Randomized Controlled Trial Examining Real-World Effectiveness of a Prescription Digital Therapeutic for the Treatment of Insomnia

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Synopsis

Primary Objective To compare patient-reported outcomes of insomnia collected through Hugo, as well as clinically validated metrics for insomnia among patients randomized to receive the Prescription Digital Therapeutic (PDT) + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization.
Secondary Objective **Secondary Objectives:** (1) To compare real-world healthcare utilization/clinical data collected through Hugo, including number of outpatient visits with primary care physicians, number of outpatient visits with specialty care, and medication refills for sleep or psychotropic medications among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization; (2) compare health utility scores (derived from SF-12) and other patient-reported outcomes among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization; (3) examine the relationship between engagement with PDT and clinical outcomes. **Exploratory Aim:** Among all patients, to compare sleep and physical activity data collected within Hugo to data collected using the Fitbit (Inspire 2) at 9, 21, 35 and 61 weeks post-randomization.
Study Duration 27 Months
Study Design This will be a multi-center, randomized, controlled trial of 100 patients wherein half of the patients with insomnia will receive the PEAR-003b digital therapeutic with linkage to Hugo and Fitbit (Inspire 2) and half of the patients with insomnia will not receive the PDT but will receive a Fitbit and be enrolled in Hugo. The treatment duration will be 9 weeks. All patients will be evaluated at baseline, as well as prompted to complete additional assessments at weeks 9, 21, 35, and 61 post-randomization. The PEAR-003b intervention will deliver CBT-I via mobile devices as 6 treatment core modules over 9 weeks. Additionally, we will use the Hugo platform to collect patient-generated engagement data, healthcare utilization data, and patient activity/clinical outcomes.
Number of Study Sites 2
Study Population We will enroll 100 patients age between 22-64 who have been diagnosed with insomnia (50 patients will be recruited at Yale New Haven Hospital (YNHH), and 50 patients will be recruited at the Mayo

Clinic). We do not have any gender, demographic, or general health status targets; we expect to enroll the distribution of patients who receive treatment at the sleep clinic across these two systems.
Number of Participants 50 patients will be recruited at YNHH.
Primary Outcome Variables Change in the Insomnia Severity Index (ISI) Score.
Secondary and Exploratory Outcome Variables Change in: Epworth Sleepiness Score (ESS); Patient Health Questionnaire (PHQ-8); ISI, Perceived Stress Scale (PSS-10); Short-form 12 (SF-12); General Anxiety Disorder-7 scale (GAD-7); sleep outcomes, healthcare utilization outcomes, health utility scores (derived from SF-12), and relationship between engagement with PDT and clinical outcomes.

Abbreviations

Abbreviation	Explanation
CBT-I	**Cognitive-behavioral**
ESS	**Epworth Sleepiness Scale**
GAD-7	**General Anxiety Disorder-7 scale**
ISI	**Insomnia Severity Index**
PDT	**Prescription Digital Therapeutic**
PHQ-8	**Patient Health Questionnaire- 8**
PSS-10	**Perceived Stress Scale-10**
SF-12	**Short-form 12**

Glossary of Terms

Glossary	Explanation
CBT-I	**Cognitive-behavioral therapy for insomnia (CBT-I) can effectively treat chronic insomnia**
Pear-003b	**Pear-003b is the PDT for insomnia that will be administered to those randomized to the treatment arm.**

Table of Contents

1 Introduction

1.1 Introductory Statement

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 ICH GCP guidelines, and according to CFR 21 Part 812, other applicable government regulations, and Institutional research policies and procedures.

2 Background

2.1.1 Device Preclinical Experience

N/A

2.1.2 Device Clinical Experience

In March 2020, the FDA granted authorization for PEAR-003b in treatment of patients with chronic insomnia. PEAR-003b was the first product submitted through FDA's 501(k) pathway while simultaneously reviewed as part of FDA's Software Precertification Pilot Program to help build and test FDA's Digital Health Precertification Working Model 1.0.[1] Similar consumer digital technologies and software applications are growing in use and are increasingly brought to FDA for authorization for treatment.

The PEAR-003b digital therapeutic will be delivered via mobile devices to patients with insomnia as 6 core CBT-I modules over 9 weeks,[2-4] based on the features and functionality originally tested in the SHUTi web-based program.[5] We will also enroll patients in the Hugo platform to understand patient experience with insomnia by aggregating patients' EHR data, survey data on patient-reported outcomes, healthcare utilization metrics, and patient activity and sleep recorded via Fitbit.

