CLINICAL STUDY PROTOCOL

Observational Study of Individual or Group Template

A photoplethysmography sensor-based personalized feedback intervention for heavy-drinking young adults targeting heart rate variability, resting heart rate, and sleep

Protocol Number
2000030417

Protocol Version

11/8/2022
Version 4

Confidentiality Statement:

Synopsis

Purpose

Heavy alcohol use among young adults is an important public health problem. Alcohol use disorder (AUD) onset peaks during young adulthood (i.e., 18-25).[1] Young adults report the highest rates of heavy drinking,[2] which puts them at increased risk for substantial negative consequences such as accidental injury, (i.e., the primary cause of death in this group),[3-5] and makes them a priority population for intervention.

Current alcohol prevention and early intervention efforts for young adults have limitations. Effective alcohol interventions are available for young adults but tend to have small effects on drinking.[6-8] Most young adults do not seek help for their drinking, often due to low perceived need.[9-12] Moreover, young adults are least likely to have medical visits with a healthcare provider[13, 14] where they could receive effective alcohol preventive services.[15] There are also gaps in access. While college students tend to have more support services, particularly free and/or low cost options, their non-college same aged peers do not. [16]

Effective strategies need to better align with young adults' health practices and preferences. Though alcohol help-seeking may be low among young adults, they are open to receiving help for other health behaviors such as sleep and exercise. [17-19] These health topics may provide alternative gateways for intervening on alcohol use, bypassing the need for self-identification. Young adults, a generation that grew up with the convenience of technology, are also increasingly turning to mobile and digital health tools. [20-22]

Mobile health interventions that embed brief alcohol intervention content may offer a novel solution. We developed and conducted a preliminary test of a mobile sleep intervention for heavy-drinking young adults for engaging them in treatment and reducing their drinking (see Preliminary Studies).[19] We targeted sleep because poor sleep is common among heavy-drinking young adults [23, 24] and an AUD risk factor, [25-31] young adults are interested in their sleep health, [32] and sleep interventions address alcohol use as standard care, thereby providing a practical opportunity to embed alcohol content. Within the last decade, there has also been an explosion in the importance of sleep [33-35] and technology options for improving it. [36, 37] Qualitative data from this pilot (N=42) and our ongoing R34-funded follow-up study (96/120 enrolled to date) generated new hypotheses. Specifically, subjects expressed an interest in receiving feedback about other health outcomes besides sleep and indicated that feedback showing the negative effects of alcohol and/or sleep on health biomarkers would further motivate them to change their behavior.

New sensor technology, that measures heart rate variability, a non-invasive, robust biomarker of health, shows potential for alcohol prevention and early intervention. In addition to sleep, there has been a rapid increase in the importance of heart rate variability (HRV) as a useful biomarker for tracking health and well-being, due in large part to new photoplethysmography (PPG) sensors and mobile apps that capture HRV, resting heart rate (RHR), and sleep. [38] HRV reflects cardiac control of the autonomic nervous system (ANS). [38] Greater HRV indicates a more resilient biological system that flexibly adjusts to changing demands and accordingly, is related to better physical and mental health. [39-43] Acute alcohol use reduces HRV; individuals with AUD have lower HRV than controls; [44] and HRV may be lower among heavy-drinking young adults compared to their non- or moderate-drinking peers. [45] Poor sleep may also reduce HRV. [46] The results of preliminary studies suggest that biofeedback interventions to improve HRV (i.e., paced breathing protocols) may reduce alcohol craving among individuals in substance use treatment

or recovery programs. [47] HRV biofeedback may also have potential as an alcohol prevention/early intervention strategy, particularly receiving feedback about alcohol effects on HRV. This hypothesis has not been tested but users of this new PPG sensor technology reported reductions in drinking after observing negative effects of alcohol use on their health data. [48] PPG sensors and integrated mobile apps analyze user health and behavior data and can tailor health advice to these data, thereby creating a unique alcohol intervention opportunity. Thus, a controlled test of HRV/RHR/sleep monitoring and feedback on drinking via this new PPG technology warrants further study.

We will conduct the first controlled test of a personalized feedback intervention targeting HRV, RHR, and sleep for heavy-drinking young adults via PPG sensors and electronic daily diaries to provide preliminary data for a larger grant application. The study is directly responsive to NIAAA strategic directions focused on novel alcohol prevention and intervention efforts for young people. This innovative strategy could have great potential as it does not rely on self-identification for alcohol treatment, [9-12] targets important substance use risk factors (i.e., sleep, HRV), [25-31, 44, 47] is applicable for all young adults, is easily accessible, and uses technology, which appeals to young adults. [20-22]

We expect that a feedback intervention targeting HRV, RHR, sleep and their association with alcohol use will reduce drinking in young adults. The study will yield preliminary data for a larger, definitive study. The rich database will allow for an exploration of the links among these health variables to inform our understanding of their role in young adult AUD risk.

Primary Objective

We propose to conduct the first controlled test of a feedback intervention targeting heart rate variability (HRV), resting heart rate (RHR), and sleep, for heavy-drinking young adults (18-25) and will leverage the capabilities of a consumer-marketed PPG sensor/mobile app, OURA™. We will evaluate the feasibility, acceptability, and preliminary efficacy of this intervention for promoting improvements in drinking.

Primary Aim 1: To examine the preliminary efficacy of a PPG-sensor based HRV, RHR, sleep feedback intervention on alcohol outcomes measured using validated assessments (Timeline Followback Interview (TLFB)[& PROMIS™) and diary data. Hypothesis: The *Feedback* group will report fewer total drinks consumed compared to the *Assessment* group. We will also examine secondary drinking outcomes: drinks per drinking day, % heavy drinking and abstinent days, alcohol-related consequences, and daily diary entries of alcohol use before bedtime.

Secondary Objective

We will evaluate the preliminary efficacy of this intervention for promoting improvements in sleep and health as secondary outcomes.

Aim 2.1: Examine condition effects on PROMIS™ sleep quality and sleep-related impairment self-ratings, controlling for baseline, using mixed effects models. Hypothesis: The *Feedback* group will have better self-reported PROMIS™ sleep quality ratings compared to the *Assessment* group. We will also examine secondary sleep outcomes: PROMIS™ sleep-related impairment ratings, sensor-derived quantitative sleep outcomes (i.e., duration, efficiency, awakenings, % of time in sleep stages, bed/wake times), and daily diary ratings of sleep quality.

Aim 2.2: To examine the preliminary efficacy of a PPG-sensor based HRV, RHR, sleep feedback intervention on HRV measured using sensor data. Hypothesis: The *Feedback* group will report greater HRV compared to the *Assessment* group. We will also examine RHR as a secondary outcome.

Third Objective

Aim 2.3: To evaluate intervention feasibility and acceptability using subject post-treatment ratings and interviews and use metrics. Hypothesis: *Feedback* will rate higher than *Assessment*.

Study Design

The purpose of this study is to test a mobile health intervention for young adults who report heavy alcohol use. The health intervention includes: (1) alcohol use and other health self-monitoring including use of a wearable biosensor, (2) a mobile application, and (3) personalized feedback and tailored health tips about your health and alcohol use data. This study is the first controlled test of an HRV/RHR/sleep feedback intervention for heavy-drinking young adults (N=60; ages 18-25) and will take advantage of a marketed PPG sensor and mobile app, OURA™. Subjects will be randomly assigned to 1 of 2 conditions: (1) Assessment (n=30) or (2) Feedback (n=30). The *Assessment* group will not have access to the OURA™ mobile app and will not receive any health feedback. The *Feedback* group will have access to the OURA™ app and will receive feedback. The OURA™ app provides daily summaries of HRV, RHR, and sleep that subjects can view on the app. In addition, every 2 weeks, we will send a written report via text/email that: (1) summarizes subjects' alcohol use and the links with their HRV/RHR/sleep data and (2) provides health advice tailored to this data.

Following intake, all subjects will wear the OURA™ daily for 6 weeks and will complete daily electronic diaries of alcohol use and sleep. All subjects will then complete follow-ups at Weeks 6 and 10. We will use standardized assessments to measure alcohol consumption and consequences (TLFB, PROMIS™)[56, 57] and self-reported sleep outcomes (PROMIS™).[58] The OURA™ will measure quantitative sleep outcomes, HRV, and RHR. Daily electronic diaries will measure sleep quality and alcohol use. The primary alcohol outcome will be TLFB total drinks consumed, a composite measure of drinking quantity/frequency sensitive to change in our young adult research [19] and other brief alcohol interventions for this population. [6, 7, 51] Secondary alcohol outcomes will examine other effects on drinking: TLFB % heavy drinking and abstinent days; drinks per drinking day; PROMIS™ alcohol-related consequences; and daily diary entries of alcohol use before bedtime. The primary sleep outcome will be PROMIS™ sleep quality ratings, sensitive to change in our young adult research. [19] Secondary sleep outcomes will include PROMIS™ sleep-related impairment ratings, OURA™ quantitative sleep outcomes (i.e., duration, efficiency, latency, wakefulness, % time in sleep stages, bed/wake times) and sleep quality daily diary entries. The primary health outcome will be OURA™ HRV due to its strong association with heavy drinking. [43, 44] OURA™ RHR will be a secondary outcome. We will evaluate feasibility and acceptability with treatment-exit interviews and OURA™ use metrics (below).

Eligible subjects will be randomized to: (1) *Assessment or* (2) *Feedback.* All subjects will begin wearing an OURA™ right after intake and will complete daily diary assessments. **Assessment (A) (n=30)**: Subjects in this group will only monitor their health/behaviors and will not receive any health feedback or advice. They will wear the OURA™ daily and complete daily electronic diaries about bedtime behaviors (e.g., amount/timing of alcohol use) and their sleep for 6 weeks. Diaries will be programmed in MEI Research and sent via text message each morning, a successful procedure for our current R34-funded study.

Feedback (F) (n=30): Subjects in this group will monitor their health/behaviors and will receive health feedback and advice. Subjects will wear the OURA™ daily and complete daily MEI Research diaries for 6 weeks. They will also have access to the OURA™ mobile app. Subjects will receive the following daily health information from the OURA™ app: (1) HRV, RHR, sleep (i.e., duration, efficiency, latency, sleep stages, timing, wakefulness), body temperature, respiratory rate, and physical activity (i.e., steps, calories burned); (2) composite scores from 0-100 (≥85 optimal) for "Sleep", "Activity", and "Readiness" (i.e.,

overall measure of recovery, based on HRV, that signals capacity to perform at physical, mental, cognitive best); and (3) advice regarding optimal bedtime, activity progress, inactivity, and recovery. At intake, we will orient subjects to OURA™ app health feedback and advice. At Weeks 2, 4, and 6, subjects will receive written reports sent via a text/email link that summarizes their alcohol use (e.g., drinks per week, # of heavy occasions, peak BAC) and the links between drinking and OURA™ health outcomes as well as tailored advice for improving health, including evidence-based brief content for alcohol (e.g., standard drinks, low risk drinking guidelines, BAC feedback, controlled drinking tips) [40-42] and sleep (e.g., sleep hygiene, stimulus control). [19, 53, 54, 59, 60] We will derive these reports using the OURA™ Teams dashboard and daily diaries; subjects will not have dashboard access.

Study Date Range and Duration

Study procedures will include: an initial, in-person intake appointment (Week 0), a 6- week intervention phase, and 2 follow-up visits (Weeks 6 and 10). We anticipate that recruitment to follow-up will take 2 years.

Number of Study Sites

Sites: Screening appointments will take place at the Connecticut Mental Health Center (CMHC) main campus or the Substance Abuse Treatment Unit, a satellite location of CMHC. The Yale School of Nursing Biobehavioral Laboratory is also available as a back-up space for appointments. Follow-up visits will be conducted virtually using ZOOM.

Primary Outcome Variables

Standardized, consensus-based measures for assessing alcohol, sleep and other health outcomes were selected to assess primary and secondary aims. These measures are described below.

Timeline Follow-back Interview (TLFB): Valid/reliable/standardized interview to obtain alcohol quantity/frequency estimates [56] for a 30-day period prior to enrollment in the study and monthly following intake for a total of 3 months.(51) Calendar prompts and memory aids (e.g., holidays) are used to facilitate accurate recall of substance use during the targeted period. We will derive the following 30-day summary variables for: total drinks, drinks per drinking day, % heavy and abstinent days.

