35-60 year old, short-sleeping adults from diverse racial/ethnic groups with the Metabolic Syndrome in the greater New York City area.
Study Sites	NYU Langone Health NYU Rory Meyers College of Nursing

	Bellevue Hospital 462 1st Avenue, New York, NY 10016 in C/D Building, 4th Floor New York, NY.

Number of participants	We will screen approximately 220 individuals for a final sample of N= 60 participants. Of these 220 participants, we anticipate that 65% will become ineligible through the multi-stage screening process and 20% will be lost to attrition during the intervention leaving 60 participants with evaluable data.
Description of Study Intervention/Procedure	SASI is based on Cognitive Behavioral Therapy for Insomnia (CBTI). Like CBTI, SASI extends sleep based on sleep efficiency (the proportion of time spent sleeping during a sleep episode). Bedtimes and wake times will be prescribed each week for each participant and allow for gradual increases in sleep opportunity. Bedtimes will be set 15 minutes earlier each week provided sleep efficiency remains >90%. Earlier bedtimes will extend sleep duration by increasing the opportunity for sleep. Wake times will not be changed because wake times are often determined by external demands, such as work schedules.
Reference Therapy	Not applicable.
Key Procedures	Surveys, patient reported outcomes, anthropometric measurements, blood pressure measurement, daily sleep diaries, wrist accelerometry, blood draw (3 ml CTSI visit 1), open-ended interview.
Statistical Analysis	Primary endpoints: 1) Acceptability based on the percentage of pre and post intervention acceptability surveys with total scores < 21 (unacceptable), 21 (neutral), greater than 21 (acceptable). 2) Feasibility will be based on recruitment, retention, and study protocol adherence rates.

Schematic of Study Design

Screening/ CTSI Visit 1

- Research Assistants will identify eligible participants through EPIC, Datacore, and other recruitment strategies. N= 220 individuals will be screened for inclusion / exclusion criteria using a multi-stage screening process that includes 1) a telephone screen, 2) a CTSI visit to obtain informed consent, complete screening surveys, and obtain anthropometric and blood pressure measurements, 3) a 2-week baseline data collection to objectively confirm short sleep and establish treatment of OSA (at home).

Baseline data collection (at home)

- Objectively screen for short sleep: Wrist accelerometry and fitbit 24/7 for 14 days, daily sleep diaries. Objectively establish OSA treatment: Wear pulse oximeter for 1-night. Complete baseline surveys: Acceptability survey, Composite Scale of Morningness, Economic Vulnerability Survey, Family Assessment: General Functioning Scale, Sleeping Environment Survey, 36-item Short Form Health Survey (SF -36) version 1, ASA24, Demographics-Social Determinants of Health (SDOH): Alcohol use (AUDIT C), Demographics- SDOH: Alcohol Use, Index of Self- regulation, SAFTEE Questionnaire, PROMIS Depression 6a. Otherweekly surveys : Epworth Sleepiness Scale, PROMIS Fatigue 6a – morning PROMIS Fatigue 6a – evening,

Intervention (at home)

- Sleep diaries (daily), fitbit 24/7, Phone/videoconference calls (weekly with study team), Epworth Sleepiness Scale (weekly), PROMIS Fatigue 6a- morning (weekly)– PROMIS Fatigue 6a- evening (weekly).

Last 2 weeks of intervention (at home)

- Sleep diaries (daily), Phone calls (weekly with study team), Wrist accelerometry and fitbit 24/7 for 14 days, 36-item Short Form Health Survey (SF-36) version 1, ASA24, Demographics- SDOH: Alcohol use (AUDIT C), Demographics- SDOH: Alcohol Use, Index of Self-regulation, SAFTEE Questionnaire; PROMIS Depression 6a. Other weekly surveys: PROMIS Fatigue 6a– morning, PROMIS Fatigue 6a–evening, Epworth Sleepiness Scale.

Final Visit (at home)

- Acceptability survey.
- Open-ended Interview.

Key Roles

Susan Kohl Malone, PhD, RN,
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Principal Investigator: Dr. Malone will direct and oversee all aspects of the pilot study, ensuring that study procedures are implemented and maintained for the enrollment of participants, form development, collection of data, data management, and budget maintenance. She will have primary responsibility for oversight of data analysis, preparation of manuscripts, and the submission of annual and final reports.

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Co-investigator: Dr. Seixas is well experienced leading funded projects related to sleep, cardio-metabolic health and racial/ethnic disparities. Dr. Seixas has worked as a project manager on several NIH-funded sleep-related studies including a NIMHD-funded R01 study on sleep obstructive sleep apnea among Blacks and as a principal investigator on a NIH-funded K01 award investigating the relationship between insufficient sleep and cardiovascular disease markers between Blacks and Whites. Dr. Seixas' expertise will also be brought to bear on recruiting community participants and identifying barriers to extending sleep across diverse subgroups. Dr. Seixas will contribute to the dissemination of study findings.

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Co-investigator: Dr. Dickson is an Associate Professor in the NYU Rory Meyers College of Nursing, Director of the Pless Center for Nursing Research, program director of the NYU Meyers NIOSH-funded T42 Program in Occupational and Environmental Health Nursing, and co-director of the NIH-funded NYU School of Medicine CTSA Scholars Program. Dr. Dickson's work has led to an improved understanding of the socio- cultural influences of self-care among women and racial/ethnic minority groups and the development of innovative theory based interventions. This expertise will be brought to bear on our proposed CTSI pilot project. Dr. Dickson is also an international expert in qualitative research techniques and mixed methods research. She will provide expertise for the qualitative design and analysis where we will identify barriers and facilitators to the sleep intervention. Dr. Dickson will play a critical role in identifying and recruiting potential participants. The overarching goal of his research is to address patient- level, provider-level, and system-level barriers hindering adoption of healthful practices.

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Co-investigator: Dr. Jean Louis is Professor of Population Health and Psychiatry at NYU Langone Health. He is Director of the NHLBI-funded PRIDE Summer Institute on Behavioral Medicine and Sleep Disorders Training Institute and Director of the T32 Program on Translational Behavioral Cardiovascular Health Research. He served for three years on the NHLBI's Sleep Disorders Research Advisory Board, and for four years as a member of the Cancer, Heart, and Sleep Epidemiology (CHSB) study section, and the NHLBI Special Emphasis Panel/Scientific Review Group. As PI for several past studies, Dr. Jean Louis will play a critical role in recruiting potential participants and provide expertise in the proposed sleep intervention.

Gary Yu, PhD
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Biostatistician: Dr. Yu is a biostatistician trained at Columbia's Mailman School of Public Health. His dissertation involved creating a new dimensional-informative mixture model (DIMM) [NIH/NHLBI R01HL111195], a model-based clustering technique to create endophenotypes of major chronic conditions (MCC) (i.e. pain, fatigue, depression, CVD) under conditions of severe disease heterogeneity in the clinical diagnosis. Dr. Yu has applied a variety of advanced analysis approaches to complex longitudinal data including multiple imputation for missing data, structural equation modeling, generalized estimating equations, and linear and generalized linear mixed models. His expertise as a biostatistician will be brought to bear on the quantitative analyses of the proposed study aims and complement the qualitative analyses exploring the individual, family, and community factors influencing sleep extension. His work addressing barriers to racial/ethnic minorities for participating in research studies will inform the study design and analysis.

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Key Collaborator: Dr. Wright is Assistant Professor at the NYU Rory Meyers College of Nursing. Her expertise in fatigue research will be brought to bear on the analyses of these data. Dr. Wright will also assist in identifying and recruiting potential participants.

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Key Collaborator: Dr. Melkus is the Florence and William Downs Professor in Nursing Research, Associate Dean for Research, and Director of the Muriel and Virginia Pless Center for Nursing Research. Her expertise in conducting behavioral intervention research and serving as a career development mentor to many rising early-career scientists will benefit Dr. Malone in the conduct of this pilot study.

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One outpatient visit will take place at this site the remainder of the study will take place in the home environment

1 Introduction, Background Information and Scientific Rationale

1.1 Background Information and Relevant Literature

Name and description of the study intervention. The Self-management for Adequate Sleep Intervention (SASI) is a 12-week self-management for adequate sleep intervention (SASI) that extends sleep gradually based on individual responses to the intervention. Participants will be enrolled in the study for 18 weeks because we will be collecting baseline sleep data during weeks 1 and 2, confirming eligibility based on objectively measured sleep and personalizing the intervention during week 3, delivering SASI weeks 4-15, and completing the last study visit within 3 weeks of the last day of the intervention. SASI is based on Cognitive Behavioral Therapy for Insomnia (CBTI). Like CBTI, SASI extends sleep based on sleep efficiency (the proportion of time spent sleeping during a sleep episode). Bed times and wake times will be prescribed each week for each participant and allow for gradual increases in sleep opportunity. Bedtimes will be set 15 minutes earlier each week provided sleep efficiency remains >90%. Earlier bedtimes will extend sleep duration by increasing the opportunity for sleep. Wake times will not be changed because wake times are often determined by external demands, such as work schedules.

Summary of relevant clinical research. Diet and exercise are the first line of treatment for effectively reducing the Metabolic Syndrome (MetS)[1]. However, disappointing outcomes are reported when diet and exercise programs are translated into less intense, more affordable community based programs. Less intense programs report only half the amount of weight loss achieved by more intense programs[2]. Moreover, only 50% of Americans with elevated glucose levels attempt modifying their diets and physical activity[3]. Poor participation rates suggest that diet and exercise are only effective for select, highly motivated individuals[4]. Extending sleep is an innovative approach to reducing MetS because it shifts the first line of treatment from diet and exercise alone to include sleep, a potentially modifiable, upstream factor for MetS.

Discussion of important literature and data that are relevant to the trial and that provide background for the trial. Applicable clinical, epidemiological, or public health background or context of the study. Short sleep, defined as ≤ 6 hours/night[5], is strongly associated with MetS[6], a cluster of risk factors that profoundly increases the risk for multiple chronic conditions such as type 2 diabetes[7]. The highest prevalence of short sleep (~30%) is reported by middle-aged adults (35-60 years old)[8]. Extending sleep in short sleepers without MetS improves behavioral and clinical risk factors, as it reduces hedonic food cravings[9] and improves insulin sensitivity and blood pressure[10,11]. Average 24-hour systolic and diastolic blood pressures are reduced by 14mmHG and 8mmHG, respectively, following sleep extension[11]. Progress in extending sleep interventions to persons with MetS is limited by the absence of intervention studies in community- dwelling, racially/ethnically diverse, middle-aged adults with MetS. The extent to which this high risk, understudied group can extend sleep and the contextual factors influencing their ability to do so are not known. Also unknown is whether extending sleep improves symptoms, such as poor affective well-being and fatigue, that are associated with MetS risk behaviors[12,13].