2.2 Background/prevalence of research topic

Insomnia is one of the most prevalent health concerns and imposes a significant physical, psychological, and financial burden on patients' lives.[6] Up to 50% of the general adult population experience insomnia symptoms, with 12-20% meeting criteria for chronic insomnia.[7,8] Adults suffering from insomnia also have a higher likelihood of comorbid conditions such as depression, resulting in a reduced quality-of-life and higher rates of morbidity and mortality.[9] The documented high rates and detrimental effects of insomnia and co-occurring disorders, provide a compelling rationale for identifying effective, accessible, easy-to-use, and cost-effective treatments.

There is empirical evidence indicating that cognitive-behavioral therapy for insomnia (CBT-I) can effectively treat chronic insomnia,[10-16] with long-lasting benefits. CBT-I is now recommended as first-line therapy for insomnia.[15] However, due to challenges associated with in-person CBT-I (e.g. lack of trained clinicians and expense, poor access, and limited fidelity),[17] attention has turned towards use of technology to overcome obstacles and deliver CBT-I interventions (e.g., Sleep Healthy Using the Internet: SHUTi).[2,3,5] Despite promising clinical efficacy in randomized controlled trials (RCTs),[18] these studies have been unable to rigorously assess impact of the digital therapeutic on patient experience.

The goal of this study is to conduct a multi-center RCT to collect and evaluate real-world data from a mobile CBT-I prescription digital therapeutic (PEAR-003b) and a patient-centered data

sharing platform (Hugo). This approach will allow concurrent analysis of clinical outcomes data, healthcare utilization data, and data from connected devices. The data generated will be used alongside clinically-validated measures of insomnia to yield a multidimensional analysis of patient benefit.

3 Rationale/Significance

3.1 Problem Statement

There is empirical evidence indicating that CBT-I can effectively treat chronic insomnia.[10-16] However, due to challenges associated with in-person CBT-I such as lack of trained clinicians and expense, poor access, and limited fidelity,[17] attention has turned towards use of technology to overcome obstacles and deliver CBT-I interventions. Despite promising clinical efficacy in randomized controlled trials (RCTs),[18] these studies have been unable to rigorously assess impact of the digital therapeutic on patient experience.

3.2 Purpose of Study/Potential Impact

Significance:

Specific Aim 1 aims to enroll patients into the Hugo data sharing platform to collect patient-reported outcome measures (PROMs) of insomnia, as well as clinically validated metrics for insomnia (all modified to a mobile-friendly format). Patient self-reported data collected via Hugo will include insomnia severity using the self-reported insomnia severity index (ISI) scale.[19] This measure will be used to track sleep improvement progress over the 63-week study period. We will also collect data on depression (using the Patient Health Questionnaire [PHQ-8]),[20]daytime sleepiness (measured using the Epworth sleepiness scale [ESS]),[21] stress (measured using the perceived stress scale [PSS-10]),[22] health-related quality of life (measured using the Short-form 12 [SF-12])[23] and anxiety (measured using the general anxiety disorder-7 scale [GAD-7]).[24]

Specific Aim 2 addresses the outstanding question of whether a novel PDT (i.e., PEAR-003b) can use the Hugo platform to feasibly collect real-world healthcare utilization data from the YNHH or Mayo Clinic EHR and show trends for changes in healthcare utilization and healthy utility scores among the PDT cohort as well as the relationship between engagement with PDT and clinical outcomes. EHR data collected via the Hugo platform will include emergency department encounters, medications, inpatient visits, and outpatient visits.

We will also ask patients to link their health system data from anywhere they received care to their Hugo account. This will allow us to collect information from outside healthcare providers (i.e. if patients received care outside of YNHH or the Mayo Clinic related to their insomnia). Lastly, exploratory Aim 1 will address the feasibility of linking Fitbit (Inspire 2) to the Hugo platform in order to evaluate patient activity data including heart rate, tracking steps per day and/or exercise, sleep (total sleep time in minutes), and self-reported metrics such as weight, height and BMI.