PROMIS™ Alcohol Consequences: Valid/reliable measures of positive/negative alcohol consequences.[57]

Alcohol daily diaries: subjects will record the timing and amount of alcohol use before bedtime.[71]

Physical Fitness/Activity: Self-reported assessments with validity against objective measures. [74, 75]

Intervention Feasibility/Acceptability: OURA™ use metrics; quantitative and qualitative ratings of OURATM and diary self-monitoring and health feedback/advice components using treatment evaluation surveys and exit interviews (e.g., ease of use, helpfulness, satisfaction, suggestions for improvement).

Secondary and Exploratory Outcome Variables (if applicable)

PROMIS™ Sleep-Related Impairment and Sleep Disturbance: Valid/reliable measures of perceived alertness, sleepiness, during waking hours and functional impairments due to sleep problems and perceived sleep quality/satisfaction and

difficulty initiating/maintaining sleep.[58]
Sleep daily diaries: subjects will rate their sleep quality upon waking.[72]

PROMIS™ Positive Affect/Depression/Anxiety: Valid/reliable measures of well-being, negative affect.[57, 73]

Physical Fitness/Activity: Self-reported assessments with validity against objective measures. [74, 75]

Intervention Feasibility/Acceptability: OURA™ use metrics; quantitative and qualitative ratings of OURATM and diary self-monitoring and health feedback/advice components using treatment evaluation surveys and exit interviews (e.g., ease of use, helpfulness, satisfaction, suggestions for improvement).

Study Population
Participants are 18-25 years of age, reported ≥4 heavy drinking occasions in the last 4 weeks, and have a personal smartphone available for use along with the wearable sensor provided in the study**.**
We will recruit heavy-drinking young adults (N=60; ages 18-25 years old) from the local community through online advertising/social media (e.g., Facebook, Instagram, Snapchat) and flyers and notices displayed around the local community and college campuses. Subjects will be randomly assigned to 1 of 2 conditions: (1) Assessment (n=30) or (2) Feedback (n=30).
Urine Drug Toxicology: JANT Pharmaceuticals rapid urine drug test kit for opiates, cocaine, barbiturates, amphetamines, benzodiazepines, or phenylcyclidine. Positive tests are an exclusion criterion.

Breath Alcohol Concentrations (BAC): Subjects need to test negative on a handheld breathalyzer- an Alcohol-Sensor III (Intoximeter Inc., St. Louis, MO). Participants need to test negative to provide consent at intake and need to test <.04% at subsequent in-person treatment and assessment visits.

Number of Participants
Targeted for enrollment at Yale for this protocol: 60 subjects (Assessment group [n=30] and Feedback group [n=30]). This is a preliminary study, which if promising will lead to a larger trial of this intervention approach. Sample size estimates were based on enrolling a sufficient number of participants to determine the feasibility, acceptability, and preliminary efficacy of this PPG-sensor based feedback and brief advice intervention for reducing drinking among heavy-drinking young adults. This number is feasible to recruit for a 2-year study. Moreover, for Phase 1 psychotherapy intervention studies, the minimum recommended sample size is 15-30 subjects per group.

Study Schedule
There are 3 expected visits: an initial, in-person intake appointment (Week 0), a 6- week intervention phase, and 2 follow-up visits (Weeks 6 and 10).

Protocol Revision History

Include the IRB approved protocol version number and date for each revision of the protocol. All version history should remain in the table and never be deleted. The oldest IRB approved version of the protocol should be listed on the top row. The most recent IRB approved version should be listed on the bottom row.

Version Date	Summary of Substantial Changes
Version 2, 4/21/2021	Accepted tracked changes, included description of http://www.clinicaltrials.gov, included Oncore usage for payment, clarified clinical interviews will be conducted by licensed experts to determine if participant meets any exclusion criteria, and clarified that consenting process will occur at either in person or remotely.
Version 3 1/20/2022	Accepted tracked changes, added/changed measures that participants will complete at intake, week 6, and week 10, and clarified how participants will be completing daily diaries
Version 4 11/8/2022	Accepted tracked changes and clarified that diary administration will occur through MEI Research, not Qualtrics.

Statement of Compliance

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to the Common Rule at 45CFR46 (human subjects) and other applicable government regulations and Institutional research policies and procedures.

Abbreviations

Abbreviation	Explanation

Glossary of Terms

Glossary	Explanation

Table of Contents

1 Background/Literature Review

1.1 Background

Alcohol use disorder (AUD) onset peaks during young adulthood (i.e., 18-25).[1] Compared to older adults, young adults report more frequent and heavier alcohol consumption that is linked to substantial negative consequences including risk of accidental injury, the primary cause of death among young adults.[49] Current alcohol intervention strategies for young adults have modest effects [7, 50, 51]and young adults rarely self-identify for specialized alcohol treatment.[8, 52] Thus, more work is needed to identify effective alcohol interventions and novel treatment engagement strategies to reduce this substantial public health burden.

Effective alcohol interventions are available for young adults but tend to have small effects on drinking. [6-8] Most young adults do not seek help for their drinking, often due to low perceived need.[9-12] Moreover, young adults are least likely to have medical visits with a healthcare provider [13, 14] where they could receive effective alcohol preventive services. [15] There are also gaps in access. While college students tend to have more support services, particularly free and/or low-cost options, their non-college same aged peers do not. [16]

Though alcohol help-seeking may be low among young adults, they are open to receiving help for other health behaviors such as sleep and exercise. [17-19]These health topics may provide alternative gateways for intervening on alcohol use, bypassing the need for self-identification. Young adults, a generation that grew up with the convenience of technology, are also increasingly turning to mobile and digital health tools.[20-22]

We developed and conducted a preliminary test of a mobile sleep intervention for heavy-drinking young adults for engaging them in treatment and reducing their drinking (see Preliminary Studies). [19] We targeted sleep because poor sleep is common among heavy-drinking young adults [23, 24] and an AUD risk factor, [25, 26, 28-31] young adults are interested in their sleep health, [32] and sleep interventions address alcohol use as standard care, thereby providing a practical opportunity to embed alcohol content. Within the last decade, there has also been an explosion in the importance of sleep [33-35] and technology options for improving it. [36, 37] Qualitative data from this pilot (N=42) and our ongoing R34-funded follow-up study (96/120 enrolled to date) generated new hypotheses. Specifically, subjects expressed an interest in receiving feedback about other health outcomes besides sleep and indicated that feedback showing the negative effects of alcohol and/or sleep on health biomarkers would further motivate them to change their behavior.

In addition to sleep, there has been a rapid increase in the importance of heart rate variability (HRV) as a useful biomarker for tracking health and well-being, due in large part to new photoplethysmography (PPG) sensors and mobile apps that capture HRV, resting heart rate (RHR), and sleep. [38] HRV reflects cardiac control of the autonomic nervous system (ANS). [38] Greater HRV indicates a more resilient biological system that flexibly adjusts to changing demands and accordingly, is related to better physical and mental health. [39-43] Acute alcohol use reduces HRV; individuals with AUD have lower HRV than controls; [44] and HRV may be lower among heavy-drinking young adults compared to their non- or moderate-drinking peers. [45] Poor sleep may also reduce HRV.[46] The results of preliminary studies suggest that biofeedback interventions to improve HRV (i.e., paced breathing protocols) may reduce alcohol craving among individuals in substance use treatment or recovery programs. [47] HRV biofeedback may also have potential as an alcohol

prevention/early intervention strategy, particularly receiving feedback about alcohol effects on HRV. This hypothesis has not been tested but users of this new PPG sensor technology reported reductions in drinking after observing negative effects of alcohol use on their health data. [48] PPG sensors and integrated mobile apps analyze user health and behavior data and can tailor health advice to these data, thereby creating a unique alcohol intervention opportunity. Thus, a controlled test of HRV/RHR/sleep monitoring and feedback on drinking via this new PPG technology warrants further study.

We will conduct the first controlled test of a personalized feedback intervention targeting HRV, RHR, and sleep for heavy-drinking young adults via PPG sensors and electronic daily diaries to provide preliminary data for a larger grant application. The study is directly responsive to NIAAA strategic directions focused on novel alcohol prevention and intervention efforts for young people. This innovative strategy could have great potential as it does not rely on self-identification for alcohol treatment, [9-12] targets important substance use risk factors (i.e., sleep, HRV), [25-31, 44, 47] is applicable for all young adults, is easily accessible, and uses technology, which appeals to young adults. [20-22]

1.2 Prior Experience (if applicable)

Dr. Fucito and the research team has experience implementing and evaluating mobile behavioral interventions to help young adults with their alcohol use and sleep. This current study is a continuation of this line of work. In Dr. Fucito's current R34 clinical trial [IRB Protocol # 2000021048], young adults expressed an interest in exit interviews to receive information about health biomarkers that are related to poor sleep and/or heavy alcohol use. For this purpose, we have opted to focus on the biomarkers of heart rate variability and resting heart rate.

Rationale/Significance

1.3 Rationale and Study Significance

- The study provides the first systematic, controlled test of a HRV, RHR, sleep monitoring and feedback intervention as a novel alcohol prevention/early intervention strategy in heavy-drinking young adults. Improving these other health targets at this developmental stage could have long-term payoffs such as reduced long-term AUD risk as well as improved long-term mental and physical outcomes.
- Use of a health promotion intervention to engage young adults to change their drinking is a paradigm shift.
  Current young adult alcohol prevention/early intervention strategies largely rely on self-identification or identification by a healthcare provider. [6-8] Many young adults do not perceive a need for help with their drinking and are increasingly less likely to visit a healthcare provider. [13, 14]Thus, other "on ramps" to alcohol preventive services are urgently needed. Young adults are concerned about their health and sleep. [32] Therefore, for this population, it may be useful to embed alcohol-related content within a more comprehensive health program and connect alcohol use to other health outcomes.
- As part of the intervention and as an objective outcome measure, the research incorporates new, validated sensor technology for continuously monitoring HRV, RHR, and sleep. We will use this data and alcohol and sleep diary data to deliver innovative feedback to young adults on the links between drinking and their health.
- HRV, RHR, and sleep are non-invasive health biomarkers that are malleable. This is the first test of all 3

biomarkers as a brief alcohol intervention for young adults. All 3 are important for physical and mental health [34, 35, 39-42] and can be improved with cost-effective, easily disseminated behavioral interventions. [47, 53-55]

- Research on HRV biofeedback interventions for substance use is in its infancy. [47] To date, only a few,
  small studies have tested biofeedback interventions to improve HRV as an adjunct to substance use treatment, none of these targeted sleep.[47] No studies have explored the value of HRV feedback for substance use prevention/early intervention or the potential benefit of simply monitoring HRV and providing feedback about the effects of substance use on HRV among young adults.
- This study tests an alcohol prevention/early intervention strategy that is applicable to the broad population of young adults (i.e., civilian, college, and military young adults).

1.4 Purpose of Study/Potential Impact

Heavy alcohol use among young adults is an important public health problem. Alcohol use disorder (AUD) onset peaks during young adulthood (i.e., 18-25).[1] Young adults report the highest rates of heavy drinking,[2] which puts them at increased risk for substantial negative consequences such as accidental injury, (i.e., the primary cause of death in this group),[3-5] and makes them a priority population for intervention.

Current alcohol prevention and early intervention efforts for young adults have limitations. Effective alcohol interventions are available for young adults but tend to have small effects on drinking.[6-8] Most young adults do not seek help for their drinking, often due to low perceived need.[9-12] Moreover, young adults are least likely to have medical visits with a healthcare provider[13, 14] where they could receive effective alcohol preventive services.[15] There are also gaps in access. While college students tend to have more support services, particularly free and/or low cost options, their non-college same aged peers do not. [16]

Effective strategies need to better align with young adults' health practices and preferences. Though alcohol help-seeking may be low among young adults, they are open to receiving help for other health behaviors such as sleep and exercise. [17-19] These health topics may provide alternative gateways for intervening on alcohol use, bypassing the need for self-identification. Young adults, a generation that grew up with the convenience of technology, are also increasingly turning to mobile and digital health tools. [20-22]

Mobile health interventions that embed brief alcohol intervention content may offer a novel solution. We developed and conducted a preliminary test of a mobile sleep intervention for heavy-drinking young adults for engaging them in treatment and reducing their drinking (see Preliminary Studies).[19] We targeted sleep because poor sleep is common among heavy-drinking young adults [23, 24] and an AUD risk factor, [25-31] young adults are interested in their sleep health, [32] and sleep interventions address alcohol use as standard care, thereby providing a practical opportunity to embed alcohol content. Within the last decade, there has also been an explosion in the importance of sleep [33-35] and technology options for improving it. [36, 37] Qualitative data from this pilot (N=42) and our ongoing R34-funded follow-up study (96/120 enrolled to date) generated new hypotheses. Specifically, subjects expressed an interest in receiving feedback about other health outcomes besides sleep and indicated that feedback showing the negative effects of alcohol and/or sleep on health biomarkers would further motivate them to change their behavior.