Short sleep may directly impact MetS, a chronic inflammatory state[14], by furthering inflammation. Elevated C-reactive protein has been found in habitual short sleepers[15]. Short sleep may also impact MetS through its effect on MetS risk behaviors[16-18]. Reduced physical activity, increased sedentary behavior, and unhealthy diets are associated with habitual short sleep[19,20]. Sleep deprivation symptoms, such as poor affective well-being and fatigue[21], further increase MetS risk behaviors[12,13]. Finally, short sleep impairs executive functioning[22], such as self-regulatory capacities that are important for adopting and sustaining healthy behaviors[23].

Importance of the study and any relevant treatment issues or controversies. Critical barriers exist to using sleep interventions to address MetS. First, laboratory findings may not translate to the context of people's real lives. Community-based interventions are needed to draw conclusions about the effects of sleep extension on MetS. For example, a 3-week community-based sleep restriction study reported increased insulin resistance after 1 week, corroborating laboratory evidence[24], but reduced insulin resistance during the remaining weeks[25], contradicting laboratory evidence. This exemplifies a shortcoming of lab studies and the profound implications for treatment interventions. Second, racial/ethnic minorities are under-represented in extant sleep extension studies. Yet, Black adults are more likely to be short sleepers[26] and are more vulnerable to the adverse effects of short sleep[27]. Third, socio-ecological factors at the individual (e.g., gender)[28], microsystem (e.g., family support)[29], and exosystem (neighborhood conditions)[30] levels affect sleep. Yet, existing sleep extension studies[10,11] have relied on generic approaches advising individuals to sleep more. These recommendations lack

the precision needed to be effective in diverse populations because they do not account for individual variability in lifestyle. Additionally, these recommendations do not address how to extend sleep.

This proposed study is significant because it will determine the acceptability and feasibility of a sleep intervention in an understudied population: racially/ethnically diverse middle-aged adults with MetS. The preliminary evidence of the effectiveness of this intervention will translate laboratory evidence suggesting that sleep can improve metabolic health into a promising new treatment for individuals with MetS, a group at high risk for multiple chronic conditions in later life. The socio-ecological factors identified will contribute to targeting and tailoring future sleep interventions in high-risk, understudied groups. The preliminary data generated will be used to test this intervention in a fully powered randomized control trial. Without personalized strategies to reduce MetS severity in middle age, healthy aging will be thwarted by a higher and lengthier burden of multiple chronic conditions in later life.

1.2 Rationale

State the problem or question under study (e.g., describe the disease and current limitations of knowledge or therapy). Include a statement of the hypothesis. Progress in extending sleep extension interventions to persons with MetS is limited by the absence of intervention studies in community- dwelling, racially/ethnically diverse, middle-aged adults with MetS. The extent to which racially/ethnically diverse middle-aged adults with MetS can extend sleep and the contextual factors influencing their ability to do so are not known. Also unknown is whether extending sleep improves symptoms, such as poor affective well-being and fatigue, that are associated with MetS risk behaviors[12,13]. In this study, we will: 1) Test the feasibility and acceptability of a self-management for adequate sleep intervention (SASI) in community-dwelling, short-sleeping, middle-aged adults with MetS.

2) Assess the preliminary efficacy of SASI on sleep duration, MetS risk behaviors (physical activity, sedentary behavior, diet quality), symptoms associated with MetS risk behaviors (affective well-being, fatigue) and self- regulation.
3) Explore the perceived barriers and facilitators of SASI (e.g., socio-ecologicalfactors).

Justification for the method of administration, treatment regimen of the intervention, intervention periods, and selection of study population. The method of administration, SASI, is based on Cognitive Behavioral Therapy for Insomnia (CBTI). SASI differs from CBTI because the first step of sleep restriction prescribed by CBTI is not used in SASI. This is because the participants have already been verified as short- sleepers. However, SASI does employ CBTI's gradual approach for increasing sleep time and applies it to short sleepers. CBTI has demonstrated effectiveness in improving sleep in persons with insomnia[31,32].

Increasing sleep duration gradually has also been demonstrated to sustain sleep quality. The 12- week intervention period of gradually increasing sleep duration by advancing bedtimes 15 minutes per week (or 1 hour per month) will provide the time needed to increase sleep duration in habitual 5 hour sleepers to the recommended 7 to 8-hour sleep duration. Our preliminary data from an 8-week sleep extension intervention increased sleep duration up to 2 hours over 8 weeks using this approach (Grandner, unpublished data). Moreover, 12 weeks will provide preliminary data regarding adaptation to adequate sleep duration (7-8 hours) and the effects of the sleep intervention on key biomarkers that may be missed by shorter intervention periods, such as improved triglyceride and HDL-c measures. The study population selected was middle-aged adults with MetS because short sleep has been associated with MetS. Plausible biological and behavioral pathways have been demonstrated
and further support a relationship between MetS and short sleep[10]. Middle-aged adults were chosen for this pilot study because short sleep is more prevalent in middle-aged adults than other stages of adulthood[12].

Discuss known or potential problems associated with the control group chosen in light of the specific disease and therapies being studied. There is no control group. This is a one group pre-and post- intervention study design that will provide preliminary data for a fully powered R01 randomized controlled trial.

1.3 Potential Risks & Benefits

1.3.1 Known Potential Risks

This study involves no more than minimal risk, as defined by federal regulations, to research participants. The probability and magnitude of harm or discomfort anticipated for this research are not greater than what the population encounters in daily life or during the performance of physical or psychological examinations or tests. The only alternative to study participation is non-participation. Non-participation will in no way affect the potential participant's medical care.

Loss of confidentiality. To protect against loss of confidentiality all survey data and clinical assessment data will be entered directly into REDCap (Research Electronic Data Capture). REDCap is a secure, web-based application designed to support data capture and storage for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. REDCap has been designed to allow for compliance with such standards as HIPAA, 21 CFR Part 11, and international standards. Also included are a built-in project calendar, a scheduling module, ad hoc reporting tools, and advanced features, such as branching logic, file uploading, and calculated fields. For further information about protecting against the risk of loss of confidentiality, please see Section 8.8
Protection Participant Confidentiality. Audiotaped intervention sessions that will be used to ensure the quality of the intervention and judge treatment fidelity will be reviewed by Dr. Dickson and the PI and subsequently destroyed.

Discomfort. To protect against discomfort associated with the accelerometer, participants will be instructed in person during their CTSI intake visit on the use of these devices. Participants will be given verbal as well as written, illustrated instructions for using the devices. Study team 24/7 contact information will also be provided to assist with troubleshooting. Participants may also remove the accelerometer and note this in their sleep diary.

Sleep complaints associated with the sleep extension intervention will be protected against by carefully monitoring sleep efficiency throughout the study. Careful monitoring of sleep efficiency and excessive sleepiness will significantly reduce risk for insomnia and other negative outcomes. The treatment for insomnia on which SASI is based (Sleep Restriction Therapy) can produce sleepiness, especially in the initial weeks of treatment. The proposed intervention, though, does not begin with a curtailment of sleep opportunity, so these issues should not be present. Sleep will be extended gradually and on an individual basis using the results from the previous week's sleep diary data. Participants diagnosed with an ARES score of greater than or equal to six suggesting OSA will be referred to the Sleep Disorders Center at NYU Langone Health for further evaluation and treatment.

Blood drawing risks. The risk of blood specimen collection is within the routine of clinical care. To protect against potential risks associated with the blood draw such as dizziness, decreased alertness, and symptoms associated with low blood sugar, every effort will be made to schedule the CTSI appointment between 0800 and 1000. A free light breakfast of cereal, juice, and muffins is provided by the CTSI to all research participants. Potential risks will also be minimized by using skilled and trained personnel to perform blood collection to minimize discomfort and potential for infection. Blood will be drawn following standard procedures. Standard techniques at the NYU CTSI will be used for analysis of the blood samples according to CLIA standards. Approximately 3 ml of blood will be drawn (as needed to objectively confirm MetS) during CTSI visit 1.

Inconvenience. To minimize the most likely risk of inconvenience, the following steps will be undertaken to reduce burden. Short forms of the surveys will be used wherever appropriate.

Embarrassment. To minimize embarrassment that may be associated with survey questions and waist measurements, we have selected survey questions that have been established and used in previous research studies. Waist circumference is a routine measurement taken in health care settings for persons with MetS. To protect against embarrassment participants will be free to omit answers and or refuse waist measurements. Additionally, waists will be measured in a private exam room. Clinicians sensitive to emotional or physical

responses to these procedures will conduct these interviews and examinations. Participants who are psychologically distressed will be referred for appropriate treatment.

Rationale for the necessity of exposing human participants to such risks. There is a critical need to develop personalized strategies to reverse MetS in middle-aged adults. Without such strategies to reduce MetS severity in middle age, healthy aging will be thwarted by a higher and lengthier burden of multiple chronic conditions in later life.

Why the value of the information to be gained outweighs the risks involved. These data will provide a more complete understanding of the association between sleep and MetS. This study will determine the acceptability and effectiveness of extending sleep in a high-risk, understudied group: racially/ethnically diverse, short-sleeping middle age adults with MetS. The socio-ecological factors identified will contribute to targeting and tailoring future sleep interventions in high risk, understudied groups.

If risk is related to proposed procedures included in protocol, any alternative procedures that have been considered and an explanation on why alternative procedures were not included. Risk associated with the procedures in this protocol are minimal. Participation in this study is voluntary and separate from medical care; therefore, patients enrolled will be informed verbally and in writing that they may withdraw at any time without giving reason and without penalty.

1.3.2 Known Potential Benefits

Immediate potential benefits. It is possible that the sleep extension protocol will improve sleep duration, daytime function, and cardio-metabolic risk profile.

Long-range potential benefits. Participants may gain some satisfaction that their participation will advance our understanding of the relationship between sleep and MetS that may someday improve preventative efforts.

2 Objectives and Purpose

The purpose of this pilot study is to determine the acceptability and feasibility of a sleep extension intervention in middle age adults with MetS. We will also compare pre- and post-intervention differences in sleep duration, MetS risk behaviors, symptoms associated with MetS risk behaviors and self- regulation.

2.1 Primary Objective

To test the feasibility and acceptability of a self-management for adequate sleep intervention (SASI) in community-dwelling, short-sleeping, middle-aged adults with MetS.

2.2 Secondary Objectives (if applicable)

The secondary objectives are to compare differences between pre- and post-intervention sleep duration, MetS risk behaviors (physical activity, sedentary behavior, diet quality), symptoms associated with MetS risk behaviors (affective well-being, fatigue) and self-regulation. We will also explore the perceived barriers and facilitators of SASI (e.g., socio-ecological factors).

3 Study Design and Endpoints

3.1 Description of Study Design

This single site, one group, pilot study will test the acceptability and feasibility of the Self- management for Adequate Sleep Intervention (SASI) in racially/ethnically diverse middle-aged adults with MetS.
This is an 18-week study. In the first 2 weeks, baseline data will be collected. During week 3, the baseline data will be used to confirm study eligibility based on objectively estimated short sleep and to plan the personalized intervention. During weeks 4 to 15, the study team will call or videoconference participants once a week to prescribe a sleep schedule based on their daily sleep diaries. At the end of week 15, participants will be asked to schedule their final visit within 3 weeks.