Potential Impact:

Results from this study will advance our understanding of: (1) how novel ways of collecting and aggregating clinical and patient-reported outcomes data can support informed clinical decision-making (2) digital therapeutic engagement and its relationship to clinical outcomes; and (3)

evaluation of data from linked devices by providing novel information on a digital therapeutic for insomnia, connected with the Hugo platform. The outcome of this research will provide crucial data to inform the latest thinking about how data from both digital therapeutics and EHR systems can be utilized to evaluate real-world clinical and utilization outcomes. These data will be used to demonstrate the value of implementing technology within healthcare systems, supporting broad uptake of similar technology platforms. In addition, they will inform reimbursement discussions with payers to support coverage of and broad access to effective digital therapeutics.

3.2.1 Potential Risks

In following some intervention recommendations, participants may be asked to restrict sleep at certain times, which could lead them to initially feel more tired. This could potentially exacerbate the fatigue or sleepiness that many participants may already be experiencing. The therapeutic will direct patients to discontinue sleep restriction if they feel excessively tired.

The risk to patient privacy is no different with this study than it is with any other study that securely collects and appropriately stores personally identifiable information or protected health information. Indeed, the risk may be less since researchers are only getting access to patient data from the time of enrollment forward for 63 weeks for this study; there is no open access to the patient's entire medical record. The Hugo platform, like many other personal health records, is not a covered entity; therefore, the HIPAA privacy rule does not apply to this platform. The Hugo platform does take all necessary precautions, including industry-standard encryption, to minimize privacy and security risks to personally identifiable information stored on behalf of study participants. Hugo makes publicly available its Security Statement (http://hugophr.com/security), its Privacy Notice (http://hugophr.com/privacy-notice), and Terms of Service (http://hugophr.com/terms-of-service/)

Participants will undergo the possible inconvenience of filling out electronic patient-reported outcome measure surveys, which can take up to 60 minutes at each time point (at baseline, 9, 21, 35, and 61 weeks post-randomization). Additionally, some participants may feel uncomfortable providing data over the phone and have concerns about the confidentiality of their digital data. They may also have concerns about the legitimacy of a digital therapeutic. Patients will be provided the sleep clinic contact information in case they feel they need to seek support at enrollment in addition to at the completion of each PHQ-8 questionnaire. The PHQ-8 is a validated measure for depression that was modified from the original PHQ-9 to not include a question about suicidality and has been used in prior studies.[25-27]

Participants may also experience the possible inconvenience of wearing a Fitbit for extended periods of time and syncing these devices with the Hugo platform. Although the Fitbit has been deemed a 'Low-Risk Device' by the FDA[28] and is therefore not deemed medical grade,[29] there is the risk of inaccuracy in Heart Rate or sleep measurements. According to the Fitbit terms of

service, found at www.fitbit.com/legal/terms-of-service, “The accuracy of the data collected and presented through the Fitbit Service is not intended to match that of medical devices or scientific measurement devices.”

3.2.2 Potential Benefits

Knowledge gained from this study may improve outcomes for patients who suffer from insomnia. Also, through the Hugo platform, patients will have easy access to their medical records. Wearing a Fitbit may also give patients additional useful information regarding their health and fitness.

4 Study Objectives

4.1 Hypothesis

A PDT delivering remote based CBT for insomnia will improve patient reported outcomes, healthcare utilization/clinical outcomes, health utility scores, and sleep/physical activity for individuals with insomnia.

4.2 Primary Objective

The primary objective of this study is to compare patient-reported outcomes of insomnia (ISI), collected through Hugo, as well as clinically validated metrics for insomnia, among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization.