New sensor technology, that measures heart rate variability, a non-invasive, robust biomarker of health, shows potential for alcohol prevention and early intervention. In addition to sleep, there has been a rapid increase in the importance of heart rate

variability (HRV) as a useful biomarker for tracking health and well-being, due in large part to new photoplethysmography (PPG) sensors and mobile apps that capture HRV, resting heart rate (RHR), and sleep. [38] HRV reflects cardiac control of the autonomic nervous system (ANS). [38] Greater HRV indicates a more resilient biological system that flexibly adjusts to changing demands and accordingly, is related to better physical and mental health. [39-43] Acute alcohol use reduces HRV; individuals with AUD have lower HRV than controls; [44] and HRV may be lower among heavy-drinking young adults compared to their non- or moderate-drinking peers. [45] Poor sleep may also reduce HRV. [46] The results of preliminary studies suggest that biofeedback interventions to improve HRV (i.e., paced breathing protocols) may reduce alcohol craving among individuals in substance use treatment or recovery programs. [47] HRV biofeedback may also have potential as an alcohol prevention/early intervention strategy, particularly receiving feedback about alcohol effects on HRV. This hypothesis has not been tested but users of this new PPG sensor technology reported reductions in drinking after observing negative effects of alcohol use on their health data. [48] PPG sensors and integrated mobile apps analyze user health and behavior data and can tailor health advice to these data, thereby creating a unique alcohol intervention opportunity. Thus, a controlled test of HRV/RHR/sleep monitoring and feedback on drinking via this new PPG technology warrants further study.

We will conduct the first controlled test of a personalized feedback intervention targeting HRV, RHR, and sleep for heavy-drinking young adults via PPG sensors and electronic daily diaries to provide preliminary data for a larger grant application. The study is directly responsive to NIAAA strategic directions focused on novel alcohol prevention and intervention efforts for young people. This innovative strategy could have great potential as it does not rely on self-identification for alcohol treatment, [9-12] targets important substance use risk factors (i.e., sleep, HRV), [25-31, 44, 47] is applicable for all young adults, is easily accessible, and uses technology, which appeals to young adults. [20-22]

We expect that a feedback intervention targeting HRV, RHR, sleep and their association with alcohol use will reduce drinking in young adults. The study will yield preliminary data for a larger, definitive study. The rich database will allow for an exploration of the links among these health variables to inform our understanding of their role in young adult AUD risk**.**

1.5 Potential Risks and Benefits

1.5.1 Potential Risks

The major potential risks in this study are related to intervention components, interviews/self-report questionnaires, urine collection, and recording of treatment exit interviews.

Intervention Components:

PPG sensor use and mobile self-monitoring of alcohol use and health behaviors poses minimal risk. There are no side effects from wearing the OURA™ beyond minor inconvenience – users can shower and swim with the devices. OURA™ deidentifies user data and will distribute data to us using deidentified data via a password-protected dashboard that protects participants' confidentiality. The brief health advice provided by the OURA™ mobile app and our personalized alcohol-related feedback and advice pose minimal risk. A great deal of this information is also available to young adults through external health websites. Our experience providing brief alcohol and health interventions to young adults and cognitive-behavioral sleep interventions indicates that they are well tolerated. Our research group has several PhD-level clinical psychologists available for consultation should the need arise. Participants will be monitored regularly through daily diaries and via remote reminders regarding study procedures.

The Oura ring is a wearable ring that includes multiple sensors to detect several health biomarkers including temperature, sleep, heart rate and connects to mobile application that provides users with information about their health status. Participants will wear the device and half will have access to the mobile application to view their health data so we can test the effect of using this device and receiving this health information on drinking behavior. The device is not FDA approved and it is our understanding that they are not seeking FDA approval status at this time for any medical indications. The Oura ring is intended for general health self-monitoring and is available to the public.

These will only be given to participants and tested by research staff. They will be stored in a locked cabinet in a locked research office at CMHC in between use. The devices will also be cleaned in between use by different participants.

Interviews and Self-Reports:
Research interviews and assessments, including completing daily health diaries, are all non-invasive and should add no risk. The major disadvantage is the time it takes to complete them and possible breach of confidentiality. Our research group's experience with these measures indicates that they are acceptable to participants. Dr. Fucito, a licensed clinical psychologist, will be available to meet with individuals and will provide staff with consultation should the need arise. Careful efforts aimed at maintaining confidentiality will be made, which are described below, and only participants' study numbers will be recorded on the forms themselves in order to protect confidentiality.

Recording of Exit Interviews: Recording of interviews is necessary to evaluate participants' reactions to self-monitoring activities (i.e., daily electronic diaries and the OURA™ smart ring) as well as personalized feedback and tailored health advice for those in the feedback group. To assure the confidentiality and protection of participants with respect to these procedures, the following steps will be taken:

- Participants have the right to refuse recording. Participants who consent to recording will be informed that they have the right to stop recording at any time.
- All recording will occur using ZOOM teleconferencing software, which is HIPAA-compliant and password-protected. Only Dr. Fucito, Dr. Ash, or the Research Coordinator will record interviews.
- Interviews will be saved on a password protected secure server. Digital file names will only be identified by participants' study numbers.
- Access to digital recordings will be limited to key study personnel.

Effective screening will exclude all participants who would be at greater risk for complications from the intervention and/or study participation because of medical or specific psychiatric illnesses. Dr. Fucito, a licensed clinical psychologist, will evaluate all potential participants for inclusion regarding their psychiatric suitability. If participants are not eligible for the study and/or request further assistance with alcohol use, physical health, and/or sleep once the study is completed, appropriate referrals will be provided. Upon study enrollment, numerous safeguards will be used to monitor participants. Participants will receive at a minimum, weekly contact from Study Staff for reminders about study procedures/address any logistical problems with diaries, sensors, or other procedures. Plus, all participants will wear a sensor and complete daily diaries. Sensor data and diaries can be monitored remotely. Dr. Fucito will be available to meet with participants and will provide participants with treatment referrals if they are interested.

Right to privacy for participation in this research will be protected through alphanumeric coding of data (in place of names) and proper storage of research records, including treatment exit interviews. Collected materials will be maintained via an alphanumeric reference system maintained by Dr. Fucito. Participants' names will appear only on the consent form, the HIPAA authorization form, and a master list maintained in a physically locked file that is separate from research data. Our data collection and management procedures are fully compliant with HIPAA. Access will be limited to personnel intimately involved in the study. A Certificate of Confidentiality will also be obtained from the National Institutes of Health to protect access to the records. However, participants will also be told that if they present with suicidal or homicidal ideation and/or report any form of child/elder abuse or report plans to damage property then we will have to report this to the appropriate authorities and/or provide them with referrals for immediate treatment. Electronic data will be de-identified, and password protected. Only members of the study team will have access to the physical or electronic data. OURA™ data are deidentified and are also protected through secure, password-protected servers. We will use an alphanumeric code to sign participants up to the OURA™ mobile app in place of their names.

1.5.2 Potential Benefits

All participants will engage in self-monitoring that may help participants learn more about their alcohol use, health, and/or sleep. In this study, half of the participants will receive personalized feedback about their health and behaviors as well as tailored, evidence-based advice, which may help them improve their drinking, health, and/or sleep. All participants will be provided compensation for their participation. They will be able to withdraw from the study at any time. There is a need to reduce heavy alcohol consumption and alcohol-related risks among young adults. The purpose of this study is to test a mobile health intervention for heavy-drinking young adults. Mobile interventions that target young adults' other health concerns may provide alternative on ramps for intervening on alcohol use in this population. This study may help to engage more heavy-drinking young adults into treatment and reduce the substantial harms and healthcare costs associated with heavy alcohol use.

2 Study Purpose and Objectives

2.1 Hypothesis

Hypothesis 1: The *Feedback* group will report fewer total drinks consumed compared to the *Assessment* group. We will also examine secondary drinking outcomes: drinks per drinking day, % heavy drinking and abstinent days, alcohol-related consequences, and daily diary entries of alcohol use before bedtime.

Hypothesis 2: The *Feedback* group will have better self-reported PROMIS™ sleep quality ratings compared to the *Assessment* group. We will also examine secondary sleep outcomes: PROMIS™ sleep-related impairment ratings, sensor-derived quantitative sleep outcomes (i.e., duration, efficiency, awakenings, % of time in sleep stages, bed/wake times), and daily diary ratings of sleep quality

Hypothesis 3: The *Feedback* group will report greater HRV compared to the *Assessment* group. We will also examine RHR as a secondary outcome.

Hypothesis 4: *Feedback* will rate higher than *Assessment on measures of intervention* post-treatment ratings and interviews and use metrics.

2.2 Primary Objective

Aim 1: Examine condition effects on total drinks consumed over Weeks 2-10 (summarized over 4-week periods), controlling for baseline drinks.

2.3 Secondary Objective (if applicable)

Aim 2.1: Examine condition effects on PROMIS™ sleep quality and sleep-related impairment self-ratings, controlling for baseline, using mixed effects models**.**

Aim 2.2: To examine the preliminary efficacy of a PPG-sensor based HRV, RHR, sleep feedback intervention on HRV measured using sensor data.

Aim 2.3: To evaluate intervention feasibility and acceptability using subject post-treatment ratings and interviews and use metrics.

3 Study Design

3.1.1 General Design Description

Study Design

The purpose of this study is to test a mobile health intervention for young adults who report heavy alcohol use. The health intervention includes: (1) alcohol use and other health self-monitoring including use of a wearable biosensor, (2) a mobile application, and (3) personalized feedback and tailored health tips about your health and alcohol use data. This study is the first controlled test of an HRV/RHR/sleep feedback intervention for heavy-drinking young adults (N=60; ages 18-25) and will take advantage of a marketed PPG sensor and mobile app, OURA™. Subjects will be randomly assigned to 1 of 2 conditions: (1) Assessment (n=30) or (2) Feedback (n=30). The *Assessment* group will not have access to the OURA™ mobile app and will not receive any health feedback. The *Feedback* group will have access to the OURA™ app and will receive feedback. The OURA™ app provides daily summaries of HRV, RHR, and sleep that subjects can view on the app. In addition, every 2 weeks, we will send a written report via text/email that: (1) summarizes subjects' alcohol use and the links with their HRV/RHR/sleep data and (2) provides health advice tailored to this data.

Following intake, all subjects will wear the OURA™ daily for 6 weeks and will complete daily electronic diaries of alcohol use and sleep. All subjects will then complete follow-ups at Weeks 6 and 10. We will use standardized assessments to measure alcohol consumption and consequences (TLFB, PROMIS™)[56, 57] and self-reported sleep outcomes (PROMIS™).[58] The OURA™ will measure quantitative sleep outcomes, HRV, and RHR. Daily electronic diaries will measure sleep quality and alcohol use. The primary alcohol outcome will be TLFB total drinks consumed, a composite measure of drinking quantity/frequency sensitive to change in our young adult research [19] and other brief alcohol interventions for this population. [6, 7, 51] Secondary alcohol outcomes will examine other effects on drinking: TLFB % heavy drinking and abstinent days; drinks per drinking day; PROMIS™ alcohol-related consequences; and daily diary entries of alcohol use before bedtime. The primary sleep outcome will be PROMIS™ sleep quality ratings, sensitive to change in our young adult research. [19] Secondary sleep outcomes will include PROMIS™ sleep-related impairment ratings, OURA™ quantitative sleep outcomes (i.e., duration, efficiency, latency, wakefulness, % time in sleep stages, bed/wake times) and sleep quality daily diary entries. The primary health outcome will be OURA™ HRV due to its strong association with heavy drinking. [43, 44] OURA™ RHR will be a secondary outcome. We will evaluate feasibility and acceptability with treatment-exit interviews and OURA™ use metrics (below).

Eligible subjects will be randomized to: (1) *Assessment or* (2) *Feedback.* All subjects will begin wearing an OURA™ right after intake and will complete daily diary assessments. **Assessment (A) (n=30)**: Subjects in this group will only monitor their health/behaviors and will not receive any health feedback or advice. They will wear the OURA™ daily and complete daily electronic diaries about bedtime behaviors (e.g., amount/timing of alcohol use) and their sleep for 6 weeks. Diaries will be programmed in MEI Research and sent via a notification each morning, a successful procedure for our current R34-funded study.