Acceptability data will be collected at two time points (i.e., pre- intervention and at the final visit). The final visit will include a 30-minute open ended interview to explore perceived facilitators and barriers to implementing SASI. The intake visit will take place at the CTSI. The final visit will take place using video conferencing technology such as WebEx. Weekly contact with the study team will take place during the intervention weeks so that SASI can be personalized based on individual responses to the sleep intervention. This weekly contact will be remote in the form of telephone calls or remote video conferencing technology.

3.2 Study Endpoints

3.2.1 Primary Study Endpoints

This pilot study is designed to test the acceptability and feasibility of SASI. The primary endpoint, acceptability, will be evaluated by the percentage of participants rating SASI as acceptable (overall acceptability survey scores greater than 21), neutral (overall acceptability survey scores equal to 21), and unacceptable (overall acceptability survey scores less than 21) at each of two time points (pre- intervention and post intervention). The feasibility endpoints will be determined by the 1) recruitment rate: the percentage of potential participants screened in order to enroll 60 participants 2) attrition rate: the percentage of enrolled participants completing the 18-week study. Participants will be considered withdrawn after 4 weeks of not responding to phone calls/emails during the intervention and the 3) protocol adherence rates: the percentage of participants completing greater than or equal to 4 daily sleep diary entries per week for 80% or more of the intervention period.

3.2.2 Secondary Study Endpoints

Secondary endpoints will be evaluated by pre- and post-intervention sleep duration, physical activity, sedentary behavior, diet quality, smoking, alcohol use, affective well-being, morning fatigue, evening fatigue, and self- regulation measurements. These secondary endpoints were chosen to gain preliminary evidence of relationships between SASI and sleep duration, MetS risk behaviors, as well as symptoms associated with MetS risk behaviors, and self-regulation. Elucidating these relationships will inform potential pathways through which SASI impacts MetS.

3.2.3 Exploratory Endpoints

Exploratory endpoints are the perceived barriers and facilitators of SASI. These will be identified through bivariate correlations between specific socio-ecological factors associated with sleep duration changes. Qualitative data analysis from the post intervention interviews will be conducted. Identifying perceived barriers and facilitators will lead to future tailoring and/or targeting of SASI.

4 Study Enrollment and Withdrawal

To reach a final sample of N= 60, we will recruit 220 individuals. Of these, we anticipate that 65% will become ineligible through the multi-stage screening process and 20% will be lost to attrition during the intervention leaving 60 participants with evaluable data.

4.1 Inclusion Criteria

To be eligible to participate in this study, an individual must meet all of the following criteria:

1. Greater than or equal to 35 years of age and less than or equal to 60 years of age. Middle aged adults have the highest prevalence of short sleep compared to other stages of adulthood[8,34].
2. Objectively confirmed MetS factors defined by one or more of the following: a) waist circumference greater than 120cm (men) or 88cm (women), b) blood pressure greater than or equal to 135 mmHg systolic or greater than or equal to 85 mmHg diastolic or antihypertensive medication use, c) fasting glucose greater than or equal to 110 mg/dL or insulin or oral hypoglycemic medication use, d) serum triglycerides greater than or equal to 150mg/dL or hypertriglyceride medication use, e) HDL-c less than 40mg/dL (women) or less than 50 mg/dL (men) or medication use for low HDL-c[1]. MetS was selected because individuals with MetS are at high risk for multiple chronic conditions[35].

3. Accelerometry confirmed short sleep (average work day sleep less than or equal to 6 hours/night). Self-reported sleep may overestimate sleep duration. This will ensure that participants will have short sleep patterns that are associated with MetS outcomes.
4. English speaking. Participants will need to demonstrate adequate English comprehension (assessed during informed consent).

4.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Pregnancy/lactation (self-reported). Pregnancy and lactation can disrupt habitual sleep patterns, and hormonal changes during pregnancy increase insulin resistance and may confound MetS[37].
2. Current chemotherapy treatments (self-reported). Current chemotherapy treatments may contribute to fatigue and sleep disturbances[38].
3. Alcohol abuse will be assessed with the Alcohol Use Disorders Identification Test (a measure that has demonstrated good reliability and validity). Alcohol abuse/dependence may contribute to sleep disturbances and limit the participant's ability to take part in sleep interventions[39]. Individuals with scores > 15 (men) or > 13 (women) will be excluded.
4. Night shift or shift work (previous 2 months), trans-meridian travel (previous 4 weeks), or planned shift work or trans-meridian travel during intervention period (self-reported). These will be to ensure that sleep estimates from baseline represent participants' habitual sleep and to ensure adherence with the sleep intervention.
5. Moderate-severe or severe depression will be assessed with the Patient Health Questionnaire (PHQ-9). The PHQ-9 is reliable and has been shown to have construct and criterion validity (Kroenke et al, 2001). Using professional interviews as the criterion standard, a PHQ-9 score of 10 had a sensitivity of 88% and a specificity of 88% for detecting major depression. It has been validated in clinical populations and been used in a large number of cardiovascular studies. Moderate-severe depression or severe depression may contribute to sleep disturbances[40] and interfere with the participant's ability to adhere to the sleep interventions. Therefore, individuals with scores ≥ 15 will be excluded.
6. Chronic use of sleep-promoting medications (self-reported) defined as taking a sleep-promoting medication ≥ 3 nights per week. These may interfere with sleep patterns and limit the participant's ability to take part in the sleep interventions.
7. Habitual napping, defined as 2 naps per day or > 90 minutes of napping on 3 or more days of the week will be assessed during baseline with accelerometry. This will be to ensure adherence with the sleep intervention.
8. Untreated OSA, defined by an apnea hypopnea index (AHI)> 10 using the hypopnea scoring criteria of a 4% or more oxyhemoglobin saturation. This criterion has been used because of its independent association with cardiovascular disease (Punjabi et al 2008, Punjabi et al 2013).
9. Any condition that, in opinion of the PI, will interfere with the safe completion of the study.

4.3 Vulnerable Subjects

No special classes of people who may be considered vulnerable populations (e.g., fetuses, neonates, pregnant women, children less than 16 years of age, prisoners, institutionalized individuals) will be recruited into the study.

4.4 Strategies for Recruitment and Retention

Recruitment. Recruitment strategies will include 1) electronically posting IRB-approved flyers at NYULH, NYU College of Dentistry, NYU College of Nursing, Seastreak commuter ferries and ferry terminals, and metro terminals, 2) advertising in the community so interested individuals can contact the study team, 3) posting/distributing IRB-approved flyers in the community and in clinics, 4) contacting Co-I's past study participants who agreed to be contacted for future research studies, 5) using Epic to identify potential participants (see section below on using DataCore for recruitment/identification purposes, and 6) sending IRB-approved study recruitment messages to potential study volunteers using research registries such as Research Match. Subject identification and recruitment are described in detail below.

Retention. We will offer an incentive for completing each of the study visits, as well as for completing 6 weeks of the SASI intervention (Total incentive: $100). Multiple means of contact will be collected for enrolled participants, including email, mailing address, and phone number. Reminders for study visits will be sent via email, if available, or via one of the other means of contact.

4.4.1 Electronically-posted flyers

IRB-approved electronic flyers will be posted at selected sites with permission from the site. Potential sites include NYULH, NYU College of Dentistry, NYU College of Nursing, Seastreak commuter ferries and ferry terminals, and metro terminals. Interested persons responding to the flyers will be contacted by the RA and provided with the option of proceeding with the IRB-approved verbal telephone consent and screening. See study flyer attached with study team contact information.

4.4.2 Advertising in the community

Community members may learn of the study through electronically-posted flyers (see Section 4.4.1), or other methods, such as radio talk shows (e.g. NYU Langone Nurse Radio, sleep apnea support groups). Interested community members may contact the study team for more information about the study. After contacting the study team, the RA will provide individuals with the option of proceeding with the IRB-approved verbal telephone consent and screening.

4.4.3 Posted/distributed flyers

Flyers promoting the study will be available to individuals who visit the participating health facilities (see Section 4.4.4 NYU Langone Health Recruitment for more detailed information). Flyers will also be distributed at community sites so that interested individuals can contact the study team. Those responding to the distributed flyer will be contacted by the RA and provided with the option of proceeding with the IRB-approved verbal telephone consent and screening.

4.4.4 NYU Langone Health recruitment

This study will recruit individuals from settings affiliated with NYU Langone Health, such as employee health, occupational medicine, cardiology, endocrinology, and college of nursing faculty practices. Flyers promoting this study will be available to individuals who visit the participating health facilities or attend employee health events (e.g. flu shot clinics, health fairs). Clinical staff informed of the study protocol and provided with the IRB-approved study information may also inform individuals about the study and refer them to the study team to contact if interested in participating in the study. With approval of the clinic site, the research staff will also be available at the clinic site during specific hours to facilitate recruitment.

4.4.5 Past study participants

Only past study participants from the Co-I's previous studies who agreed to be contacted for future studies will be contacted by the RA. Contacted individuals expressing interest in the study will be provided with the option of proceeding with the IRB-approved verbal telephone consent and screening.

4.4.6 Use of DataCore/Epic Information for Recruitment Purposes

A study team member will submit a request to DataCore to identify potential participants. Data points to be searched will include age, blood pressure measurements, fasting glucose, serum triglycerides, HDL-c, medication use (antihypertensives, insulin, oral hypoglycemic, hypertriglyceridia medication, or medication use for low HDL-c) within the last 6 months. A DataCore query will be run at the start of the study and six months after the study start depending on recruitment rates. DataCore will request a report from EPIC for these patients with identifiable protected health information (name, email address) for research related purposed. Only study team members with Epic access will have access to the search results.

The Epic team will set up a recruitment message in MyChart and work with the PI and project coordinator to send it out. The IRB-approved MyChart recruitment message is attached. The text will include a description of the study, inclusion and exclusion criteria, and contact information for the PI (phone number and email). The recruitment message may be repeated two times at two-month intervals if needed for subject recruitment (total 3 Epic MyChart messages).

These data will be used solely for participant identification in order to determine patients who are initially eligible and for chart review (previous 12-month blood specimen results from Co-investigator's study). The study team will discard information from those who do not wish to participate in the study. If a subject requests information regarding opting out of further recruitment for all research, subjects will be directed to

contact the study coordinator or have subjects contact research-contact- optout@nyumc.org or 1-855-777-7858.