4.3 Secondary Objectives (if applicable)

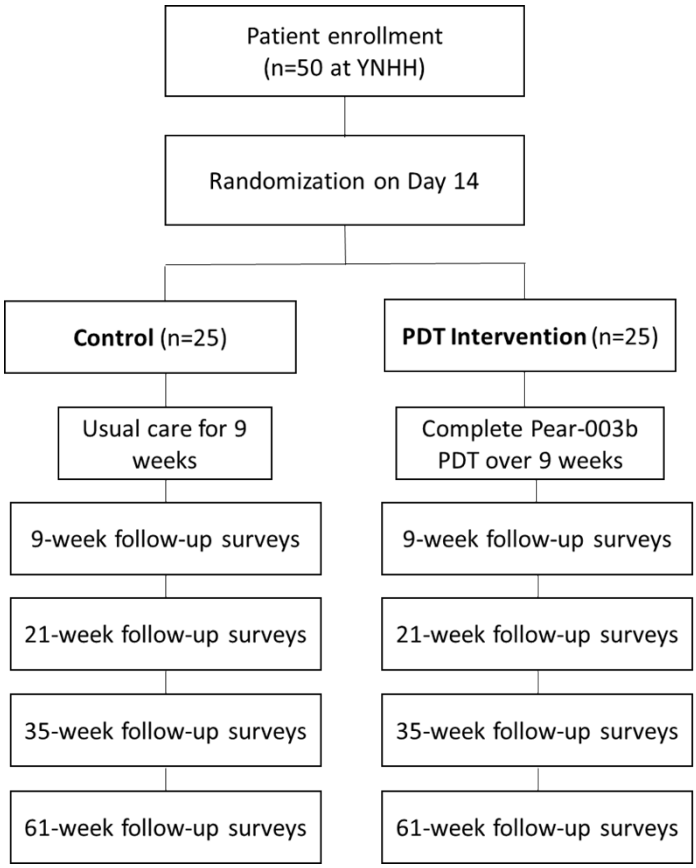
The secondary objectives of this study are to: (1) compare real-world healthcare utilization/clinical data, collected through Hugo, including number of outpatient visits with primary care physicians, number of outpatient visits with specialty care, and medication refills for sleep or psychotropic medications among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization; (2) compare health utility scores and other patient-reported outcome measures among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization; (3) examine the relationship between engagement with PDT and clinical outcomes.

The exploratory aim of this study is to compare sleep and physical activity data collected within Hugo to data collected using the Fitbit (Inspire 2) at 9, 21, 35 and 61 weeks post-randomization, among all patients.

5 Study Design

5.1 General Design Description

This will be a Phase 2 multi-center, randomized, controlled trial (2 group X 5 assessment design) whereby half of the patients with insomnia will receive the PEAR-003b digital therapeutic with linkage to Fitbit and half of the patients with insomnia will not receive the PDT, however will receive linkage to Fitbit (100 patients total: 50 at each site). The treatment duration will be 9 weeks and there will be a 21-, 35-, and 61-week follow-up. All patients will be evaluated at baseline, as well as prompted to complete additional assessments at weeks 9, 21, 35, and 61 weeks post randomization. The PEAR-003b intervention will deliver CBT-I via mobile devices as 6 treatment core modules over 9 weeks. Using the Hugo platform, we will also collect patient-generated engagement data, healthcare utilization, and patient activity/clinical outcomes for patients with insomnia.



5.1.1 Study Date Range and Duration

This project is expected to be completed no later than October 2022 with enrollment beginning in April 2021. Recruitment for patients is expected to take 14 weeks in each healthcare setting (i.e. YNHH and the Mayo Clinic) based on current patient volume, with follow up of each patient at 61 weeks post-randomization. As batches of patients complete the 21- and 61-week follow up

duration, we will begin to clean, review and verify the data as they are received from the Hugo platform on a rolling basis.

5.1.2 Number of Study Sites

Two

5.2 Outcome Variables

5.2.1 Primary Outcome Variables

The primary outcomes are a change in the ISI score from baseline to 9-weeks post randomization.

5.2.2 Secondary and Exploratory Outcome Variables (if applicable)

Secondary Outcomes (ascertained at baseline, 9-weeks, 21-weeks, 35-weeks, and 61-weeks post-randomization):

- Healthcare utilization outcomes reported in Hugo including number of outpatient visits and specialty care visits, number of medication refills for sleep and psychotropic medications), comparing PDT to control at all follow-up time points.
- Change from baseline to 21-, 35-, and 61-weeks in the ISI, comparing PDT to control.
- Change from baseline to 9-, 21-, 35-, and 61-weeks post-randomization in individual patient-reported outcomes including depressive symptoms (PHQ-8),[20] daytime sleepiness (ESS),[21] health status (SF-12),[23] stress (PSS-10)[22], and anxiety (GAD-7),[24] comparing PDT to control.
- Change in sleep outcomes collected through sleep diaries (sleep efficiency (SE), sleep onset latency (SOL) (minutes), waking after sleep onset (WASO) (minutes), number of awakenings, sleep quality (scale score), time in bed, and total sleep time), from baseline to 9-, 21-, 35-, and 61-weeks post-randomization comparing PDT to control.
- Change in (and total) health utility scores using the SF-12 among patients randomized to receive PDT + Fitbit vs. Fitbit only at 9, 21, 35, and 61 weeks post-randomization
- Examine the relationship between engagement with PDT and clinical outcomes, particularly the sleep specific outcomes (ISI and diary-derived sleep metrics).