Feedback (F) (n=30): Subjects in this group will monitor their health/behaviors and will receive health feedback and advice. Subjects will wear the OURA™ daily and complete daily MEI Research diaries for 6 weeks. They will also have access to the OURA™ mobile app. Subjects will receive the following daily health information from the OURA™ app: (1) HRV, RHR, sleep (i.e., duration, efficiency, latency, sleep stages, timing, wakefulness), body temperature, respiratory rate, and physical activity (i.e., steps, calories burned); (2) composite scores from 0-100 (≥85 optimal) for "Sleep", "Activity", and "Readiness" (i.e., overall measure of recovery, based on HRV, that signals capacity to perform at physical,

mental, cognitive best); and (3) advice regarding optimal bedtime, activity progress, inactivity, and recovery. At intake, we will orient subjects to OURA™ app health feedback and advice. At Weeks 2, 4, and 6, subjects will receive written reports sent via a text/email link that summarizes their alcohol use (e.g., drinks per week, # of heavy occasions, peak BAC) and the links between drinking and OURA™ health outcomes as well as tailored advice for improving health, including evidence-based brief content for alcohol (e.g., standard drinks, low risk drinking guidelines, BAC feedback, controlled drinking tips) [40-42] and sleep (e.g., sleep hygiene, stimulus control). [19, 53, 54, 59, 60] We will derive these reports using the OURA™ Teams dashboard and daily diaries; subjects will not have dashboard access.

3.1.2 Study Date Range and Duration

Study procedures will include: an initial, in-person intake appointment (Week 0), a 6- week intervention phase, and 2 follow-up visits (Weeks 6 and 10).

3.1.3 Number of Study Sites

Sites: Screening appointments will take place at the Connecticut Mental Health Center (CMHC) main campus or the Substance Abuse Treatment Unit, a satellite location of CMHC. The Yale School of Nursing Biobehavioral Laboratory is also available as a back-up space for appointments. Follow-up visits will be conducted virtually using ZOOM.

3.2 Outcome Variables

3.2.1 Primary Outcome Variables

Timeline Follow-back Interview (TLFB): Valid/reliable/standardized interview to obtain alcohol quantity/frequency estimates [56]for a 30-day period prior to enrollment in the study and monthly following intake for a total of 3 months.(51) Calendar prompts and memory aids (e.g., holidays) are used to facilitate accurate recall of substance use during the targeted period. We will derive the following 30-day summary variables for: total drinks, drinks per drinking day, % heavy and abstinent days.

PROMIS™ Alcohol Consequences: Valid/reliable measure of positive alcohol consequences.[57]

Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ): Valid/reliable measure of negative alcohol consequences. [81]

Protective Strategies Questionnaire (PSQ): Valid/reliable measure of direct and indirect strategies for reducing alcohol consumption and consequences. [83]
Alcohol daily diaries: subjects will record the timing and amount of alcohol use before bedtime.[71]

Physical Fitness/Activity: Self-reported assessments with validity against objective measures. [74, 75]

Intervention Feasibility/Acceptability: OURA™ use metrics; quantitative and qualitative ratings of OURATM and diary self-monitoring and health feedback/advice components using treatment evaluation surveys and exit interviews (e.g., ease of use, helpfulness, satisfaction, suggestions for improvement).

3.2.2

3.2.3 Secondary and Exploratory Outcome Variables (if applicable)

PROMIS™ Sleep-Related Impairment and Sleep Disturbance: Valid/reliable measures of perceived alertness, sleepiness, during waking hours and functional impairments due to sleep problems and perceived sleep quality/satisfaction and difficulty initiating/maintaining sleep.[58]

Sleep daily diaries: subjects will rate their sleep quality upon waking.[72]

PROMIS™ Positive Affect/Depression/Anxiety: Valid/reliable measures of well-being, negative affect.[57, 73]

Physical Fitness/Activity: Self-reported assessments with validity against objective measures. [74, 75]

Morningness/Eveningness (ME) Questionnaire: Valid/reliable measure for degree of alertness during different points in the day. [80]

Munich ChronoType Questionnaire (MCTQ): Valid/reliable measure for how individuals sleep and wake. [80]

Theory of Planned Behavior (TPB): Valid/reliable measure for predicting risky drinking behavior. [78,79]

Dietary Screening Questionnaire (DSQ): Valid/reliable measure of dietary intake. [82]

COVID-19 Experiences Questionnaire: Self-report assessment to measure the impact of COVID-19. [84]

Intervention Feasibility/Acceptability: OURA™ use metrics; quantitative and qualitative ratings of OURATM and diary self-monitoring and health feedback/advice components using treatment evaluation surveys and exit interviews (e.g., ease of use, helpfulness, satisfaction, suggestions for improvement).

3.3 Study Population

Participants: We will recruit both male and female heavy-drinking (report alcohol use that exceeds NIAAA recommended daily drinking limits (i.e., ≥5 for men; ≥4 for women) at least 4 times within the last 28 days at baseline but do not meet criteria for a severe alcohol use disorder) young adults (N=60; ages 18-25 years old) from the local community through online advertising/social media (e.g., Facebook, Instagram, Snapchat) and flyers and notices displayed around the local community and college campuses.

.

3.3.1 Number of Participants

Targeted for enrollment at Yale for this protocol: 60 subjects (Assessment group [n=30] and Feedback group [n=30]).

3.3.2 Eligibility Criteria/Vulnerable Populations

Prospective participants will be screened on initial eligibility criteria via a web-based screener on the study website. Our research group has successfully recruited participants, including heavy-drinking young adults utilizing these recruitment strategies.

Following completion of the pre-screener, research staff will contact potential subjects and inform them of their initial eligibility status. Those who meet initial criteria will attend an intake to provide written informed consent and complete final screening for inclusion/exclusion criteria. Eligible individuals will be randomized to their condition to begin immediately after intake.

All research staff and research participants will be screened for COVID-19 symptoms prior to entry into CMHC. These include: fever of 99.9°F or higher, cough, shortness of breath/difficulty breathing, fatigue, repeated shaking with chills, muscle pain or body aches, chills, headache, sore throat, new loss of taste or smell, congestion or runny nose, nausea or vomiting, or diarrhea. Research staff and research participants must additionally affirm that they have not been in close

proximity to anyone who is experiencing symptoms, or who have tested positive for COVID- 19, within 14 days of a scheduled in-person visit. Research staff and research participants will indicate whether they have traveled anywhere outside of Connecticut within 14 days prior to a scheduled in-person visit. Current Connecticut state guidance on quarantine requirements for those traveling into Connecticut from other states in the USA, or internationally, will be observed. This section will be updated as Connecticut and Yale guidelines change.

Inclusion Criteria:
(1) 18-25 years of age
(2) report ≥ 4 heavy drinking occasions in the past 28 days (i.e., ≥5 drinks on 1 occasion for men; ≥4 for women)
(3) report Alcohol Use Disorders Identification Test – Consumption (AUDIT-C) scores indicative of risk of drinking harm (i.e., ≥7 for men; ≥5 for women) [70]
(5) English speaking
(6) have a smartphone for syncing OURA™ data and receiving OURA™ feedback. *An estimated 96% of young adults own a smartphone*.[76]

Exclusion Criteria:
(1) history of a sleep disorder
(2) night or rotating shift work; travel beyond 2 time zones in month prior and/or planned travel >2 time zones during study participation
(3) clinically severe AUD in past 12 months defined by: a) history of seizures, delirium, or hallucinations during alcohol withdrawal; b) report drinking to avoid withdrawal symptoms or have had prior alcohol withdrawal treatment; c) required medical treatment of alcohol withdrawal in the past 6 months which is concluded through a clinical interview with either Dr. Fucito or Dr. Ash.
(4) currently enrolled in alcohol or sleep treatment
(5) current, severe psychiatric illness (i.e., bipolar disorder, schizophrenia, panic disorder, borderline personality disorder, organic mood or mental disorders, or suicide or violence risk) by history or exam which is verified by clinical interview with either Dr. Fucito or Dr. Ash.
(6) current DSM-V substance use disorder as obtained by clinical interview with either Dr. Fucito or Dr. Ash

No fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations will be included.

4 Study Methods/Procedures

4.1 Study Procedures

The goal of this study is to determine the feasibility and preliminary efficacy of this intervention for reducing drinking among heavy-drinking young adults, which if promising will lead to a larger trial of this approach.

Young adults in our previous studies expressed strong interest in both sleep and health feedback. Our current R34-funded study is testing sleep feedback alone, and our goal is to develop a program that is appealing to young adults. We will use this information to optimize and automate future intervention iterations. Inclusion of a condition in which health feedback/advice is limited to the OURA™ mobile app. Our goal is to motivate alcohol behavior change.

Screening: We will recruit and screen subjects using methods Dr. Fucito has used successfully for other studies of heavy-drinking young adults, including online ads/social media posts (e.g., Facebook, Instagram, Snapchat), and notices posted around local

colleges and the community. Interested individuals who contact investigators by phone or email or who respond to mobile ads will be directed to complete a 5-minute, web-based pre-screening survey. Before completing the pre-screener, volunteers will provide informed consent. Following completion of the pre-screener, research staff will contact potential subjects and inform them of their initial eligibility status. Those who meet initial criteria will attend an intake to provide written informed consent and complete final screening for inclusion/exclusion criteria. Eligible individuals will be randomized to their condition to begin immediately after intake.

Randomization to Condition: Dr. Gueorguieva will create the randomization list, stratified by gender and implemented through an electronic clinical trial management system to ensure allocation concealment.

Photoplethysmography (PPG) Sensor: For 6 weeks following randomization, all subjects will wear a marketed PPG sensor, OURA™, daily. We will obtain the following health data (i.e., sleep duration, efficiency, latency, awakenings, % of time in sleep stages, bed/wake times, HRV, RHR). PPG is a non-invasive, low-cost technology that uses a light source and a photodetector at the skin surface to measure physiological parameters such as RHR, HRV, temperature, motion, movement. [61] PPG sensors are easy to use, discrete, low cost, and suitable for use in non-clinical/research settings, thereby enhancing ecological validity. PPG, including OURA™, is reliable/valid for HRV/RHR[62-65] and sleep stage prediction relative to actigraphy and PSG.[49, 50, 66-68]

At intake, the Research Coordinator will demonstrate how to wear and charge the OURA™ (device needs charging every 7 days). To encourage OURA™ adherence, we will provide daily reminders and support including when to recharge, and compensation for wearing and returning them, which we used successfully in our other studies. We will monitor OURATM use for all subjects through the OURA™ Teams dashboard. Subjects in Assessment will not have access to the OURA™ mobile app. We will sync their data to one of our study phones at the Week 6 visit. The OURA™ ring can hold 6-weeks of data. Subjects in Feedback will have the OURA™ mobile app downloaded on their phone to sync their data daily and receive immediate health feedback. They will then receive 3 electronic feedback reports sent via text/email at Weeks 2, 4 and 6, for which we will use the OURA™ Teams dashboard.

Diary Self-Monitoring: All subjects will complete daily alcohol and sleep diaries for 6 weeks following intake, using diaries from our current R34-funded study. We will program diaries in MEI Research and send links via text message each morning. To encourage adherence, we will compensate subjects $1 for each completed daily diary, a successful strategy in our prior research. We will monitor use via the MEI Research dashboard.

Follow-up Visits and Exit Interviews: At Weeks 6 and 10, all subjects will complete follow-up visits remotely via ZOOM (HIPAA-compliant and password-protected) which will be recorded using ZOOM with subjects' consent. Using remote procedures to conduct follow-up visits for our current R34-funded study and prior studies has resulted in very high retention (i.e., 95%). Follow-up visits will assess alcohol use, health characteristics, and the feasibility and acceptability of self-monitoring activities and health feedback/advice. At the Week 6 follow-up, we will conduct exit interviews to evaluate helpful components. For subjects in the assessment group, we will also sync their OURA TM data to the study phone at Week 6.

Randomization:

Subjects will be randomly assigned to 1 of 2 conditions: (1) Assessment (n=30) or (2) Feedback (n=30). The *Assessment* group will not have access to the OURA™ mobile app and will not receive any health feedback. The *Feedback* group will have access to the OURA™ app and will receive feedback. The OURA™ app provides daily summaries of HRV, RHR, and sleep that subjects can view on the app. In addition, every 2 weeks, we will send a written report via text/email that: (1) summarizes subjects' alcohol use and the links with their HRV/RHR/sleep data and (2) provides health advice tailored to this data.