4.4.7 Research Match

We will also utilize Research Match (ResearchMatch.org), a national, electronic, web-based recruitment tool that was created through the Clinical and Translational Science Awards Consortium in 2009 to send study recruitment messages to potential study participants. This study's recruitment content will be inserted into the standard Research Match electronic notification that informs possible matched participants that they have been identified as a potential match for this study. The Research match recruitment message is attached. The secure Research Match clearinghouse will route this standard Research Match notification to each of these Research Match participants. These potentially matching participants will have the option of replying "yes", "no", or "not respond" through a set of quick links available in this notification of the study announcement. The contact information of the "yes" responding participants will be made available on the PI's "Manage my Study" dashboard. A member of the research team will contact the individual who expresses interest and provide the option for the verbal/telephone consent and screening or an in-person meeting. If a subject requests information regarding opting out of further recruitment for all research, subjects will be directed to contact the study coordinator or have subjects contact research-contact-optout@nyumc.org or 1-855-777- 7858.

4.5 Duration of Study Participation

The study is expected to last 18 weeks. This period includes the initial visit at the CTSI, the first 2 weeks of baseline data collected during the participant's everyday routine, a third week to evaluate the sleep baseline data to confirm short sleep using the accelerometry data and to plan the personalized intervention, weeks 4-15 delivering the SASI intervention, and then a final visit by WebEx videoconferencing within 3 weeks of completing the intervention.

4.5.1 Reasons for Withdrawal or Termination

Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study if:

- Any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
- The participant does not respond to phone calls/emails for 4 weeks during the intervention.

4.5.2 Handling of Participant Withdrawals or Termination

Participants will be considered withdrawn if they cannot be contacted for 4 weeks during the intervention using all of the contact information collected. No further efforts will be made to contact the participant and that participant will be considered lost to follow-up. Abrupt termination of participation in the study intervention poses no safety risk to participants. As this study is minimal risk, efforts will not be made to collect safety and efficacy data after withdrawal.

Any data collected before withdrawal from the study will be retained for analysis, and no new data will be collected. If the participant requests that data be destroyed, all paper records will be shredded, and any data already processed into computer files will be removed. However, if results based on the participant's data have been submitted for publication or presentation before the request is made, the results cannot be removed from the publication or presentation.

4.5.3 Premature Termination or Suspension of Study

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the PI and the appropriate funding agency, and New York University IRB. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension. As this study will evaluate acceptability, feasibility, and preliminary efficacy, it will not be possible to determine whether the intervention is efficacious or futile for the population studies. Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

If the study is temporarily suspended, the study may resume once concerns about safety, protocol compliance, data quality is addressed and satisfy the sponsor and/or IRB.

5 Behavioral/Social Intervention

5.1 Study Behavioral or Social Intervention(s) Description

SASI, is based on Cognitive Behavioral Therapy for Insomnia (CBTI). SASI differs from CBTI because the first step of sleep restriction prescribed by CBTI is not used in SASI. This is because the participants have already been verified as short-sleepers. However, SASI does employ CBTI's gradual approach for increasing sleep time and applies it to short sleepers. The 12-week intervention period of gradually increasing sleep duration by advancing bedtimes 15 minutes per week (or 1 hour per month) will provide the time needed to increase sleep duration in habitual 5 hour sleepers to the recommended 7 to 8 hour sleep duration. Like CBTI, SASI extends sleep duration based on sleep efficiency (the proportion of time spent sleeping during a sleep episode). Bed times and wake times will be prescribed each week for each participant and allow for gradual increases in sleep opportunity. Bedtimes will be set 15 minutes earlier each week provided sleep efficiency remains >90%. Earlier betimes will extend sleep duration by increasing the opportunity for sleep. Wake times will not be changed because wake times are often determined by external demands, such as work schedules. There will be no control intervention in this pilot study.

5.1.1 Administration of Intervention

This intervention will be delivered by a trained study team member for 15 weekly sessions that consist of approximately 15 to 30-minute phone calls or NYU WebEx videoconferencing based on the participant's preference. During these individual weekly sessions, the participant and the study team member will review the participant's previous week's consensus sleep diary, discuss challenges implementing the sleep intervention, and determine the work day bedtime-wake time schedule for the upcoming week. Daily text message or email reminders will be sent to participants to complete their daily sleep diary as needed.

5.1.2 Procedures for Training Interventionalists and Monitoring Intervention Fidelity

The PI and trained study team members will be responsible for administering the intervention. We will use recommendations of the Treatment Fidelity Workgroup of the NIH Behavior Change Consortium[45] to enhance SASI fidelity. The treatment fidelity plan includes audiotaping of each SASI session and reviewing content against an a priori performance checklist to ensure consistency in SASI delivery. Treatment fidelity will be monitored by the research team with guidance from Dr. Dickson, Co-investigator. Barriers to implementing SASI will be identified and resolved together with the participant and the PI or Co-I's.

5.1.3 Assessment of Subject Compliance with Study Intervention

The study team will track feasibility data, including completion of daily sleep diaries and retention rates. Participant engagement will be assessed through attendance records for weekly sessions and by the number of sleep diaries completed each week. Daily texts or email reminders will be sent to participants to remind them to complete the diary as needed.

6 Study Procedures and Schedule

6.1 Study Procedures/Evaluations

6.1.1 Study Specific Procedures

Participants meeting the telephone screen eligibility criteria will be invited to the CTSI for an intake visit (CTSI visit 1). The enrollment procedures at the CTSI visit 1 will include the 1) informed consent process, 2) further screening for eligibility using surveys, and 3) further screening to objectively confirm MetS (anthropometric measurements and 3 ml. blood draw if needed for glucose and lipids). (Participants will have the option of providing an optional 8ml blood sample for blood storage.).

Assessments will be done at the following time points: 1) CTSI visit 1, 2) during 2-week baseline assessment at home, 3) during the last 2-weeks of the intervention, and 4) within three weeks of completing the intervention (Final visit – at home).
The screening surveys, physical exam, and blood draw will be completed at the CTSI at Bellevue Hospital 462 1st Avenue, New York, NY 10016 in C/D Building, 4th Floor New York, NY. About 220 subjects will be in the study. Accelerometry, pulse oximetry (as needed), acceptability (pre- and post- intervention), Composite Scale of Morningness, Economic Vulnerability Survey, Family Assessment Device – General Functioning Scale, 36-item Short Form Health Survey (SF-36) version 1, ASA24, Demographics- SDOH: Alcohol use (AUDIT C), Demographics – SDOH: Tobacco use, Index of Self- regulation, SAFTEE questionnaire, Sleeping Environment Survey, PROMIS Fatigue 6a –morning, PROMIS Fatigue 6a – evening, Epworth Sleepiness Scale, Daily sleep diaries, acceptability survey (post- intervention), and the open-ended interview will take place at home.

Demographic and Clinical Characteristics.

- Demographic:
  - BRICS NINR Demographic Data Elements ○ BRICS NINR Demographics (with race clarifying questions)
  - BRICS Demographics - Diagnosis
- General health questions (self-reported) ○ Pregnancy/lactation ○ Current chemotherapy treatments ○ Habitual napping ○ Sleep promoting medication use (prescribed or over the counter) ○ Cardio-metabolic disease medication use:
    - insulin
    - oral hypoglycemic medication
    - anti-hypertensive medications
    - hypertriglyceridemia medication
    - medications for low HDL-c
- Physical exam**:** All measurements will be completed by a qualified and trained RA.
  - Height ○ Weight ○ BMI
  - Waist circumference ○ Blood pressure
    - average of 3 recordings each taken 1 minute apart, following 10 minutes of inactivity.
    - A 4th recording will occur if any two systolic or diastolic readings are >5 mmHg apart.
      - Neck circumference

Surveys. Participants enrolled in the study will be asked to complete several surveys. All surveys will be completed using REDCap. At home surveys will be administered through the Assessment Center Application Programming Interface in REDCap (Research Electronic Data Capture). For the PROMIS-fatigue morning scale and the PROMIS-fatigue evening scale, the REDCap system will be programed to send two separate timed emails, at each time point, to subjects with instructions to answer the questions based on how they felt when they woke up for morning fatigue severity and how they felt when they went to bed for evening fatigue severity.

- **CTSI visit 1 surveys** ○ BRICS NINR Demographic Data elements ○ BRICS NINR Demographics (with race clarifying questions)
  - BRICS Demographics - Diagnosis

- ARES
- Alcohol Use Disorders Identification Test (AUDIT)
- General health questions
- PHQ-9
- Primary Care Provider
- Contact form

- **Baseline Surveys (weeks 1 or 2)**
  - Acceptability survey (pre-intervention)
  - Composite Scale of Morningness
  - Economic Vulnerability Survey
  - Family Assessment Device – General Functioning Scale
  - Sleeping Environment Survey
  - 36-item Short Form Health Survey (SF-36) version 1
  - ASA24
    - The ASA24 (ASA24-2016) is a freely available web-based tool designed to collect self-report dietary recall data. While under- reporting and inaccuracy in self-report of dietary intake is a known limitation, 24-hour recalls provide more accurate data than other screeners or food frequency questionnaires, and the ASA24 has demonstrated similar criterion validity against actual food intaketo other more complex and time consuming recall methods.
  - Demographics – SDOH: Alcohol use (AUDIT C)
  - Demographics – SDOH: Tobacco use
  - Index of Self-Regulation
  - SAFTEE questionnaire
  - PROMIS-Depression 6a
- **End of study surveys at home (week 15)** ○ 36-item Short Form Health Survey (SF-36) version 1
  - ASA24
    - The ASA24 (ASA24-2016) is a freely available web-based tool designed to collect self-report dietary recall data. While under-reporting and inaccuracy in self-report of dietary intake is a known limitation, 24-hour recalls provide more accurate data than other screeners or food frequency questionnaires, and the ASA24 has demonstrated similar criterion validity against actual food intaketo other more complex and time consuming recall methods.
  - Demographics – SDOH: Alcohol use (AUDIT C)
  - Demographics – SDOH: Tobacco use
  - Index of Self-Regulation
  - ○ SAFTEE questionnaire
  - PROMIS- Depression 6a
- **Intervention surveys at home (weeks 1-15)** ○ Epworth Sleepiness Scale (weekly) ○ PROMIS Fatigue 6a - morning (weekly) ○ PROMIS Fatigue 6a - evening (weekly) ○ Sleep Diary (daily)

Objective Sleep and Physical Activity Measures. Participants will wear a wrist accelerometer 24/7 for 14 continuous days during the first 2 weeks of baseline data collection and the last 2 weeks of the SASI intervention. The accelerometer may be removed for bathing and contact sports. Data collected from the accelerometer will be used to estimate sleep duration and physical activity levels. A wrist worn fitbit will also be worn during the 2-week baseline and 12 week SASI intervention by the study by participants.

Objective OSA Measures. Participants being treated for OSA will wear a pulse oximeter on their fingertip for one night during the first 2-week baseline data collection.

Training and Treatment Fidelity: SASI facilitators will be individuals with prior training and experience delivering sleep interventions. Facilitators will complete training in intervention content and telephone

facilitation skills through didactic instruction and roleplaying. They will be trained to refer participants to their providers for any medical questions.