Definition of sleep outcomes:

- ***Sleep efficiency*** **(SE):** The ratio of total sleep time (TST) to time in bed (TIB).
- **Sleep onset latency (SOL):** The length of time that it takes to accomplish the transition from full wakefulness to sleep, normally to the lightest of the non-REM sleep stages.
- **Sleep quality:** One's satisfaction of the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening.
- **Waking after sleep onset (WASO):** Periods of wakefulness occurring after defined sleep onset.

Exploratory Outcomes (ascertained at 9-weeks 21-weeks, 35-weeks, and 61-weeks post-randomization):

- Physical and sleep activity measured using Fitbit (steps per day, sleep [total sleep time in minutes], and self-reported metrics such as weight, height, and BMI) from baseline to 9-, 21-, 35-, and 61-weeks post randomization comparing PDT to control.

5.3 Study Population

Participants who have been diagnosed with insomnia between the ages of 22-64 years will be enrolled in this study.

We will recruit 50 participants from YNHH, which represents a geographic and racial diversity of populations as well as diversity of patients attending sleep clinics in the US. YNHH is the largest and most comprehensive healthcare system in Connecticut (1,541-bed tertiary care hospital with 12,000 employees). Last year YNHH treated over 70,000 inpatients and more than 800,000 outpatient visits. The medical staff exceeds 3,500, and it serves as the primary teaching hospital for the Yale School of Medicine. Women and minorities are strongly represented in the population. More specifically, the gender racial mix is approximately 51% women; 50% White, not of Hispanic Origin; 33% Black, not of Hispanic Origin, 15% Hispanic; 1% Asian and 1% other. Approximately 42% of patients have private insurance, 29% have Medicare, 27% are covered by Medicaid or other public assistance, and 2% are uninsured.

Patients from YNHH will be recruited from the Yale Sleep Center. This center opened in 1997 and became accredited by the American Academy of Sleep Medicine (AASM) the same year. The Yale Sleep Center is renowned nationally and internationally for its excellence in clinical care and research. It is a multidisciplinary center with active participation of faculty from various departments in clinical, research and educational missions of the Center. The Yale Sleep Center has performed over 11,078 polysomnographies and numerous Multiple Sleep Latency Tests (MSLT). The Yale Sleep Center has become a major referral center in Connecticut, performing about 200 polysomnographies and 4 MSLTs each month. The Center is comprised of three fully American Academy of Sleep Medicine (AASM) accredited centers with a total of 15 monitored bed units. The Center receives referrals from all Connecticut counties as well as northeast states. The YNHH Sleep Medicine program offers comprehensive diagnostic testing and treatment services for those who are unable to get a restful night sleep. As an interdisciplinary program, clinicians work closely with a network of specialty providers who are board-certified in bariatric surgery, cardiology, dentistry, neurology, otolaryngology and psychology. The program is accredited by the AASM.

Patients from Mayo Clinic will be recruited from the Mayo Center for Sleep Medicine. This center opened in 1983 and became accredited by the AASM in 1985. The Mayo Center for Sleep Medicine is renowned nationally and internationally for its excellence in clinical care and research. It is a multidisciplinary center with active participation of faculty from various departments in clinical, research and educational missions of the Center. The Mayo Center for Sleep Medicine has performed over 120,000 polysomnograms (PSG), Multiple Sleep Latency Tests (MSLT), Maintenance of Wakefulness tests (MWT), and Home Sleep Apnea Tests (HSAT). The Mayo Center for Sleep Medicine has become a major national and international referral center performing about 330 PSGs, 100 HSATs and 15 MSLTs and MWTs each month. The Center is accredited by the American Academy of Sleep Medicine (AASM) and operates 24 monitored

beds. The Center receives referrals primarily from Minnesota, Wisconsin, Iowa, Illinois, and North and South Dakota with a significant volume of national and international referrals.

5.3.1 Number of Participants

We will enroll 50 patients at YNHH and 50 patients at the Mayo Clinic (100 total). Approximatly 350 patients are anticipated to be screened at Yale.