Intervention Conditions: Eligible subjects will be randomized to: (1) Assessment or (2) Feedback. All subjects will begin wearing an OURA™ right after intake and will complete daily diary assessments.

Assessment (A) (n=30): Subjects in this group will only monitor their health/behaviors and will not receive any health feedback or advice. They will wear the OURA™ daily and complete daily electronic diaries about bedtime behaviors (e.g., amount/timing of alcohol use) and their sleep for 6 weeks. Diaries will be programmed in MEI Research and sent via text message each morning, a successful procedure for our current R34-funded study. These subjects will not have access to the OURATM mobile app. We will sync their data to one of our study phones at the Week 6 visit. The OURATM ring can hold 6-weeks of data.

Feedback (F) (n=30): Subjects in this group will monitor their health/behaviors and will receive health feedback and advice. Subjects will wear the OURA™ daily and complete daily MEI Research diaries for 6 weeks. They will also have access to the OURA™ mobile app. Subjects will receive the following daily health information from the OURA™ app: (1) HRV, RHR, sleep (i.e., duration, efficiency, latency, sleep stages, timing, wakefulness), body temperature, respiratory rate, and physical activity (i.e., steps, calories burned); (2) composite scores from 0-100 (≥85 optimal) for "Sleep", "Activity", and "Readiness" (i.e., overall measure of recovery, based on HRV, that signals capacity to perform at physical, mental, cognitive best); and (3) advice regarding optimal bedtime, activity progress, inactivity, and recovery. At intake, we will orient subjects to OURA™ app health feedback and advice. At Weeks 2, 4, and 6, subjects will receive written reports sent via a text/email link that summarizes their alcohol use (e.g., drinks per week, # of heavy occasions, peak BAC) and the links between drinking and OURA™ health outcomes as well as tailored advice for improving health, including evidence-based brief content for alcohol (e.g., standard drinks, low risk drinking guidelines, BAC feedback, controlled drinking tips) [40-42] and sleep (e.g., sleep hygiene, stimulus control).[19, 53, 54, 59, 60] We will derive these reports using the OURA™ Teams dashboard and daily diaries; subjects will not have dashboard access.

b. **Sources of Materials**

b.1.The research material and data that will be collected include self-reports, interviews, sensor data.

b.2.These materials will be used to determine study eligibility and obtain information about drinking, health and sleep, and other related assessments.

b.3.The principal investigator and her designates will have access to individually identifiable private information. We will code research data by a number that does not include identifiable private information. All investigators and key personnel are required

to take the Yale University HIPAA training. Documentation of this training is required before research staff are allowed to take part in research activities.

b.4.The specimens and data are collected directly from the participants as described above (b.1.) specifically for the purpose of this project.

4.1.1 Data Collection

Describe how and where the data will be recorded and identify all sources of data. This description should be specific but not over-detailed. However, you must make sure that data collected supports the objectives and endpoints stated above. Indicate whether:

- The information obtained will be recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects; OR
- If any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; OR
- If the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

Specify any assessments being used including methods and timing for assessing, recording and analysis.

Include any questionnaire administration and identify the questionnaire to be used for the study related assessment. State how these assessments contribute to the overall study aims. Include as appendices copies of each questionnaire.

Socio-demographic information: Will be assessed with interviews and self-reported age, race/ethnicity, marital & occupational status, education.

Diagnostic/Substance Use History: Dr. Fucito, a licensed clinical psychologist, will

conduct the Mini International Neuropsychiatric Interview (The M.I.N.I.). [69]

Alcohol Use Disorders Identification Test-Consumption (AUDIT-C): Reliable/valid alcohol use screener to confirm at-risk drinking inclusion criterion based on cut-off scores for young adults.[70]

Table 1. Schedule of Assessments

Variables	Assessments	Intake	Intake-Wk 6	6, 10
Eligibility/ Lab/ Medical	Demographics	X		
		X		
	The M.I.N.I.	X		
	AUDIT-C	X		
Alcohol/ Health Outcomes	TLFB	X		6, 10
	PROMIS™ measures	X		6, 10
	BYAACQ	X		6, 10
	PSQ	X		6,10
	TPB	X		6
	DSQ	X		6,10
	Munich Chrono Type Questionnaire	X		
	ME Questionnaire	X		
	Physical fitness	X		6, 10
	Alcohol/sleep diaries		X	
	COVID-19 Experiences Questionnaire	X		6,10
	OURA™ HRV, RHR, sleep		X	
Feasibility	OURA™ use metrics		X	
Acceptability	Treatment eval; exit interview			6

Alcohol Use

Timeline Follow-back Interview (TLFB):

Valid/reliable/standardized interview to obtain alcohol quantity/frequency estimates [56]for a 30-day period prior to enrollment in the study and monthly following intake for a total of 3 months.(51) Calendar prompts and memory aids (e.g., holidays) are used to facilitate accurate recall of substance use during the targeted period. We will derive the following 30-day summary variables for: total drinks, drinks per drinking day, % heavy and abstinent days.

PROMIS™ Alcohol Consequences: Valid/reliable measure of positive alcohol consequences.[57]

Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ): Valid/reliable measure of negative alcohol consequences. [81]

Protective Strategies Questionnaire (PSQ): Valid/reliable measure of direct and indirect

strategies of reducing alcohol consumption and consequences. [83]

Theory of Planned Behavior (TPB): Valid/reliable measure for predicting risky drinking behavior. [79,79]

Alcohol daily diaries: subjects will record the timing and amount of alcohol use before bedtime.[71]

Health Characteristics

PROMIS™ Sleep-Related Impairment and Sleep Disturbance: Valid/reliable measures of perceived alertness, sleepiness, during waking hours and functional impairments due to sleep problems and perceived sleep quality/satisfaction and difficulty initiating/maintaining sleep.[58]
Sleep daily diaries: subjects will rate their sleep quality upon waking.[72]

PROMIS™ Positive Affect/Depression/Anxiety: Valid/reliable measures of well-being, negative affect.[57, 73]

Physical Fitness/Activity: Self-reported assessments with validity against objective measures. [74, 75]

Morningness/Eveningness (ME) Questionnaire: Valid/reliable measure for degree of alertness during different points in the day. [80]

Munich Chrono Type Questionnaire (MCTQ): Valid/reliable measure for how individuals sleep and wake. [80]

Dietary Screening Questionnaire (DSQ): Valid/reliable measure of dietary intake. [82]

COVID-19 Experiences Questionnaire: Self-report assessment to measure the impact of COVID-19. [84]

Intervention Feasibility/Acceptability: OURA^{TM} use metrics; quantitative and qualitative ratings of OURATM and diary self-monitoring and health feedback/advice components using treatment evaluation surveys and exit interviews (e.g., ease of use, helpfulness, satisfaction, suggestions for improvement).

4.1.2 Adverse Events Definition and Reporting

Dr. Fucito, the principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting monthly safety reviews. During the review process, Dr. Fucito, will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

Dr. Fucito, the Institutional Review Board (IRB) or NIH have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems

Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 48 hours of Dr. Fucito becoming aware of the event to NIAAA and within 5 days per the guidelines of the Yale IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies.

Dr. Fucito will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project. Dr. Fucito will hold weekly study meetings with investigators to review study progress, including any adverse events. Investigators who are not present at these meetings will be alerted via email by Dr. Fucito. The protocol's research monitor(s), e.g., the Yale IRB and NIH will be informed of any adverse events that meet these 3 criteria: (1) unexpected, (2) related/possibly related to study participation, and (3) places subjects or others at greater risk of harm than previously known/recognized. These adverse events will be reported within 48 hours of the event becoming known to Dr. Fucito.

4.2 Study Schedule

Intake (Week 0):

Prior to attending the intake and upon arrival, subjects will be screened for COVID-19 symptoms. These include fever of 99.9°F or higher, cough, shortness of breath/difficulty breathing, fatigue, repeated shaking with chills, muscle pain or body aches, chills, headache, sore throat, new loss of taste or smell, congestion or runny nose, nausea or vomiting, or diarrhea. We will also discuss COVID-19 risks with you. Subjects will then be asked to complete a number of questionnaires and self-assessments that will ask them about Their sleep, alcohol use, health behaviors, mood, and psychological characteristics. We will also ask for demographic information including age, race, socioeconomic status, and educational and occupational levels. A licensed clinical psychologist will conduct an interview with them to determine their substance use history and other relevant medical and psychiatric history. We will measure their height and weight. This visit will take about 1 hour.

Randomization (Week 0): Subjects will be randomly assigned (like the flip of a coin) to 1 of 2 conditions: (1) Assessment or (2) Feedback.

If they are assigned to the Assessment group, they will wear the OURA™ ring and complete daily diaries for 6 weeks but will not have access to the OURA™ mobile app and will not receive any feedback about their health data. They will have an opportunity to receive this health data after they complete their final follow-up visit at Week 10.

If they are assigned to the Feedback group, subjects will wear the OURA™ ring and complete daily diaries for 6 weeks. During this time, they will have access to the OURA™ mobile app and will receive personalized feedback and tailored health tips about their data.

Treatment Phase (Intake-Week 6): They will begin wearing the OURA™ after the intake every day for a 6-week period. During these weeks, monitoring will occur continuously with the OURA™ and subjects will also complete daily diaries using the MEI Research application. We will arrange to pick up the biosensor from them at the end of the 6-week monitoring period. If they are in the Feedback group, subjects will also receive health feedback and advice through the OURA™ mobile app and reports that are sent to . The OURA™ app provides daily summaries of their resting heart rate, heart rate variability, and sleep that they can view on the app. The research staff will orient them to the OURA™ app health feedback and advice. In addition, every 2 weeks (i.e., Weeks 2, 4, and 6), we will send a written report via text/email that: (1) summarizes their alcohol use and the links with their heart and sleep health data and (2) provides health advice tailored to this data.

Follow-up (Week 6): Subjects will complete the Week 6 follow-up visit remotely via ZOOM, which will be recorded using ZOOM with their consent. The research staff will conduct exit interviews and treatment evaluation surveys to understand the feasibility/acceptability of the health intervention program including wearing the biosensor. They will also complete questionnaires and interviews about their alcohol use, health characteristics, and the feasibility and acceptability of self-monitoring activities and health feedback/advice.

Follow-Up (Week 10): Subjects will also complete the Week 10 follow-up visit remotely via ZOOM, which will be recorded using ZOOM with their consent. They will complete questionnaires and interviews about your alcohol use and health characteristics.

4.3 Informed Consent

After giving consent via a web-based screener, potentially eligible participants will be invited for an in-person intake visit. At the start of the initial intake session, informed consent to participate will be obtained from all participants after the research procedures and risks associated with participation have been explained. The entire consent form will be reviewed in detail with the participant in a private, one-on-one setting at the intake appointment with a research staff member. All risks and potential benefits will be described and discussed. The consent form will provide clear and explicit language about the intervention components, diary monitoring procedures, and sensor use. Any questions that the participant may have will be addressed. If the participant wishes, they may take the consent form home and consider it further before signing. They may also request to speak to anyone on the research team about questions they have or to consult others, including their physician and family members. Participants will sign 2 copies of the consent, retain one, and the researchers will keep the second copy on file.

Participants will then complete all assessments to determine eligibility. Participants will be informed that they are free to decline participation and withdraw from the study at any time and that neither action will adversely affect their relationship with any study personnel. Following resolution of any questions, the participant will be asked to sign the consent form, if he/she agrees to participate.

4.3.1 Screening (if applicable)

We will recruit and screen subjects using methods Dr. Fucito has used successfully for other studies of heavy-drinking young adults, including online ads/social media posts (e.g., Facebook, Instagram, Snapchat), and notices posted around local colleges and the community. Interested individuals who contact investigators by phone or email or who respond to mobile ads will be directed to complete a 5-minute, web-based pre-screening survey. Before completing the pre-screener, volunteers will provide informed consent. Following completion of the pre-screener, research staff will contact potential subjects and inform them of their initial eligibility status. Those who meet initial criteria will attend an intake to provide written informed consent and complete final screening for inclusion/exclusion criteria. Eligible individuals will be randomized to their condition to begin immediately after intake.

4.3.2 Recruitment, Enrollment and Retention (if applicable)

Interested individuals who contact investigators by phone or email or who respond to mobile ads will be directed to complete a 5-minute, web-based pre-screening survey. Before completing the pre-screener, volunteers will provide informed consent. Following completion of the pre-screener, research staff will contact potential subjects and inform them of their initial eligibility status. Those who meet initial criteria will attend an intake to provide written informed consent and complete final screening for inclusion/exclusion

criteria. Eligible individuals will be randomized to their condition to begin immediately after intake.