All sessions will be digitally audio-recorded using a WebEx conference call line recording capability. A subset of 20% of SASI sessions will be reviewed to evaluate treatment fidelity and provide feedback to intervention facilitators. Facilitators' degree of adherence to the protocol will be rated using a SASI Adherence Scale.

6.1.2 Standard of Care Study Procedures

Not applicable.

6.2 Laboratory Procedures/Evaluations

6.2.1 Clinical Laboratory Evaluations

Biochemistry: Participants *without* evidence of fasting glucose, triglyceride, and HDL-c results during the previous 12 months will have 3 ml. in total blood drawn at CTSI Visit 1.

Participants recruited from outside the Langone system will have the option to provide documentation of their most recent blood work. Long term changes in blood lipid levels has been documented as small (0.7% per year) (Glaszious et al 2008). This approach is consistent with other studies examining the relationship between sleep and metabolic outcomes whereby most recent bloodwork from subject's medical records were used (Reutrakul et. Al 2015).

The blood specimens will be collected at the NYU Langone Health CTSI Clinical Research Center (CRC) at Bellevue Hospital C/D Building, 4th floor by the Clinical Research Coordinators. The estimated total volume of blood drawn is 3 ml (for participants needing a fasting glucose, triglyceride, and HDL-c analyses). All vacutainer tubes will be labeled with participants' unique study ID without PHI (e.g. P20+123). The unique study ID will stored in a locked cabinet in the PI's locked office.

Analysis will be completed at the CTSI lab using standard techniques for analyzing the blood samples. The laboratory will report the results through the CRC EMR integration with the NYU Clinical Research Management System and REDCap.

Table 1: Biomarker collection for MetS verification

Biomarker	Volume required	Specimen type	Collection tube	Lab analysis method	Collection requirement
FBG	1 ml	serum	Red top	spectrophotometry	Fasting 8 hours prior to collection
TG	1 ml.	serum	Light green PST gel and lithium heparin	spectrophotometry	Fasting 8 hours prior to collection
HDL-c	1 ml.	serum	Light green PST gel and lithium heparin	spectrophotometry	Fasting 8 hours prior to collection

Research Subjects will be asked to abstain from food, alcohol use, recreational drug use, and caffeinated beverages for 8 hours before the blood collection. Blood will be collected by peripheral vein venipuncture by the coordinators at the CRC between 0800-1000 to control for diurnal variation and to support subject abstinence requirements. Additionally, to control for diurnal variability we will document the time the patient awoke and evaluate the time lapse during analysis.

6.2.2 Other Assays or Procedures

Future use of Stored Specimens

De-identified optional blood samples will be stored for future analysis of biomarkers of metabolic disorders or other health conditions, no genetic material will be collected. These optional blood samples will be collected, used, stored, distributed, and transferred only in accordance with all applicable laws and regulations, all applicable policies of NYU Langone Health, NYU Langone Health's IRB Policies and Procedures and the written consent and authorization signed by the research subject. The

protocol submitted, reviewed and approved by NYU Langone Health's IRB will guide the collection of all biomarkers. Written informed consent signed by the research subject will be obtained before any blood samples are collected.

Subjects can opt-out of the optional blood draw and the storage of these specimens in the biorepository through a question on the written consent form.
Subjects will not be contacted when their stored samples are used for future analysis, as they will provide their consent to store and use their samples until they are used up at the time of informed consent. If a subject revokes his/her consent to allow storage of his/her samples, the samples will not be drawn.

Purpose of Future Research

The specimens will be shared with members of the research team and the P20 center at NYU Meyers. With the authorization of the PI and the P20 center director the samples will be made available to researchers whose scope of work would fall under the scope described in the consent and this protocol for analysis of metabolic conditions and other health conditions.

Type of Sample and Amount

The optional 20 ml. of whole blood will be drawn in an EDTA tube. Fasting will not be required.

Location of Storage and Security Protections

The optional blood specimens obtained for future analysis will be hand transported from the data collection site to the biorepository at the NYU Rory Meyers College of Nursing 433 First Ave New York NY 10010. The Research Assistant will log in the specimen for storage in the defined storage space for the study. The repository is secured by an alarm, the code for which will be known only to the research staff. With the authorization of the PI and the P20 center directors the samples will be made available to researchers whose research meets the requirements of federal regulations and the IRB.

Duration of Storage for Future Research

The specimens will be stored until they are used up, or if the subject requests to withdraw their specimen from future use. Subjects will be informed that they can withdraw their specimens at any time and if they so request, the specimens will be destroyed and not used for future research.

Labeling of and Access to Stored Specimens

The stored samples will be identified by a unique study ID number without PHI. We will keep one separate and password-protected and encrypted computer file that contains identifiable data that is necessary to keep if subjects contact us to withdraw their samples from storage (phone numbers, email, and U.S. mailing addresses). This file will be the only file that can link subject names, addresses, and/or telephone numbers to the study unique codes and is only accessible by the study PI.

The PI and members of the P20 research team will have access to the specimens.

7.3 Study Schedule

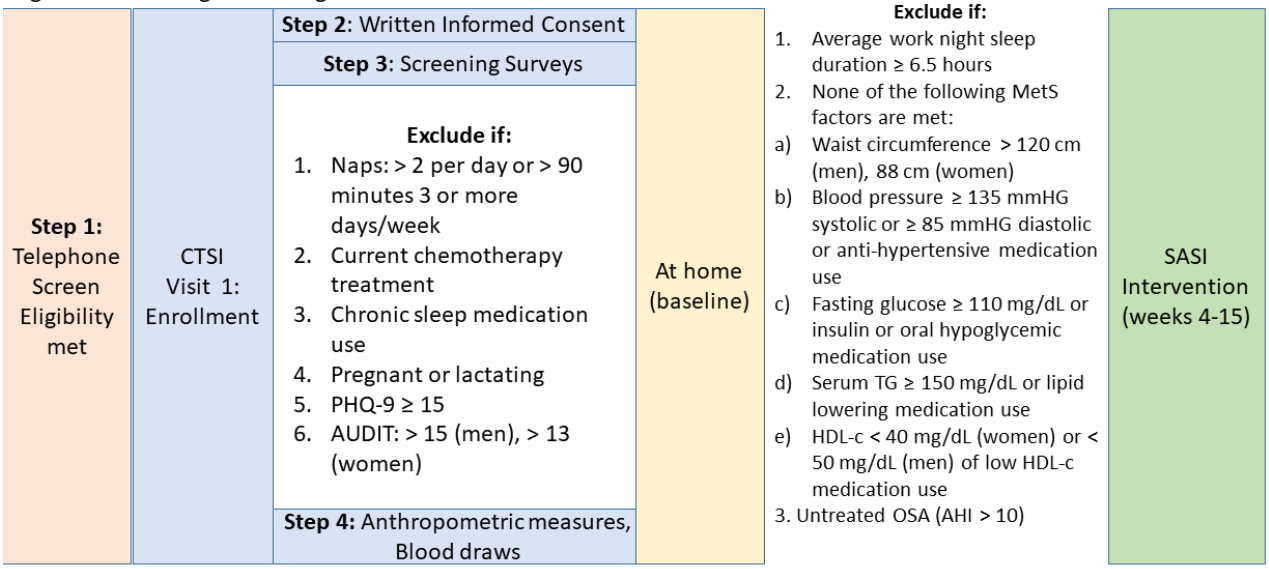
7.3.1 Screening

Telephone Screening (within 4 weeks of CTSI visit 1)

- Telephone screen administered (Duration: approximately 15 minutes) ○ If eligible and interested, schedule CTSI visit 1 within 4 weeks of the telephone screen
- Figure 1 for Multi-stage Screening and Enrollment Flowchart

Figure 1: Multi-stage Screening and Enrollment Flowchart

Figure 1: Multi-stage Screening and Enrollment Flowchart



7.3.2 Enrollment/Baseline

Enrollment Visit (CTSI Visit 1, within 4 weeks of screening interview): Duration of visit: approximately 120 minutes

- Review informed consent form and, if desired by potential participant, obtain written informed consent. Provide copy of signed form to participant.
- Review intervention audio consent and, if desired by potential participant, obtain written audio consent. Provide copy of signed form to participant.
- See Table 2 for eligibility measurements and surveys during CTSI Visit 1

Table 2: Eligibility tests and surveys during Enrollment CTSI Visit 1		
	Number of measurements/volume/questions	Estimated time
Anthropometric measurements		
Height	3	30 minutes
Weight	1	
Waist circumference	3	
Neck circumference	1	
Blood pressure	3-4	
Blood Draw within 12 months of visit 1		
FBG	1 ml	15 minutes
TG	1 ml.	
HDL-c	1 ml.	
Optional blood sample stored for future analyses	20 ml.	

Surveys		
BRICS NINR Demogrpahic Data Elements	n/a	Study team enters
BRICS NINR Demographics with race clarifying question	14	< 5 minutes
BRICS NINR Demographics - Diagnosis	n/a	Study team enters
ARES questionnaire	17	< 5 minutes
AUDIT	10	5 minutes
General health questions	10	< 5 minutes
PHQ-9	9	< 5 minutes
Primary Care Provider	5	< 5 minutes
Contact Form	12	< 5 minutes
TOTAL TIME		**~75 minutes**

- Instruct participant on the use of the following (20 minutes total):
  - o wrist accelerometer o consensus sleep diary o surveys to be completed during the 2-week baseline home assessment.
- Arrange for a method (daily texts and/or emails sent through a secure email server) for participants to receive reminders to complete the daily sleep diaries as needed.
- Arrange for a convenient day of week and time for the participant to receive weekly phone or videoconferencing calls during the intervention period.

7.3.3 Intermediate Visits

Week 1: Baseline Data Collection

- See Table 3 for study related procedures during week 1
- See Table 4 for baseline surveys to be completed during week 1 or 2.
- Daily texts and/or emails will be sent through a secure email server to remind to participants to complete the daily sleep diaries as needed Arrange for pick up or UPS return of pulse oximeter as needed.

Table 3: Baseline Data Collection Week 1

	Number of times to complete per week	Number of questions	Estimated time
Wrist accelerometer and fitbit	Wear 24/7	n/a	n/a
Pulse oximeter (as needed per protocol)	Wear for 1 night	n/a	n/a
Daily sleep diary	7	9	< 5 minutes/day < 35 minutes/week
PROMIS Fatigue 6a -morning	1	6	< 5 minutes
PROMIS Fatigue 6a - evening	1	6	< 5 minutes
Epworth Sleepiness Scale	1	8	< 5 minutes/week
TOTAL TIME			**< 50 minutes/week**

Table 4: Baseline Surveys Completed during Baseline Weeks 1 or 2		
	Number of questions	Estimated time
Acceptability Survey (pre-intervention)	7	< 5 minutes
Composite Scale of Morningness	13	5 minutes
Economic Vulnerability Survey	8	5 minutes
Family Assessment Device – General Functioning Scale	12	< 5 minutes
Sleeping Environment Survey	11	5 minutes
36-item Short Form Health Survey (SF-36) version 1	36	40 minutes
ASA24	varies	24 minutes
Demographics – SDOH: Alcohol use (AUDIT C)	3	< 5 minutes
Demographics – SDOH: Tobacco use	2	< 5 minutes
Index of Self-Regulation	9	5 minutes
SAFTEE	128	10 minutes
PROMIS Depression 6a	6	< 5 minutes
TOTAL TIME		**~114 minutes**

7.3.3.2 Week 2: Baseline Data Collection

- Record adverse events as reported by participant or observed by investigator.
- See Table 5 for study related procedures.
- Daily texts and/or emails sent through a secure email server will be sent to remind to complete the daily sleep diaries as needed
- Arrange for the pick-up or UPS return of the accelerometry devise.
- Arrange for convenient date/time to call or WebEx videoconference during week 3.