5.3.2 Eligibility Criteria/Vulnerable Populations

Inclusion Criteria:

- Age between 22-64 years
- English-speaking (both reading and writing in English required)
- Diagnosis of chronic insomnia
- Participant is willing and able to give consent and participate in study
- Participant has an email account or is willing to create one and a smartphone able to download the necessary applications
- Participant is willing and able to use the PDT, the Hugo data sharing platform and the syncable devices (e.g. Fitbit)
- Participant has primary care at YNHH or Mayo Clinic

Exclusion Criteria:

- Pregnancy
- Shift work or family/other commitments that interfere with establishment of regular night-time sleep patterns, and if wake/sleep time is outside the ranges of 4:00h – 10:00h (wake time) and 20:00h – 02:00h (bed time)
- Absence of a reliable internet access and smartphone
- A reported diagnosis of psychosis, schizophrenia or bipolar disorder, or any medical disorders contraindicated with sleep restriction
- Current involvement in a **non-medication** treatment program for insomnia (participants are still eligible if they are taking traditional sleep medications)
- Those with untreated co-existing sleep conditions (e.g. sleep apnea)
- Those who have failed CBT for insomnia in the past

6 Methods

6.1 Treatment – Device

6.1.1 Intended Use for Device (provide the following information for each device being investigated in the study)

The PDT being studied in this protocol was authorized by the FDA under the name Somryst. The PDT has not been modified from its usual commercial state for this study. Somryst is intended to improve insomnia symptoms by providing neurobehavioral intervention (cognitive behavioral therapy for insomnia – CBT-I) to adults 22 years of age and older with chronic insomnia. This study will evaluate outcomes in adults age 22-64 who have chronic insomnia.

6.1.2 Device Administration and Schedule

Patients will be consented and enrolled in person on the enrollment date where they will complete their baseline surveys. Over the following 14 days, patients will complete their baseline sleep diaries. Patients randomized to the PDT will be contacted by the Research Associate (RA) and provided information on how to install the app to their mobile devices and receive a unique access code for the PDT.

6.1.3 Method of Assignment/Randomization (if applicable)

Patients will be randomized 1:1 to the digital therapeutic or the control arm by the RA using a randomization algorithm via Hugo. Patients will be notified if they are randomized to the treatment arm on day 14 by the RA and will be provided with instruction on how to set up and create their Pear-003b account if randomized to the Pear-003b arm. The study will not employ blinding as patients will need to know if they are completing the treatment

6.1.4 Device Calibration

N/A

6.1.5 Storage Conditions

N/A

6.1.6 Concomitant therapy

Participants are eligible for this study if they are taking traditional sleep medications (e.g. Temazepam, Triazolam, Zaleplon and Zolpidem). Concomitant non-medication treatment programs for insomnia are not allowed during the study. However, non-medication treatments, such as psychotherapy, are allowed for conditions not contraindicated with sleep restriction. (as mentioned in section 5.3.2).

6.1.7 Restrictions

There are no restrictions.

6.2 Assessments

6.2.1 Efficacy

The sleep outcomes identified in this study (Insomnia Severity Index and sleep diary-derived metrics of SOL and WASO) are considered together when evaluating efficacy of the PDT. These measures are part of recent guidelines from the American Academy of Sleep Medicine[30,31] as outcomes to be considered in evaluation of efficacy and clinical significance.

6.2.2 Safety

N/A. This study has been deemed minimal risk because the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests and will therefore not be required to be reviewed by a data safety monitoring committee. Information about the minimal risks for this study can be found in Section 3.2.1.

If the study team learns that a participant has clinical depression during screening, or identifies a participant as having clinical depression during the study, the participant will be instructed to schedule an appoint with their primary care clinician; if the participant does not have a primary care clinician, the study team will offer to help the participant schedule an appointment with a primary care clinician at the New Haven Primary Care Consortium (NHPCC).

6.2.3 Adverse Events Definition and Reporting

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, they will be reported immediately, followed by a written report within 5 calendar days of the PIs becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigators will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project via email as they are reviewed by the PIs. The protocol's research monitor(s), e.g. study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies, will be informed of a data breach within 5 days of the event becoming known to the PI.