The PI and research staff will recruit potential subjects

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify the subject. At most, the website will include a summary of the results. The subject can search this website at any time.

4.3.3 Study Visits (is applicable)

Table 1. Schedule of Assessments

Variables	Assessments	Intake	Intake-Wk 6	6, 10
Eligibility/ Lab/ Medical	Demographics	X		
		X		
	The M.I.N.I.	X		
	AUDIT-C	X		
Alcohol/ Health Outcomes	TLFB	X		6, 10
	PROMIS™ measures	X		6, 10
	Physical fitness	X		6, 10
	BYACCQ	X		6, 10
	PSQ	X		6,10
	TPB	X		6
		X		6, 10
	DSQ	X		6,10
	Munich Chrono Type Questionnaire	X		
	ME Questionnaire	X		
	Alcohol/sleep diaries		X	
	COVID-19 Experiences Questionnaire	X		6,10
	OURA™ HRV, RHR, sleep		X	
Feasibility	OURA™ use metrics		X	
Acceptability	Treatment eval; exit interview			6

4.4 Statistical Method

4.4.1 Statistical Design

Dr. Gueorguieva, a biostatistician, will oversee data analyses. We will use a type I error of 5% (two-sided) significance testing using SAS V9.4 (SAS Institute, Cary, NC). We will examine data for conformity to the normal distribution and transformation or non-parametric methods will be used if necessary.

4.4.2 Sample Size Considerations

Sample Size and Power Calculations: The goal of this proof-of-concept proposal is to determine the feasibility and preliminary efficacy of this intervention for reducing drinking among heavy-drinking young adults, which if promising will lead to a larger trial of this approach. We propose to recruit 60 subjects (30 per group), in line with the recommended sample size of 15-30 subjects per group for Phase 1 behavioral intervention studies. [78] This sample size is feasible to recruit within the time period, will allow us to derive effect size estimates for primary and secondary outcomes to inform a more definitive study, and is sufficient for detecting a clinically significant, large difference between groups in total drinks controlling for baseline with 80% power at a 2-sided 0.05 significance level

4.4.3 Planned Analyses

Statistical analyses will utilize an ITT approach and mixed models, one of two gold standards (together with multiple imputation) for handling missing outcome data in longitudinal studies.

For Primary Aim 1, we will examine condition effects on total drinks consumed over Weeks 2-10 (summarized over 4-week periods), controlling for baseline drinks. For this analysis, we will use mixed effects models with condition and sex as between-subject factors and time as a within-subject factor. We will also use the same modeling approach for secondary alcohol outcomes: drinks per drinking day, % heavy drinking, abstinent days (summarized in 4-week periods), and alcohol-related consequences, controlling for baseline, and will focus on effect size estimation rather than statistical testing. Using all repeated measures on individuals in the context of a mixed model will allow us to assess temporal patterns of change over time and to use all available data on individuals. Thus, this approach helps to avoid imputation of missing data and allows us to obtain unbiased and efficient estimates of the main and interactive effects. Mixed models will account for the correlation in alcohol outcomes measured in the same individual. We will use the Schwartz-Bayesian Information Criterion to elect the best-fitting variance-covariance structure. We will consider time as a categorical factor but will also test whether alcohol outcomes change linearly by condition over time. If an alcohol outcome is not normally distributed, we have several options including transforming data, utilizing alternative methods (e.g., generalized linear mixed models, nonparametric tests, Poisson and negative binomial generalized linear mixed models for count data). Hypothesis: The feedback group will report fewer total drinks than the assessment group.

For Secondary Aims 2.1-2.2, we will examine condition effects on PROMIS™ sleep quality and sleep-related impairment self-ratings, controlling for baseline, using mixed effects models. We will also analyze OURA™ sleep, HRV, and RHR data (summarized over 2-week periods) using mixed effects models. We will transform or utilize alternative methods for non-normally distributed outcomes. We will also characterize the daily variations in OURA™ sleep, HRV, RHR data and potential dynamic relationships between them and daily diary drinking data using methods for longitudinally intensive data (e.g., time-varying effects models). Hypothesis: The feedback group will report better sleep/health than the assessment group.
For Secondary Aim 2.3, we will summarize interview themes. We will also summarize use metrics and ratings for feedback and/or monitoring using descriptive statistics. We expect higher scores in the feedback group.

4.4.4 Analysis of Subject Characteristics (if applicable)

We will use descriptive statistics were used to summarize frequencies and percentages of sociodemographic characteristics (age, race, ethnicity, gender, college status) and clinical characteristics (drinking, sleep, and other health behaviors).

4.4.5 Interim Analysis (if applicable)

N/A

4.4.6 Handling of Missing Data

We will also use the same modeling approach for secondary alcohol outcomes: drinks per drinking day, % heavy drinking, abstinent days (summarized in 4-week periods), and alcohol-related consequences, controlling for baseline, and will focus on effect size estimation rather than statistical testing. Using all repeated measures on individuals in the context of a mixed model will allow us to assess temporal patterns of change over time and to use all available data on individuals. Thus, this approach helps to avoid imputation of missing data and allows us to obtain unbiased and efficient estimates of the main and interactive effects. Mixed models will account for the correlation in alcohol outcomes measured in the same individual. We will use the Schwartz-Bayesian Information Criterion to elect the best-fitting variance-covariance structure. We will consider time as a categorical

factor but will also test whether alcohol outcomes change linearly by condition over time. If an alcohol outcome is not normally distributed, we have several options including transforming data, utilizing alternative methods (e.g., generalized linear mixed models, nonparametric tests, Poisson and negative binomial generalized linear mixed models for count data).

5 Trial Administration

5.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

Consent forms will be Institutional Review Board (IRB)-approved and the participant will be

This section should include any applicable ethical considerations. They should also be addressed in the Informed Consent form, including if informed consent and/or HIPAA authorization will be obtained or a waiver of informed consent and/or HIPAA authorization will be requested. The Informed Consent form should be included as an attachment to the protocol.

Describe the following:

- Any possible deception
- Rationale if payment will be provided for participation.
- Any sensitive data that may be collected and how it will be protected.
- Any possibility that a previously unknown condition (disease, genetic disposition, etc.) will be discovered as the result of the study procedures and how this will be handled.
- Any information that may be added to the subject's permanent medical records with rationale.
- If informed consent/assent and HIPAA authorization will be obtained, the following should be addressed:
- Who will obtain consent/authorization
- When and where will the consent/authorization discussion occur
- How will subject privacy be assured
- How will consent/authorization be documented
- How will subject understanding of the study be assessed
- What steps are in place to avoid subject coercion

If your study involves children, additional information should be provided to describe:

- How parental permission will be obtained
- From how many parents will parental permission be obtained
- Whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. The process used to determine these individual's authority to consent for the child should be provided
- Whether or not assent will be obtained from the child
- How will assent be documented
- Whether child subjects may be expected to attain legal age to consent to the procedures for research prior to the completion of their participation in the research. If so, describe the process that will be used to obtain their legal consent to continue participation in the study. Indicate what will occur if consent is not obtained from the now-adult subjects.

asked to read and review the document. The members of the research team will explain the research study to the participant and answer any questions that may arise. This conversation will take place in a private room.

Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records

We will not be enrolling participants with limited decision-making capacity. We plan to exclude individuals with current serious psychiatric or medical illnesses. The research assistant will read and review the consent form either in-person or via televideo while COVID-19 social distancing requirements remain in place. Due to the ongoing COVID-19

pandemic, it is not always possible to consent a new study participant in person. Due to this, many participants will be consented via televideo, therefore a physical consent form will not be signed by the participant. Instead, a REDCap consent will be created, where participants will be able to view the entire consent form and then electronically sign/date/initial the consent form. The research assistant will share their screen while on televideo so the consent form can be read along with the participant. This is to explain the study in detail to the participant, so they are aware of all aspects of the study and fully informed. Participants will be able to ask research staff any questions during this consenting period. The research assistant will then ask the potential participant various questions about the consent form and study protocol to ensure the prospective participant sufficiently understands the study and the nature of their consent to participate. If concerns arise that a potential individual does not have sufficient capacity to provide informed consent, we will have a clinical member of the team conduct a mini mental status exam to verify capacity. We will allow sufficient time for research staff to explain the study and potential participants to review the consent, study procedures, and ask questions to avoid coercion.

The data will be stored in a locked room for 7 years after the final data is collected. After this point, the Data Manager and Principal Investigator, Dr. Fucito, will oversee the process in which data is destroyed or de-identified.
We have obtained a Certificate of Confidentiality (CoC) issued by the NIH. Once granted, the researchers can use this Certificate to legally refuse to disclose information that may identify the participant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify the participant, except as explained below.

The protection offered by the CoC does not stop the research team from voluntarily reporting information about suspected or known sexual, physical, or other abuse of a child or older person, or a participant's threats of violence to self or others. If any member of the research team is given such information, he or she will make a report to the appropriate authorities. When the CoC is obtained, we will inform all active study participants.

The anticipated funding for this study is from an NIH grant (R21AA028886).

Even when a CoC is in place, the participant and their family members must still continue to actively protect their own privacy. If they voluntarily give their written consent for anyone to receive information about their participation in the research, then we may not use the CoC to withhold this information.

Participants will be paid $30 for completing the intake, $45 for completing the week 6 follow-up visit, and $60 for completing the week 10 follow-up visit, total=$135. Participants will also be compensated for at-home monitoring activities: (1) $1 per day for wearing the OURA (42 possible days for a total of $42), (2) $50 for returning the OURA, and (3) $1 per day for completing each daily diary (42 possible days for a total of $42). The total possible compensation for at-home monitoring is $94. Therefore, the total possible compensation for participants is $279. Participants will be registered through Oncore to receive payments for taking part in the study. We will use a Bank of America pre- paid debit card to provide payment. We will have to share participant name, address, and telephone number with Bank of America for ePayments and this information is communicated in the consent form. The participant will receive a card in the mail with the first payment. Each additional payment will be automatically added to the card.

5.2 Institutional Review Board (IRB) Review

The protocol will be submitted to the IRB for review and approval. Approval of the protocol must be obtained before initiating any research activity. Any change to the protocol or study team will require an approved IRB amendment before implementation. The IRB will determine whether informed consent and HIPAA authorization are required.
A study closure report will be submitted to the IRB after all research activities have been completed.

5.3 Subject Confidentiality

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. 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.
All research activities will be conducted in as private a setting as possible.
The study monitor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.
At the end of the study, all records will continue to be kept in a secure location for 7 years.
Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored on Yale redcap servers and in locked cabinets in locked office at CMHC. 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 will be secured and password protected. At the end of the study, all study databases will be de-identified and archived on Yale servers and CMHC.
Identifiable information including participant’s name, address, phone number, and date of birth, will be collected and used to enroll and contact participants. It will only be used for this purpose. This information will be stored in locked cabinet apart from the research records.

Research data will be collected using interviews, self-reports, wearable devices, and computer tasks. All identifiable information will be stored in a locked research cabinet. All participants will be assigned a study participant number. Subsequently, participants will be identified in the Case Report Forms (CRFs) only by that number and an encoded version of their initials (i.e., John Doe = JDO). A list of numbers and the corresponding names will be maintained by Dr. Fucito and stored in a locked research cabinet.

The data will be stored on secured server, laptop computer and desktop computer. The data will be stored in a locked room for 7 years after the final data is collected. After this point, the Data Manager and Principal Investigator, Dr. Fucito, will oversee the process in which data is destroyed or de-identified.

Several steps will be taken to safeguard the confidentiality of subjects and their data. All research data that is collected will be assigned a study participant number and that number will only identify participants in digital databases. The names of participants will not be associated with this data and assessments will be maintained according to participant study number. A master list connecting participant study numbers to participant names will be kept in a locked file cabinet where it can only be accessed by senior level project staff. Any information published as a result of the study will be such that it will not permit identification of any participant.

Right to privacy for participation in this research will be protected through alphanumeric coding of data (in place of names) and proper storage of research records, including treatment exit interviews. Collected materials will be maintained via an alphanumeric reference system maintained by Dr. Fucito. Participants' names will appear only on the compound authorization form, and a master list maintained in a physically locked file that is separate from research data. Our data collection and management procedures are fully compliant with HIPAA. Access will be limited to personnel intimately involved in the study. A Certificate of Confidentiality will also be obtained from the National Institutes of Health to protect access to the records. However, participants will also be told that if they present with suicidal or homicidal ideation and/or report any form of child/elder abuse or report plans to damage property then we will have to report this to the appropriate authorities and/or provide them with referrals for immediate treatment. Electronic data will be de-identified, and password protected. Only members of the study team will have access to the physical or electronic data.