Table 5: Baseline Data Collection Week 2			
	Number of times to complete per week	Number of questions	Estimated time
Wrist accelerometer and fitbit	Wear 24/7	n/a	n/a
Daily sleep diary	7	9	< 5 minutes/day < 35 minutes/week
PROMIS Fatigue 6a morning	1	6	< 5 minutes
PROMIS Fatigue 6a evening	1	6	< 5 minutes
Epworth Sleepiness Scale	1	8	< 5 minutes
TOTAL TIME			**~50 minutes/week**

7.3.3.3 Week 3

- The study team will evaluate participants ongoing eligibility for SASI based on the accelerometry data confirming that participants are short sleepers.
- Contact participants to notify them of their eligibility status for the SASI intervention phase of the study.
  - Retained participants are those who have objectively confirmed MetS , objectively confirmed short sleep based on the 2-week baseline home sleep test, and objectively confirmed treatment of OSA, if applicable.
- For retained participants, review baseline week 2 sleep diary data from work days to prescribe bed times and wake times for the first week of the intervention.
- Administer the study intervention in accordance with the SASI protocol.
  - Briefly, bedtimes will be set 15 minutes earlier each week provided sleep efficiency remains >90%. Earlier betimes will extend sleep duration by increasing the opportunity for sleep. Wake times will not be changed because

wake times are often determined by external demands, such as work schedules.

- Arrange for the weekly phone or WebEX videoconferencing meeting to administer the intervention for the following week.

7.3.3.4 Week 4

- Participant will initiate new sleep schedule as prescribed by the study team.
- See Table 6 for study related procedures.
- Send daily text message or email reminders via a secure email server to participants to complete their daily sleep diary as needed.
- Record participant's adherence to the intervention program.
- Record adverse events as reported by participant or observed by investigator.
- Arrange for the weekly phone or WebEx videoconferencing meeting to administer the intervention for the following week.

Table 6: SASI Data Collection Weeks 4 – 13

	Number of times to complete per week	Number of questions	Estimated time
Fitbit	Wear 24/7	n/a	n/a
Daily sleep diary	7	9	< 5 minutes/day < 35 minutes/week
PROMIS Fatigue 6a morning	1	6	< 5 minutes/week
PROMIS Fatigue 6a evening	1	6	< 5 minutes/week
Epworth Sleepiness Scale	1	8	< 5 minutes/week
TOTAL TIME			**< 50 minutes/week**

7.3.3.5 Weeks 5-13

- Participant will initiate new sleep schedule each week as prescribed by study team.
- See Table 6 for study related procedures.
- Send daily text message or email reminders via a secure email server to participants to complete their daily sleep diary as needed.
- Record participant's adherence to the intervention program.
- Record adverse events as reported by participant or observed by investigator.
- Arrange for the weekly phone or WebEx videoconferencing meeting to administer the intervention for the following week
- Week 13: Arrange for the delivery of the accelerometry devise by the study team or UPS.

7.3.3.6 Week 14

- Participant will initiate new sleep schedule as prescribed by the study team.
- See Table 7 for study related procedures.
- Send daily text message or email reminders via a secure email server to participants to complete their daily sleep diary as needed.
- Arrange for the weekly phone or WebEX videoconferencing meeting to administer the intervention for the following week.
- Record participant's adherence to the intervention program.
- Record adverse events as reported by participant or observed by investigator.

Table 7: Data Collection Week 14

	Number of times to complete per week	Number of questions	Estimated time
Wrist accelerometer and fitbit	Wear 24/7	n/a	n/a
Daily sleep diary	7	9	< 5 minutes/day < 35 minutes/week

PROMIS Fatigue 6a morning	1	6	< 5 minutes
PROMIS Fatigue 6a evening	1	6	< 5 minutes
Epworth Sleepiness Scale	1	8	< 5 minutes/week
TOTAL TIME			**< 50 minutes/week**

7.3.3.7 Week 15

- Participant will initiate new sleep schedule as prescribed by the study team.
- See Table 8 for study related procedures
- Send daily text message or email reminders via a secure email server to participants at a mutually agreed upon time to remind them to complete their daily sleep diary.
- Record participant's adherence to the intervention program.
- Record adverse events as reported by participant or observed by investigator.
- Arrange for the return of the accelerometry devise to the study team or UPS
- Arrange for a date and time for the final CTSI visit 2 (Time Point 2, post-intervention) within three weeks of completing the intervention

Table 8: Data Collection Week 15

	Number of times to complete per week	Number of questions	Estimated time
Wrist accelerometer and fitbit	Wear 24/7	n/a	n/a
Daily sleep diary	7	9	< 5 minutes/day < 35 minutes/week
PROMIS Fatigue 6a morning	1	6	< 5 minutes
PROMIS Fatigue 6a evening	1	6	< 5 minutes
Epworth Sleepiness Scale	1	8	< 5 minutes
36-item Short Form Health Survey (SF-36) version 1	1	36	40 minutes
ASA24	1	varies	24 minutes
Demographics – SDOH: Alcohol use (AUDIT C)	1	3	< 5 minutes
Demographics – SDOH: Tobacco use	1	2	< 5 minutes
Index of Self-Regulation	1	9	5 minutes
SAFTEE	1	128	10 minutes
PROMIS Depression 6a	1	6	< 5 minutes
TOTAL TIME			**~140 minutes/week**

7.4 Final Study Visit (within 3 weeks of completing SASI): Duration < 60minutes

- Record any new medications prescribed during the study period to treat hyperglycemia, hypertension, hypertriglyceridemia, or low HDL-c.
- See Table 10 for study related procedures.
- Record adverse events as reported by participant or observed by investigator.
- Notify participant that aggregate-level results will be available after dissemination of study findings begins.
- Instruct participant to report any subsequent event(s) that the participant, or the participant's physician, believes might reasonably be related to participation in this study.

Table 10: Final Study Visit (at home)

	Number of questions	Estimated time
Acceptability survey (post intervention)	7	< 5 minutes

Open ended interview	varies	30 minutes
TOTAL TIME		**~ 35 minutes**

7.5 Withdrawal Visit

If a participant withdraws or is withdrawn from the study, no further study visits or procedures will be completed.

7.6 Unscheduled Visit

Not applicable.

7.7 Concomitant Medications, Treatments, and Procedures

Any medications prescribed by treating health care provider for hyperglycemia, hypertension, hypertriglyceridemia, or low HDL-c levels during study participation will be recorded on the case report forms (CRFs). For this protocol, a prescription medication is defined as a medication that can be prescribed only by a properly authorized/licensed clinician.

8 Assessment of Safety

8.1 Specification of Safety Parameters

The study will involve no more than minimal risk to research participants. The probability and magnitude of harm or discomfort anticipated for this research are not greater than what this same population encounters in daily life or during the performance of physical or psychological examinations or tests. The only alternative to study participation is non-participation.

8.1.1 Definition of Adverse Events (AE)

An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

8.1.2 Definition of Serious Adverse Events (SAE)

Serious Adverse Event

Adverse events are classified as serious or non-serious. A serious adverse event is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events.

8.1.3 Definition of Unanticipated Problems (UP)

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc.)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

8.2 Classification of an Adverse Event

8.2.1 Severity of Event

For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

8.2.2 Relationship to Study Intervention

The clinician's assessment of an AE's relationship to study intervention is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported. All AEs must have their relationship to study intervention assessed. In a clinical trial, the study intervention must always be suspect. To help assess, the following guidelines are used.

- Related – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- Not Related – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

8.2.3 Expectedness

Dr. Malone will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention. As this study is minimal risk, no adverse events are expected.

9.3 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study intervention (assessed only by those with the training and authority to make a diagnosis),

and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.
The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study.

9.4 Reporting Procedures – Notifying the IRB

9.4.1 Adverse Event Reporting

AEs are not expected due to participation in this minimal risk study. However, AE forms will be completed at each of the study assessments as well as any AEs reported during the weekly intervention sessions.

Study participants will be encouraged to contact study staff immediately should any AEs occur during study participation. Periodic adverse event reporting will include any AE that occurs while a participant is on the research protocol, regardless of whether it is considered related to study participation.
The PI will submit as part of annual progress reports to the IRB a summary of monitoring that took place; cumulative adverse event data; assessments that were performed to evaluate external factors or relevant information that may have an impact on the safety of study participants or ethics of the research study; outcomes of procedural reviews conducted to ensure participant privacy and confidentiality; and final conclusions regarding changes to the anticipated risk-to-benefit ratio of study participants and recommendations related to continuing, changing, or terminating the study.

9.4.2 Serious Adverse Event Reporting

SAEs are not expected due to participation in this minimal risk study. The procedure for AE reporting will be followed for SAEs. In addition, if a serious adverse event occurs, it will be reported in a timely fashion after adjudication: All SAE reports will be made to the IRB within 5 working days; any participant deaths will be reported to the NINR Program Officer within 24 hours of realization, and all other serious adverse events will be reported to NINR within 72 hours of realization.

9.4.3 Unanticipated Problem Reporting

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. It is the site investigator's responsibility to report UPs to their IRB and to the DCC/study sponsor. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, oroutcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;

- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB and to the study sponsor within the timeframe described in 8.4.2
- Any other UP will be reported to the IRB and to the study sponsor within the timeframe described in 8.4.1 for AEs.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within the Time frame described for AEs or SAEs, as appropriate, after the IRB's receipt of the report of the UP from the investigator.

9.4.4 Reporting of Pregnancy

Pregnant or breastfeeding participants will not be able participate in the study because pregnancy and lactation can disrupt habitual sleep patterns, and hormonal changes during pregnancy increase insulin resistance and may confound MetS[37]. If participants become pregnant during the course of the study, their data will not be used in the analyses.

10.5 Reporting Procedures – Notifying the Study Sponsor

The study clinician will complete a SAE Form within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form and submitted to the DCC/study sponsor within 24 hours of site awareness. See Section 1, Key Roles for contact information.
- Other SAEs regardless of relationship will be submitted to the DCC/study sponsor within 72 hours of site awareness.