6.2.4 Pharmacokinetics (if applicable)

N/A

6.2.5 Biomarkers (if applicable)

N/A

6.3 Study Procedures

6.3.1 Study Schedule

Timeline	Event
Enrollment Visit	Informed Consent Hugo and Fitbit account setup Baseline Surveys
Enrollment to 13 days post enrollment	Complete Sleep diaries (at home)
Day 14 post enrollment (+3 days)	Patient randomization Register treatment arm patients onto the PDT
9-weeks post randomization	Follow-up survey
21-weeks post randomization	Follow-up survey
35-weeks post randomization	Follow-up survey
61-weeks post randomization	Follow-up survey Closeout survey

6.3.2 Informed Consent

Please see attached informed consent in IRB submission

6.3.3 Screening

Patients will be identified by the sleep clinic coordinator and/or the sleep physician after their initial consult. Eligible patients must be aged between 22-64 years, English speaking, and have a diagnosis of chronic insomnia (see inclusion/exclusion criteria above in section 5.3.2). If they are interested clinic staff will notify the RA. Additionally, the patient will be provided with the study team's contact information if they wish to follow up. Eligibility will be determined by the sleep physician or coordinator stating that the patient is being seen for insomnia. The RAs will approach the patient for consent into the study while they are waiting for their sleep consult appointment/referral to see the sleep specialist. The wait time between enrollment and follow

up with sleep specialist is up to 12 weeks; therefore, this is a prime opportunity for patient enrollment and completion of this project.

The RA will also reach out to patients on the waitlist for in-person CBT-I upon the sleep clinician's approval. If the patient is interested in the study, the RA will attempt to arrange an in-person visit to conduct the consent and enrollment process. If an in-person visit is not possible, the RA will arrange a time for a Zoom call with the patient.

Additionally, a flyer will be circulated to the Sleep Clinic staff to provide to any patients who may express interest in the study (Appendix 7).

6.3.4 Enrollment

Patients with insomnia will be seen initially by a sleep coordinator or sleep physician at the Sleep Center. If deemed eligible for the study, the sleep coordinator or sleep physician will contact the Research Associate (RA) about the potential participant. If the RA is present in clinic, they will introduce themselves to the patient and provide additional information about the study. Should a clinician identify an eligible patient at a time when the RA is not present, the clinician will inform the patient about the study and ask if the patient would be willing to be contacted by the RA. If so, the clinician will email the RA, who will then contact the patient via phone and ask if they would like to participate in the study. If yes, the RA will attempt to arrange an in-person visit to conduct the consent and enrollment process. If an in-person visit is not possible, the RA will arrange a time for a Zoom call with the patient to complete all steps of consent and enrollment (minus the Fitbit set-up) via Zoom. The coordinator will then mail the Fitbit to the patient for arrival within 7 days.

Upon enrollment, patients will be asked to sign an electronic consent and link their electronic health records and share them with the research team. Patients will need to have their smartphone and any relevant phone account passwords at the time of enrollment. As part of the consent process, the RA will advise patients that they should contact their doctor or emergency services directly if they begin having new or worrying symptoms, exactly as the patient would have done so if they were not enrolled in our study.

Upon consent into the study, the patients will receive a Fitbit. For both arms of the study, Hugo will be used as a data collection platform as it aggregates data from multiple real-world data sources, thereby enabling the assessment of patient-reported outcomes, clinical outcomes, and healthcare utilization metrics. All participants will receive materials on sleep hygiene and healthy sleep tips. These sleep hygiene recommendations and healthy sleeping tips include behavioral information regarding getting a good night's sleep (e.g. setting a regular bed-time, getting out of bed if remaining awake, exercising regularly, not smoking). A full list of these tips can be found in **Appendix 1**. Patients will also receive a informational wallet card with study contact information (Appendix 8). Participants randomized to PEAR-003b will receive access to the therapeutic for 9

weeks a in addition to the sleep hygiene material. Post assessment data will be collected post intervention via diaries and questionnaires as outlined in the "Follow-up" section.

Because the Hugo platform obtains patient data through patient portals, all patients who connect will need a YNHH MyChart account. If the patient does not yet have a MyChart account, the RA will assist the patient in creating one. The RA will then assist the patient in linking their YNHH electronic health records to the Hugo platform as well as other health systems where they have received care by showing the study participant how to enter their patient portal credentials, provided that these health systems are connected to the Hugo platform.