For the wearable devices, data will only be linked to participants' study numbers not the participants themselves. Only members of the study team will have access to the physical or electronic data. OURA™ data are deidentified and are also protected through secure, password-protected servers. We will use an alphanumeric code to sign participants up to the OURA™ mobile app in place of their names. After downloading the data, the data will be immediately deleted from the devices. OURA follows strict policy guidelines relating to both health privacy and teams privacy. OURA™ complies with all legal requirements regarding data sharing and only shares user information with trusted service providers. Users can withdraw consent from having their data collected at any time. OURA™ teams is a feature that allows health data to be shared with trusted individuals, such as healthcare professionals and researchers. There are safeguards in place to ensure this data is processed and collected efficiently and appropriately, users can withdraw from providing data to OURA™ teams at any time.

All investigators and key personnel have taken the required Yale University HIPAA training. Right to privacy for participation in this research will be protected through coding of data and proper storage of research records. A list of numbers and the corresponding names will be maintained by the Principal Investigator in a locked research cabinet.

Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996 and by additional protections of substance abuse treatment records afforded under Code of Federal Regulations (CFR) Part 2, Subpart E. All research personnel will be trained on human subjects' protection and HIPAA procedures.

We may share participant information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Those representatives at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator
- The study sponsor
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

- Other researchers through a shared data agreement through a required policy from NIAAA

5.4 Deviations/Unanticipated Problems

A protocol deviation is any noncompliance with the study protocol. 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.
It is the responsibility of the site investigator to identify and report deviations within 2 working days of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the study sponsor, and the reviewing Institutional Review Board (IRB) per their policies.
Unanticipated problems involving risks to participants or others include, in general, any incident, experience, or outcome that meets all of the following criteria:
Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
Related or possibly related to participation in the research ("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); and
Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the 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, or outcome;
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 serious adverse events (SAEs) will be reported to the IRB and study sponsor, if applicable immediately (if possible) followed by a written report within **5 calendar days** using the appropriate forms from NIH and Yale University IRB.
Any other UP will be reported to the IRB and study sponsor within 14 calendar days of the investigator becoming aware of the problem.
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 the Office for Human Research Protections (OHRP) within 30 calendar days of the IRB's receipt of the report of the problem from the investigator.

5.5 Data Quality Assurance

Describe the quality control and assurance for the conduct of the study to ensure that Good Clinical Practice is followed. Any steps that will be implemented as part of the study to ensure standardization of the collection of accurate, consistent, complete and reliable data, such as training sessions, monitoring of investigator sites, instruction manuals, use of central laboratory or reading center should be included.

Multiple measures are in place to ensure the validity and integrity of the data. First, all research staff receive Human Subjects Protection training, as well as training in Good Clinical Practice. Second, Dr. Fucito will supervise and train the Research Coordinator and key personnel on study procedures to ensure that all procedures are followed and are in compliance with the approved Yale University IRB protocol. Dr. Fucito will also provide training and oversight to study staff to ensure data are generated, documented, and reported according to requirements by the Yale University IRB and NIH. She will then monitor adherence to protocol procedures and use individual supervision to address any data quality concerns. Third, weekly research meetings will be held for all research staff as a forum for in-service training as well as to discuss questions regarding issues that arise in complex clinical research protocols. Fourth, all research staff will be cross-trained to 'cover' for each other; thus, review by multiple staff with oversight by the PI will facilitate early identification of errors and oversight. Fifth, Dr. Fucito will also oversee quality assurance of data. The Research Coordinator, in collaboration with Dr. Fucito, will review the study database on a monthly basis to ensure data accuracy. Any data quality issues will be addressed immediately. Last, the use of an electronic system for data capture will minimize data entry errors.

5.6 Study Records

Specify the documents considered study records (subject diaries, regulatory documents, protocols, consents forms, case report forms, subject medical records, surveys, specimens, etc.).

- Protocol
- Consent form
- Alcohol/sleep diaries
- Surveys

5.7 Access to Source

Source data will be maintained per Medical Records policy in a password protected, secure, Health Insurance Portability and Accountability Act (HIPAA) compliant, web-based electronic database with a built-in audit trail.
Only Institutional Review Board (IRB) approved research team members who have current HIPAA and Collaborative Institutional Training Initiative (CITI) Good Clinical Practice (GCP) and human subjects protection training will be authorized to access records.

5.8 Data or Specimen Storage/Security

Describe method in which data will be collected, stored (digital, hard copy, etc.) and maintained in a secure manner (encryption, password protection, etc.).

Data Acquisition and Transmission. We have selected psychometrically sound assessments that are brief and feasible with young adults and adequate to test study hypotheses. Trained research staff will administer assessments and collect measurements. They will enter data directly into a secure electronic database, which will be backed up on a secure, password protected Yale University network drive. De-identified data will be stored in the database and only accessible by research staff using a password protected login. All data with identifiable information will be stored in locked file cabinets in locked offices and will only be accessible by research staff. The transfer of any identifiable administrative data will be through Yale University's secure, password-protected Secure File Transfer system. OURA™ data will also be de-identified and distributed to Yale through an agreement with OURA™ that ensures data confidentiality.

Data Entry Method. Trained research staff will enter data directly into the electronic database. No personally-identifiable information will be entered into the electronic database, which will be stored on a secure, password protected Yale University network drive.

5.9 Retention of Records

The data will be stored in a locked room for 7 years after the final data is collected. After this point, the Data Manager and Principal Investigator, Dr. Fucito, will oversee the process in which data is destroyed or de-identified.

5.10 Study Modification

Study modifications will be undertaken in response to ongoing study monitoring. Any potential modifications that could have a major impact on the study objectives will be discussed with the NIH Program Officer before submission to the IRB. More minor modifications that do not impact study objectives but help with study recruitment and implementation or allow for additional assessment of important questions will be submitted to the IRB for approval.

5.11 Study Monitoring

Dr. Fucito, the PI, will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency that must be conducted at a minimum of every 6 months (including when reapproval of the protocol is sought), which is appropriate for a study deemed to be of minimal risk. Dr. Fucito will review the frequency of anticipated and unanticipated adverse events overall and by study arm with key personnel. The focus of the evaluation will be to determine whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Dr. Fucito, the Yale University IRB, and the National Institutes of Health have the authority to stop or suspend the study or require modifications.

Dr. Fucito will also lead a weekly research meeting with key personnel to review the status of all enrolled participants and discuss the eligibility of potential participants. At this weekly meeting, Dr. Fucito will review study progress (i.e., recruitment goals, retention, protocol adherence). Any adverse events will be reviewed at this meeting including serious adverse events that may have been attended to outside of this weekly meeting. An annual progress report will be submitted to NIH and the Yale University IRB that lists and summarizes adverse events; documents whether adverse event rates are consistent with pre-study assumptions; summarizes recruitment and retention and reason for dropouts; and summarizes study progress related to the stated aims.

5.12 Study Completion

Intended to complete in 2 years. The IRB will be notified in writing upon study completion and the study will be archived with the IRB when all final analyses have been conducted on identifiable information.

5.13 Funding Source

The anticipated funding for this study is from an NIH grant (R21AA028886).

5.14 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 appropriate conflict of interest review committee 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 [specify 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 investigators will follow the applicable conflict of interest policies.

5.15 Publication Plan

Study results will be made available via articles written for professional and layperson publications; presentations at scientific and professional conferences; special lectures/talks in academic and professional settings; collaborating agencies/research sites, and interest groups. No identifiable information will be disclosed. Data will be presented and published in aggregate. Dr. Fucito, as PI, has primary responsibility for publishing the study results. She will acknowledge NIH grant funding for all presentations and publications and will ensure all publications are submitted to PMC in accordance with NIH's policy on public access.

Consistent with the NIH resource sharing policy, we will share data with other qualified investigators. Once all of the data have been cleaned and validated, and main findings have been published, the data will be made available to the scientific community. Datasets will be made available to any qualified individual who makes a direct request to the PI and indicates the data will be used for the purposes of research (as defined in CFR Title 45 Part 46). Data will be provided to HIPPA-compliant, de-identified files. The following plan specifies the following conditions that need to be met before data are shared in the form of a data sharing agreement.

- A formal research question is specified *a priori*;
- Names, affiliations, and roles of any other individuals who will access the shared data;
- The deliverable(s)—e.g., manuscript, conference presentation—are specified *a priori*;
- Proper acknowledgement of the source of the data;
- A statement indicating an understanding that the data cannot be further shared with any additional individual(s) or parties without the PI's permission;
- IRB approval for use of the data (or documentation that the data are exempt);
- Agreement to maintain the data in a physically and electronically secure location.

Data will be shared in electronic format and accessible to the software used by the Investigators; upon completion of the analyses, the requestor will be instructed to destroy all copies of the data.

The agreement to share data will be revisited annually to determine whether the current policy should be modified based upon our prior experiences in sharing the data with other investigators.

In addition, consistent with new regulations for the NIAAA Data Archive (NIAAA(DA), all data will be shared with the NIAAA(DA). We will upload data to the NIAAA(DA) at least every 6 months.

1. Falk, D., H.-y. Yi, and S. Hiller-Sturmhöfel, *An epidemiologic analysis of co-occurring alcohol and drug use and disorders: findings from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC).* Alcohol Research & Health, 2008. **31**(2): p. 100.
2. Administration, S.A.a.M.H.S. *Key substance use and mental health indicators in the United States: Results from the National Survey on Drug Use and Health, Center for Behavioral Health Statistics and Quality*. 2019; Available from: https://www.samhsa.gov/data/.
3. Hingson, R.W., W. Zha, and E.R. Weitzman, *Magnitude of and trends in alcohol-related mortality and morbidity among US college students ages 18-24, 1998-2005.* Journal of Studies on Alcohol and Drugs, Supplement, 2009(16): p. 12-20.
4. NIAAA, *Alcohol involvement over the life course*, E. U. S. Department of Health and Human Services, Editor. 2000 Bethesda, MD. p. p. 28-53.
5. NIAAA, *Alcohol and Other Drugs.* Alcohol Alert, 2008. **76**.
6. Cronce, J.M. and M.E. Larimer, *Individual-focused approaches to the prevention of college student drinking.* Alcohol Research & Health, 2011. **34**(2): p. 210.
7. Carey, K.B., et al., *Individual-level interventions to reduce college student drinking: A meta-analytic review.* Addictive behaviors, 2007. **32**(11): p. 2469-2494.
8. Carey, K.B., et al., *Computer-delivered interventions to reduce college student drinking: A meta-analysis.* Addiction, 2009. **104**(11): p. 1807-1819.
9. Buscemi, J., et al., *Help-seeking for alcohol-related problems in college students: correlates and preferred resources.* Psychology of addictive behaviors, 2010. **24**(4): p. 571.
10. Black, D.R. and D.C. Coster, *Interest in a stepped approach model (SAM): Identification of recruitment strategies for university alcohol programs.* Health Education Quarterly, 1996. **23**(1): p. 98-114.
11. Wu, L.-T., et al., *Alcohol use disorders and the use of treatment services among college-age young adults.* Psychiatric Services, 2007. **58**(2): p. 192-200.
12. Caldeira, K.M., et al., *College students rarely seek help despite serious substance use problems.* Journal of substance abuse treatment, 2009. **37**(4): p. 368-378.
13. Fortuna, R.J., B.W. Robbins, and J.S. Halterman, *Ambulatory care among young adults in the United States.* Annals of internal medicine, 2009. **151**(6): p. 379-385.
14. O'hara, B. and K. Caswell, *Health status, health insurance, and medical services utilization: 2010.* Curr Pop Rep, 2012. **2012**: p. 70-133.
15. Kaner, E.F., et al., *Effectiveness of brief alcohol interventions in primary care populations.* Cochrane database of systematic reviews, 2018(2).
16. Cadigan, J.M., C.M. Lee, and M.E. Larimer, *Young adult mental health: A prospective examination of service utilization, perceived unmet service needs, attitudes, and barriers to service use.* Prevention Science, 2019. **20**(3): p. 366-376.
17. Orzech, K.M., D.B. Salafsky, and L.A. Hamilton, *The state of sleep among college students at a large public university.* Journal of American College Health, 2011. **59**(7): p. 612-619.
18. Weinstock, J., et al., *Sedentary college student drinkers can start exercising and reduce drinking after intervention.* Psychology of Addictive Behaviors, 2016. **30**(8): p. 791.
19. Fucito, L.M., et al., *Using sleep interventions to engage and treat heavy-drinking college students: A randomized pilot study.* Alcoholism: Clinical and Experimental Research, 2017. **41**(4): p. 798-809.
20. Rideout, V., *Generation RX. com.* Marketing health services, 2002. **22**(1): p. 26.
21. Rideout, V. and S. Fox, *Digital health practices, social media use, and mental well-being among teens and young adults in the US.* 2018.
22. Wartella, E., et al., *Teens, health and technology: A national survey.* Media and