All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the adherence to be stable. Other supporting documentation of the event may be requested by the DCC/study sponsor and should be provided as soon as possible.

As a follow-up to the initial report, within the following 48 hours of awareness of the event, the investigator shall provide further information, as applicable, on the unanticipated event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse effects shall be provided promptly to the study sponsor.

10.6 Reporting Procedures – Participating Investigators

As the study intervention and data collection will be conducted only at NYU, procedures for monitoring and reporting across sites are not provided.

10.7 Study Halting Rules

As this study is minimal risk, it is not anticipated that the study may be halted. However, if there is a determination of unexpected, significant, or unacceptable risk to participants, the study may be temporarily suspended or prematurely terminated as described in section 6.7.

10.8 Safety Oversight

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

Following are plans for data and safety monitoring during the pilot study.

Monitoring entity. This study will be monitored by the PI, the research coordinator, the bio-statistician, and the IRB. The PI will ensure that the research coordinator and statistician undergo training in the study protocol. The research coordinator will also be trained in the safety protocol for depression. The PI will oversee adherence to the study protocol to ensure the safety, reliability, and validity of data collection. The PI will be responsible for submitting all necessary reports to the study sponsor and the IRB. The research coordinator will prepare weekly reports on participant demographics, recruitment, attrition, data collection, data entry updates, and any other issues or concerns since the last research team meeting. The statistician will prepare monthly reports about missing, invalid, or inconsistent data on selected key variables. The reports will also contain a summary of monthly accrual and cumulative accrual, a summary of key characteristics of the study participants, and a summary of the completeness and quality of data.
Monitoring Study Safety. Once enrollment is initiated, the PI will arrange weekly meetings. These meetings will consist of retrospective and concurrent evaluation of all research procedures, including participant screening for inclusion/exclusion criteria, the informed consent process, and participant study instructions, as well as any necessary staff training in the IRB approved study protocol. Participant demographics, recruitment, retention, data collection, and data entry updates will be monitored weekly.

Quality control assurances of data will be reviewed in monthly meetings and will include information about missing, invalid, inconsistent data on selected key variables, and a summary of key characteristics of the study participants. A random sample of participants' research records will be reviewed to ensure compliance with IRB requirements, conformance with informed consent requirements, verification of source documents, and investigator compliance by the PI monthly. Meetings will also be arranged by the PI if an adverse event occurs.

Minimizing research-associated risk. We do not believe that there are any major risks associated with the proposed study, although a subject may be identified with moderate/severe or severe depression. This is not a research-associated risks but may be detected during screening or participation in the study. The sleep intervention and accelerometry monitoring have minimal risk. Trained research personnel will perform all testing and will be monitored by the PI. Throughout the study, the PI and the research coordinator will monitor participants for adverse events and for adherence to the study protocols. We have developed the following medical alert and reporting policies:

1. ARES questionnaire
    a. Scores greater than or equal to six.
        i. Send letter to participant and the participant's primary care provider, if available, referring the participant to a nearby sleep disorders center for further evaluation and treatment.

2. Depression

Depressive symptoms will be assessed using PHQ-9 during the screening interview. Individuals identified with moderate/severe or severe depression during the screening interview will not be enrolled in the intervention phase of the study as per study protocol. If moderate/severe or severe depression is identified, a medical alert and reporting policy has been developed along with a Depression Safety and Referral Plan (see Depression Safety and Referral Protocol and Arranging Care).

a. PHQ-9 score ≥15
    i During screening, the interviewer will proceed to assess the participant for thoughts of suicide using the Columbia-Suicide Severity Rating Scale, before continuing with other pre-screening surveys. The interviewer shall stay with the participant during this time and proceed with the response protocol for the Columbia-Suicide Severity Rating Scale based on the participant responses, as well The Depression Safety and Referral Protocol and Arranging Care.

Participant Screening and Enrollment. When individuals are contacted to determine their interest in participating in the study, no language will be used that will indicate any study opportunity/eligibility or personal health information unless research personnel are speaking directly with the party of interest. All data from participants screened for the study will be entered into the Research Electronic Data Capture (REDCap). The collected data will be helpful in examining the patient population and feasibility of enrollment criteria and will include gender, age, race, and reason for exclusion. For retained participants, the research staff will collect

and enter required data (written informed consent and demographics) onto study data forms in REDCap. Individuals will be assigned a unique study ID number.

This study ID number will be linked to the participant name only. Only the PI and the research coordinator will have access to the linkage between the participant identity and the study identification number. This linking file will be password protected and stored on a secure NYU server separate from study data. This linking file will be destroyed at closure of the study, and the study will remain open with the IRB until these identifiers are destroyed. The unique study identification number will be used on all data forms, and no personal identifiers will be connected to the data. Paper records, such as the informed consent documents, will be kept in a locked file cabinet in a locked office. All data will be reported in aggregate.

Binders. The research coordinator will prepare and maintain a participant-specific binder for each participant containing all non-electronic Case Record Files. A regulatory file will also be maintained to include the IRB-approved protocol, original informed consent documents, and other study-related regulatory documents. All paper research records and case record files will be maintained in a locked file cabinet in a secure facility within the College of Nursing. Access to the research records, study database and PHI's will be restricted to study personnel as approved by the PI and IRB.

Data entry, processing, monitoring. This study will use REDCap for data capture and management. Data exports will be limited to the PI, the research coordinator, and the statistician for generating reports and conducting statistical data analysis. Weekly meetings will include reports on participant recruitment and retention, adverse events, and protocol deviations. Monthly meetings will consist of summaries of monthly accrual and cumulative accrual, key characteristics of the study participants, and the completeness and quality of data. Information on missing, invalid, and inconsistent data on selected key variables will be reviewed.

Data Security. All data will be saved in an electronic database on a secure NYU server. All system logins, data entries, and data updates are recorded, enabling efficient data tracking. Access to the server is available only to authorized users with passwords; overall data security is ensured by a firewall. Additional security is provided by database software requiring a password for data entry and allowing for password protection at the record level within a database. Patient confidentiality will be ensured by eliminating from the design of the data systems any information that could be used to identify individual participants. Each participant will be identified in the database only by a project-specific ID number. Identifiable information (e.g., name, birthdate, home address, or other personal information) will not be stored on any of the devices used in this study. For mobile devices and software such as the tablets or cell phones that will be used to gather survey data, guidelines established by NYU IRB will be followed including documentation of security controls, incident response program, compliance certifications, privacy practices, physical data security, and subcontractors. The packages that are shipped to and from study participants will not have any information on the exterior of the box indicating that they are a research participant.

External factors. The PI will monitor developments in the literature as the study progresses. Should it become clear that the intervention would be in any way harmful to participants, would increase risk, or would be unethical to continue, the IRB and study sponsor will be notified and the study will be stopped.

Futility analysis. As this pilot study is designed to determine acceptability and feasibility for a future well-powered R01 application, it will not be possible to determine whether the intervention is futile for this population during the proposed study.

11 Clinical Monitoring

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

Authorized representatives of the IRB and the NINR may review de-identified information, as well as participants' identifiable information, for the purposes of assuring proper conduct of the research, addressing a specific reported incident, or verifying appropriate use of funds. The Quality Assurance and Quality Improvement Division of NYU's Research and Regulatory Services may audit the study to confirm compliance. Access of any protected health information will be done in the offices of the PI in his presence. No identifiable information may be copied or taken off-site.
The project manager (or clinical research coordinator) will audit one case per quarter, selected at random, to confirm compliance with IRB requirements, including conformance with informed consent requirements, verification of source documents, and investigator compliance.

12 Statistical Considerations

12.1 Statistical and Analytical Plans
A formal SAP will be developed for this study in consultation with the study biostatistician. Only a general overview of study statistics is included in this protocol.

12.2 Statistical Hypotheses
The sample size is too small to make inferences about relationships evaluated in the pilot study to the larger population of middle aged adults with MetS. For the primary aim, acceptability will be evaluated by the percentage of participants rating SASI as acceptable (overall acceptability survey scores greater than 21), neutral (overall acceptability survey scores equal to 21), and unacceptable (overall acceptability survey scores less than 21) on the Acceptability Survey at each of two time points (pre- intervention and post intervention). Feasibility will be evaluated by the 1) recruitment rate: the percentage of potential participants screened in order to enroll 60 participants with evaluable data, 2) attrition rate: the percentage of enrolled participants completing the 18-week study. Participants will be considered withdrawn after 4 weeks of not responding to phone calls/emails during the intervention, and the 3) protocol adherence rates: the percentage of participants completing greater than or equal to 4 daily sleep diary entries per week for 80% or more of the intervention period. For the secondary endpoints, paired t-tests will be used to compare the mean pre-intervention and mean post-intervention estimates for SAFTEE scores, physical activity, sedentary behavior, diet quality, smoking, alcohol use, affective well-being, morning fatigue, evening fatigue, and self- regulation measurements. For the exploratory endpoints of perceived barriers and facilitators of SASI, bivariate correlations between specific socio-ecological factors and sleep duration change will be identified. The qualitative data from the post intervention interviews will be analyzed using content analysis. Content analysis includes a line- by-line review that yields clusters of data that are coded. This coding is linked to interview questions. Summarization of coding will be performed across individual interviews, and subsequently cross-classified to yield a rich descriptive analysis. Emerging themes within and across interviews will be identified, and review of fit with data verified.

12.3 Analysis Datasets
The analysis dataset will include all participant (e.g., intent to treat).

12.4 Description of Statistical Methods

12.4.1 General Approach
This is a 1-group pretest-posttest pilot study of the acceptability and feasibility of a sleep intervention.

Using descriptive analyses, the investigators will describe each variable using measures of central tendency (means, medians) and variability (standard deviations, interquartile ranges) for continuous variables; counts and percentages for categorical variables. Data will be evaluated for anomalies (e.g., nonrandom missing data, erroneous outliers, multicollinearity, possible confounding) that may invalidate planned analyses. Data transformations, imputation, and/or robust and tailored analysis approaches will be used for non-normally distributed variables.

12.4.2 Analysis of the Primary Efficacy Endpoint(s)

For Aim 1: Acceptability will be based on the pre- and post-intervention acceptability survey measurements. The acceptability survey is an ordinal scale with higher scores indicating greater acceptability. Results will be reported as a categorical outcome indicating the count and percentage of participants rating SASI at the pre-intervention assessment as well as the post intervention assessment as acceptable (total scores greater than or equal to 21), neutral (total score equal to 21), and unacceptable (total scores less than 21).

Feasibility will be based on recruitment, retention, and study protocol adherence. Recruitment will be measured as the number and percentage of participants screened and their determination as eligible or ineligible based on inclusion/exclusion criteria. Results will be reported as a recruitment rate indicating the count and percentage of participants eligible and ineligible. Attrition rates will be reported as the number

and percentage of participants who withdraw from the study. Attrition rates >20% will suggest lack of feasibility. Recruitment and attrition rates will also be examined for differences in specific subgroups. Study protocol feasibility will be indicated by percentage of participants providing at least 4 work day sleep diaries per week for greater than or equal to 80% of the intervention period.