communication, 2016. **4**(3): p. 13-23.
23. DeMartini, K.S. and L.M. Fucito, *Variations in sleep characteristics and sleep-related impairment in at-risk college drinkers: A latent profile analysis.* Health Psychology, 2014. **33**(10): p. 1164.
24. Singleton, R.A. and A.R. Wolfson, *Alcohol consumption, sleep, and academic performance among college students.* Journal of studies on alcohol and drugs, 2009. **70**(3): p. 355-363.
25. Hasler, B.P., et al., *A longitudinal study of insomnia and other sleep complaints in adolescents with and without alcohol use disorders.* Alcoholism: Clinical and Experimental Research, 2014. **38**(8): p. 2225-2233.
26. Hasler, B.P., L. Kirisci, and D.B. Clark, *Restless sleep and variable sleep timing during late childhood accelerate the onset of alcohol and other drug involvement.* Journal of studies on alcohol and drugs, 2016. **77**(4): p. 649-655.
27. Miller, M.B., et al., *Adequate sleep moderates the prospective association between alcohol use and consequences.* Addictive behaviors, 2016. **63**: p. 23-28.
28. Wong, M.M., et al., *Sleep problems in early childhood and early onset of alcohol and other drug use in adolescence.* Alcoholism: Clinical and Experimental Research, 2004. **28**(4): p. 578-587.
29. Wong, M.M., et al., *Childhood sleep problems, response inhibition, and alcohol and drug outcomes in adolescence and young adulthood.* Alcoholism: Clinical and Experimental Research, 2010. **34**(6): p. 1033-1044.
30. Wong, M.M., K.J. Brower, and R.A. Zucker, *Childhood sleep problems, early onset of substance use and behavioral problems in adolescence.* Sleep medicine, 2009. **10**(7): p. 787-796.
31. Wong, M.M., G.C. Robertson, and R.B. Dyson, *Prospective relationship between poor sleep and substance-related problems in a national sample of adolescents.* Alcoholism: Clinical and Experimental Research, 2015. **39**(2): p. 355-362.
32. Fucito, L.M., et al., *Perceptions of heavy-drinking college students about a sleep and alcohol health intervention.* Behavioral sleep medicine, 2015. **13**(5): p. 395-411.
33. Liu, Y., et al., *Prevalence of healthy sleep duration among adults—United States, 2014.* Morbidity and Mortality Weekly Report, 2016. **65**(6): p. 137-141.
34. Irwin, M.R., *Why sleep is important for health: a psychoneuroimmunology perspective.* Annual review of psychology, 2015. **66**: p. 143-172.
35. Worley, S.L., *The extraordinary importance of sleep: the detrimental effects of inadequate sleep on health and public safety drive an explosion of sleep research.* Pharmacy and Therapeutics, 2018. **43**(12): p. 758.
36. Choi, Y.K., et al., *Smartphone applications to support sleep self-management: review and evaluation.* Journal of Clinical Sleep Medicine, 2018. **14**(10): p. 1783-1790.
37. Goldman, D., *Investing in the growing sleep-health economy.* Prevalence, 2016.
38. Campos, M. *Heart rate variability: A new way to track well-being*. 2019 Available from: https://www.health.harvard.edu/blog/heart-rate-variability-new-way-track-well-2017112212789.
39. Beauchaine, T.P. and J.F. Thayer, *Heart rate variability as a transdiagnostic biomarker of psychopathology.* International journal of psychophysiology, 2015. **98**(2): p. 338-350.
40. Thayer, J.F., et al., *A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health.* Neuroscience & Biobehavioral Reviews, 2012. **36**(2): p. 747-756.
41. Buccelletti, E., et al., *Heart rate variability and myocardial infarction: systematic literature review and metanalysis.* Eur Rev Med Pharmacol Sci, 2009. **13**(4): p. 299-307.
42. Young, H.A. and D. Benton, *Heart-rate variability: a biomarker to study the influence of nutrition on physiological and psychological health?* Behavioural pharmacology, 2018. **29**(2-): p. 140.

43. Kemp, A.H. and D.S. Quintana, *The relationship between mental and physical health: insights from the study of heart rate variability.* International Journal of Psychophysiology, 2013. **89**(3): p. 288-296.
44. Ralevski, E., I. Petrakis, and M. Altemus, *Heart rate variability in alcohol use: A review.* Pharmacology Biochemistry and Behavior, 2019. **176**: p. 83-92.
45. Vaschillo, E.G., et al., *Early signs of cardiovascular dysregulation in young adult binge drinkers.* Psychophysiology, 2018. **55**(5): p. e13036.
46. Stein, P.K. and Y. Pu, *Heart rate variability, sleep and sleep disorders.* Sleep medicine reviews, 2012. **16**(1): p. 47-66.
47. Leyro, T.M., J.F. Buckman, and M.E. Bates, *Theoretical implications and clinical support for heart rate variability biofeedback for substance use disorders.* Current opinion in psychology, 2019. **30**: p. 92-97.
48. Ahmed, W., *Podcast No. 43: Alcohol's effect on sleep, recovery and performance*, in *Whoop Podcast*. 2019.
49. de Zambotti, M., et al., *The sleep of the ring: comparison of the ŌURA sleep tracker against polysomnography.* Behavioral sleep medicine, 2019. **17**(2): p. 124-136.
50. Roberts, D.M., et al., *Detecting sleep using heart rate and motion data from multisensor consumer-grade wearables, relative to wrist actigraphy and polysomnography.* Sleep, 2020. **43**(7): p. zsaa045.
51. Portnoy, D.B., et al., *Computer-delivered interventions for health promotion and behavioral risk reduction: a meta-analysis of 75 randomized controlled trials, 1988–2007.* Preventive medicine, 2008. **47**(1): p. 3-16.
52. Stepanski, E.J. and J.K. Wyatt, *Use of sleep hygiene in the treatment of insomnia.* Sleep medicine reviews, 2003. **7**(3): p. 215-225.
53. Friedrich, A. and A.A. Schlarb, *Let's talk about sleep: a systematic review of psychological interventions to improve sleep in college students.* Journal of Sleep Research, 2018. **27**(1): p. 4-22.
54. Chung, K.-F., et al., *Sleep hygiene education as a treatment of insomnia: a systematic review and meta-analysis.* Family practice, 2018. **35**(4): p. 365-375.
55. Prinsloo, G.E., H.L. Rauch, and W.E. Derman, *A brief review and clinical application of heart rate variability biofeedback in sports, exercise, and rehabilitation medicine.* The Physician and sportsmedicine, 2014. **42**(2): p. 88-99.
56. Sobell, L.C., et al., *Comparison of a quick drinking screen with the timeline followback for individuals with alcohol problems.* Journal of studies on alcohol, 2003. **64**(6): p. 858-861.
57. Pilkonis, P.A., et al., *Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger.* Assessment, 2011. **18**(3): p. 263-283.
58. Yu, L., et al., *Development of short forms from the PROMIS™ sleep disturbance and sleep-related impairment item banks.* Behavioral sleep medicine, 2012. **10**(1): p. 6-24.
59. Trockel, M., et al., *An e-mail delivered CBT for sleep-health program for college students: effects on sleep quality and depression symptoms.* Journal of Clinical Sleep Medicine, 2011.
60. Kloss, J.D., et al., *The delivery of behavioral sleep medicine to college students.* Journal of Adolescent Health, 2011. **48**(6): p. 553-561.
61. Castaneda, D., et al., *A review on wearable photoplethysmography sensors and their potential future applications in health care.* International journal of biosensors & bioelectronics, 2018. **4**(4): p. 195.
62. Kinnunen, H., et al., *Feasible assessment of recovery and cardiovascular health: accuracy of nocturnal HR and HRV assessed via ring PPG in comparison to medical grade ECG.* Physiological measurement, 2020. **41**(4): p. 04NT01.
63. Pernice, R., et al., *Comparison of short-term heart rate variability indexes evaluated through electrocardiographic and continuous blood pressure monitoring.* Medical &

biological engineering & computing, 2019. **57**(6): p. 1247-1263.
64. Hernando, D., et al., *Validation of the apple watch for heart rate variability measurements during relax and mental stress in healthy subjects.* Sensors, 2018. **18**(8): p. 2619.
65. Pernice, R., et al. *Reliability of short-term heart rate variability indexes assessed through photoplethysmography*. in *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. 2018. IEEE.
66. Walch, O., et al., *Sleep stage prediction with raw acceleration and photoplethysmography heart rate data derived from a consumer wearable device.* Sleep, 2019. **42**(12): p. zsz180.
67. Fonseca, P., et al., *Validation of photoplethysmography-based sleep staging compared with polysomnography in healthy middle-aged adults.* Sleep, 2017. **40**(7): p. zsx097.
68. De Zambotti, M., et al., *Wearable sleep technology in clinical and research settings.* Medicine and science in sports and exercise, 2019. **51**(7): p. 1538.

69. Sheehan, D.V., et al., *Reliability and Validity of the MINI International Neuropsychiatric Interview (M.I.N.I.): According to the SCID-P.* European Psychiatry, 1997. **12**: p. 232-241.
70. DeMartini, K.S. and K.B. Carey, *Correlates of AUDIT risk status for male and female college students.* Journal of American College Health, 2009. **58**(3): p. 233-239.
71. Sobell, M.B. and L.C. Sobell, *Problem drinkers: Guided self-change treatment*. 1996: The Guilford Press.
72. Monk, T.H., et al., *The Pittsburgh sleep diary.* Journal of sleep research, 1994. **3**(2): p. 111-120.
73. Pilkonis, P.A., et al., *Assessment of self-reported negative affect in the NIH Toolbox.* Psychiatry Research, 2013. **206**(1): p. 88-97.
74. Ortega, F., et al., *Self-reported and measured cardiorespiratory fitness similarly predict cardiovascular disease risk in young adults.* Scandinavian journal of medicine & science in sports, 2013. **23**(6): p. 749-757.
75. Craig, C.L., et al., *International physical activity questionnaire: 12-country reliability and validity.* Medicine & science in sports & exercise, 2003. **35**(8): p. 1381-1395.
76. Anderson, M., *Technology Device Ownership: 2015.* Pew Research Center 2015.

77.. Rounsaville, B.J., K.M. Carroll, and L.S. Onken, *A stage model of behavioral therapies research: Getting started and moving on from stage I.* Clinical Psychology: Science and Practice, 2001. **8**(2): p. 133-142.
78. Collins SE, Witkiewitz K, Larimer ME. The theory of planned behavior as a predictor of growth in risky college drinking. Journal of Studies on Alcohol and Drugs. 2011;72(2):322-32.
79. Azjen I. Constructing a TPB questionnaire: Conceptual and methodological considerations 2002; Retrieved from: http://www.people.umass.edu/aizen/pdf/tpb.measurement.pdf.
80. Zavada A, Gordijn MC, Beersma DG, Daan S, Roenneberg T. Comparison of the Munich Chronotype Questionnaire with the Horne-Ostberg's Morningness-Eveningness Score. Chronobiology International. 2005;22(2):267-78.
81. Kahler CW, Hustad J, Barnett NP, Strong DR, Borsari B. Validation of the 30-day version of the Brief Young Adult Alcohol Consequences Questionnaire for use in longitudinal studies. J Stud Alcohol Drugs. 2008 Jul;69(4):611-5.

82. Thompson, F.E., et al. *Development and evaluation of the National Cancer Institute's Dietary Screener Questionnaire scoring algorithms*. J Nutr. 2017. **147**(6): p.1226-1233.
83. DeMartini, K.S., et al. *Drinking less and drinking smarter: direct and indirect protective*

strategies in young adults. Psychol Addict Behav. 2013. **27**(3): p.615-626.
84. Hamilton, et al. (2011) *The PhenX Toolkit: Get the Most From Your Measures.* American Journal of Epidemiology. **174**(3):p. 253-60.

Appendices

Appendix #	Title	Section	Topic

List of Tables