12.4.3 Analysis of the Secondary Endpoint(s)

The main secondary endpoint of interest is sleep duration. Paired-samples t-tests will be used to compare differences in repeated measures of sleep duration (baseline and intervention). Mean sleep duration will be calculated as a weighted mean using the formula [(weekday sleep duration x 5) + weekend sleep duration x 2)]/7. Weekday nights will be Sunday through Thursday nights; weekend nights will be Friday and Saturday nights. The primary secondary outcome for sleep duration data will be obtained from the two-week baseline sleep dairy data and the last two weeks of intervention sleep diary data. Other secondary endpoints that will be compared between baseline and intervention using paired sample t-tests include measures for 1) diet quality (defined as the percentage of fat, percentage of carbohydrate, and total caloric intake estimated from the ASA24 at baseline and intervention), 2) physical symptoms (estimated from SAFTEE Questionnaire), 3) cigarette and alcohol use estimated from the Demographics- SDOH: Alcohol use (AUDIT C), Demographics – SDOH: Tobacco use , 4) affective well-being (estimated from 36-item Short Form Health Survey (SF-36) version 1) self- regulation (estimated from the Index for Self-regulation), 6) physical activity (defined as moderate/vigorous [100-429 millgravity units] and light [10-99 millgravity units]) estimated from the two-week baseline accelerometry data and the last two weeks of the intervention accelerometry data, and 8) sedentary behavior (defined as less than 10 millgravity units) estimated from the two-week baseline accelerometry data and the last two weeks of the intervention accelerometry data.

12.4.4 Safety Analyses

As this study is minimal risk, it is not anticipated that the study may be halted. However, if there is a determination of unexpected, significant, or unacceptable risk to participants, the study may be temporarily suspended or prematurely terminated.

12.4.5 Adherence and Retention Analyses

Adherence and retention are the primary endpoints for this pilot study.

12.4.6 Baseline Descriptive Statistics

Baseline characteristics, including demographic and clinical characteristics of the sample, using descriptive statistics will be compared between participants for whom the intervention was acceptable and for whom the intervention was unacceptable at each time point (pre-intervention and post- intervention). Inferential statistics will not be used.

12.4.7 Planned Interim Analysis.

The research coordinator will prepare weekly reports on participant demographics, recruitment, attrition, and protocol adherence. The statistician will prepare monthly reports about missing, invalid, or inconsistent data on selected key variables. The reports will also contain a summary of monthly accrual and cumulative accrual,

a summary of key characteristics of the study participants, and a summary of the completeness and quality of data.

12.4.7.1 Safety Review

As this study is minimal risk, it is not anticipated that the study may be halted. However, if there is a determination of unexpected, significant, or unacceptable risk to participants, the study may be temporarily suspended or prematurely terminated.

12.4.7.2 Efficacy Review

This study will not evaluate efficacy.

12.4.8 Additional Sub-Group Analyses

Primary or secondary endpoints may be analyzed for descriptive purposes by age, race/ethnicity, or any other participant characteristic as described in detail in the SAP.

12.4.9 Multiple Comparison/Multiplicity

Not applicable.

12.4.10 Tabulation of Individual Response Data

For these analyses, the investigators will generally not control for multiple comparisons.

12.4.11 Exploratory Analyses

Explore the perceived barriers and facilitators of SASI (e.g., socio-ecological factors).

12.5 Sample Size

Our final sample size is N=60. To achieve this, it is anticipated that 220 interested potential participants will go through the telephone screening procedures. The reason we will need to screen 220 is because OSA is often a co-morbid condition with MetS and we anticipate 65% of participants screened will become ineligible after the initial CTSI visit[33]. We also anticipate that 20% will not complete the study protocol.

12.6 Measures to Minimize Bias

12.6.1 Enrollment/Randomization/Masking Procedures

Not applicable.

12.6.2 Evaluation of Success of Blinding

Not applicable.

12.6.3 Breaking the Study Blind/Participant Code

Not applicable.

13 Source Documents and Access to Source Data/Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays,

subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write “N/D”. If the item is not applicable to the individual case, write “N/A”. All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

14 Quality Assurance and Quality Control

QC procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written SOPs, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

15 Ethics/Protection of Human Subjects

15.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46.

15.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials have been submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

15.3 Informed Consent Process

15.3.1 Consent/Assent and Other Informational Documents Provided to Participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention. The following consent

materials are submitted with this protocol Informed Consent, audio consent for interview during the final study visit.

15.3.2 Consent Procedures and Documentation

Information will be obtained during screening for the study by the study team to determine eligibility. During screening, study staff will review the purpose, nature, risks, and benefits of the study; and determine eligibility. The period of time between recruitment and enrollment will be less than or equal to four weeks. This process will give the potential participant time to consider whether he/she wants to participate in the study. Participants will be reminded when the study is introduced, during recruitment and screening that participation is voluntary and that choosing not to participate in no way affects the quality or quantity of medical or nursing care provided to them. If at any point the candidate prefers not to proceed, the enrollment visit will be canceled. The candidate will be offered time after the in-person review of the consent form during the enrollment visit to think about her potential participation and to ask any questions before choosing to sign the study consent. In addition, participants are told that they may choose to withdraw from the study at any time.

Audio informed consents will be obtained for the fidelity checks and for the 30-minute audio-taped open ended interview during the final visit. As indicated above, participants will be reminded that participation is voluntary and that choosing not to participate in no way affects the quality or quantity of medical or nursing care provided to them. The candidate will be offered time after the in-person review of the consent form to think about her potential participation and to ask any questions before choosing to sign the study consent. In addition, participants are told that they may choose to withdraw from the study at any time.

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to potential participants. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. The participant will sign the informed consent document prior to any procedures being done for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. A copy of the signed informed consent document will be stored in the participant's research record. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject's research record. Any alteration to the standard consent process and the justification for such alteration will likewise be documented.

15.4 Participant and Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor, other authorized representatives of the sponsor, or representatives of the IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored in the research offices of the PI at the NYU Meyers College of Nursing. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by NYU Meyers College of Nursing research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the NYU Meyers College of Nursing.

To further protect the privacy of study participants, a Certificate of Confidentiality will be obtained from the NIH. This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.

16 Data Handling and Record Keeping

16.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant's official electronic study record.

Clinical data (including AEs, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into REDCap, a data capture system provided by the New York University. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

16.2 Study Records Retention

Study documents will be retained for the longer of 3 years after close out or 5 years after final reporting/publication. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

16.3 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or MOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH E6:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, section 5.1.1 □ 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site to use continuous vigilance to identify and report deviations within three working days of identification of the protocol deviation, or within three working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents, reported to NYU IRB as per their guidelines. Protocol deviations must be reported to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

16.4 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy, and the Section 801 of the Food and Drug Administration Amendments Act of 2007, requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. For interventional clinical trials performed under NIH IC grants and cooperative agreements, it is the grantee's responsibility to register the trial in an acceptable registry, so the research results may be considered for publication in ICMJE member journals. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

FDAAA mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials". NIH grantees, such as the PI, will take specific steps to ensure compliance with NIH implementation of FDAAA, including registering the trial with clinicaltrials.gov.

17 Study Finances

17.1 Funding Source

This study is funded through a grant from the National Institutes of Health, National Institute of Nursing Research 1P20NR018075-01.

17.2 Costs to the Participant

Participants will not be charged for any procedures of this study.

17.3 Participant Reimbursements or Payments

This payment system reflects the significant commitment and effort that data collection is anticipated to require on the part of participants. Therefore, the guidelines for the market model of payment from Dickert and Grady will be used for the remuneration plan[47]. The function of payment in the market model is that of an incentive

rather than a reward. Using this model, participants will receive a $25 gift card at enrollment, a $25 gift card after 6-weeks of the intervention is complete, and a $50 when they complete the study, for a total remuneration of $100 per participant in the form of gift cards for the 18-week commitment. Transportation cost incurred by the participant for required CTSI visits will be reimbursed.

18 Study Administration

18.1 Study Leadership

The study team will govern the conduct of the study. The study team will be composed of the PI, three Co-Is, a key collaborator, a biostatistician, a project coordinator, and research assistants, as listed in section 1. The PI will schedule monthly study team meetings. In addition, the PI will meet individually with study team.

19 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. The study leadership in conjunction with the NIH has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the NYU Langone Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All NYULMC investigators will follow the applicable conflict of interest policies.

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Attachment A

Schedule of Events

Activity	**Recruitment** ≤ 4 weeks	**Enrollment CTSI Visit 1**	**Baseline** Week 1	**Baseline** Week 2	**Intervention** Weeks 3-13	**Intervention** Week 14	**Intervention** Week 15	**Final Visit** ≤ 3 weeks from completing intervention
Study team procedures								
Telephone Screen	X							
Schedule CTSI Visits	X						X	
Study Consent		X						
Height, Weight, and Neck Measurements		X						
Waist Measurements		X						
Blood Pressure		X						
Blood Samples		X as needed						
Text/email daily diary reminders as needed		X	X	X	X	X	X	
Weekly Intervention Call					X	X	X	
Assess for AEs, SAEs, UPs					X	X	X	
Fitbit wear time			X	X	X	X	X	
Deliver accelerometer		X			X during week 13			
Accelerometer wear time			X	X		X	X	
Pick up/drop off accelerometer				X after week 2			X after week 15	

Pulse oximeter			X one night					
Pick up pulse oximeter			X after one night of study recording					

Post-intervention Interview								X
Surveys								
CTSI screening and enrollment surveys								
Data Elements		X						
Additional Element Group – Form Administration		X						
BRICS NINR Demographics with race clarifying questions		X						
BRICS NINR Demographics-Diagnosis		X						
ARES		X						
AUDIT		X						
General Health Questions		X						
PHQ-9		X						
Baseline surveys								
Acceptability Survey			X Pre-intervention					X Post-intervention
Composite Scale of Morningness			X					

Economic Vulnerability Survey			X					
Family Assessment Device- General Functioning Scale			X					
Sleep Environment Survey			X					
Baseline and End of Study Surveys								
36-item Short Form Survey (SF-36) version 1			X					
ASA24			X				X	
Demographic- SDOH: Alcohol use (AUDIT C)			X				X	
Demographic- SDOH: Tobacco use			X				X	
Index of Self- regulation			X				X	
SAFTEE			X				X	
PROMIS Depression 6a			X				X	
Weeks 1-15 Surveys								
PROMIS Fatigue 6a morning			X	X	X	X	X	
PROMIS Fatigue 6a evening			X	X	X	X	X	
Epworth Sleepiness Scale			X	X	X	X	X	
Daily Sleep Diary			X (daily)	X (daily)	X (daily)	X (daily)	X (daily)	