Upon enrollment and following syncing of the Hugo and Fitbit devices (with assistance from the RA), patients in both study arms will complete a baseline assessment that will include questionnaires as well as 10 days of sleep diaries within a 14-day window. Questionnaires will relate to insomnia severity (ISI),[19] depression (PHQ-8)[20], daytime sleepiness (ESS)[21], stress (PSS-10)[22], health-related quality of life (SF-12)[23] and anxiety (GAD-7).[24] Please see **Appendix 2** for original paper versions of questionnaires. These PROMs will also be administered using the Hugo platform at 9-, 21-, 35-, and 61- weeks post-randomization. The RA will also ask patients to obtain credentials, if necessary, and connect portals to health systems where they receive care that are connected to Hugo but were unable to connect at enrollment. Patients will also receive a follow-up email from the RA that includes user guides for the Fitbit Inspire 2 **(see Appendix 3)**. After the 14-day window, the patients will be randomized. Patients randomized to PEAR-003b will be contacted by the RA and will be guided through installing and initiating the CBT-I app.

The RA will collect the following data at enrollment:

- Number of people asked for study participation and number enrolled.
- Number of study participants who required assistance setting up YNHH portal.
- Number who had YNHH portal who could not be enrolled (e.g. because they had forgotten password, no space on mobile device, technical glitch, etc.).

If a patient refuses to participate, then we will note the number of people who refused. If the patient is agreeable, we will then administer a short questionnaire to understand their rationale for not participating in the study, to understand potential reasons for non-participation. We will also ask these people who chose not to participate about basic demographics, if they are willing to answer (age, sex, race/ethnicity, major co-morbidities, insurance status). Please see **Appendix 4** for questionnaire.

6.3.5 On Study Visits

All patients will be asked to use the Hugo platform and Fitbit wearable for the entire 63-week period. Those randomized to PEAR-003b will be asked to complete the 6 core modules in 9 weeks, and at completion will be asked to fill out a questionnaire via Hugo to determine their satisfaction with the process of answering queries and will provide the opportunity for them to offer comments and suggestions for improvement. Patients will be asked to charge their Fitbit for the minimum necessary time during the day and try to wear it for as much time as possible. We will cycle patient reminders about charging the Fitbit for continuous study use based on the anticipated battery life of the Fitbit wearable. Based on our prior experience conducting both SHUTi and Hugo projects, we anticipate being able to stream electronic health record and patient-generated data from the Fitbit into our researcher database using the Hugo platform. The enrollment visit is the only time patients will need to come in for an in-person visit. All subsequent visits will be completed at home. For all patient-reported outcome measures, we will query patients regarding whether they prefer a secure email link or text message link to receive questionnaires at baseline, 9, 21, 35, and 61 weeks. If patients do not respond to this prompt within 24 hours, they will receive an email reminder. Should there be still be no response after an additional 48 hours, the RA will follow up with the patient via phone to ask the patient to complete the unanswered survey.

Patients will be contacted by the RA via phone at 35 and 61 weeks to ascertain any new health systems in which they sought care and the Hugo platform will be checked to ensure that data from those health systems are included (and patients will be asked to link those health systems or provide data, as appropriate). Multiple attempts will be made to contact patients if they are not contacted on the first attempt. Patients will receive automatic reminders to complete questionnaires at 9, 21, 35, and 61 weeks post-randomization via email. Similarly, patients will receive automatic reminders to sync their Fitbit at these time points.

- **Enrollment Visit (in-person) [~3 hours total]:**
    - Informed Consent/study enrollment
    - Fitbit setup
    - Hugo account setup
    - Baseline Surveys: Baseline Questionnaire; ISI; PHQ-8; GAD-7; ESS; PSS-10; SF-12
    - Begin sleep diaries
- **Day 15 post-enrollment**
    - Patients are randomized by RA
    - Patients randomized to the PDT arm will be contacted by the RA and instructed on how to download and sign-up for Pear-003b.
- **Randomization through 9-week post-randomization**
    - Intervention Arm: Complete the Pear-003b PDT
    - Control Arm: Standard of Care
- **9-weeks post-randomization [~3 hours total]**

- Complete follow-up surveys: ISI; PHQ-8; GAD-7; ESS; PSS-10; SF-12
- Begin sleep diaries

- **21-weeks post-randomization [~3 hours total]**
  - Complete follow-up surveys: ISI; PHQ-8; GAD-7; ESS; PSS-10; SF-12
  - Begin sleep diaries
- **35-weeks post-randomization [~3 hours total]**
  - Complete follow-up surveys: ISI; PHQ-8; GAD-7; ESS; PSS-10; SF-12
  - Begin sleep diaries
- **61-weeks post-randomization [~3 hours total]**
  - Complete follow-up surveys: ISI; PHQ-8; GAD-7; ESS; PSS-10; SF-12
  - Begin final sleep diaries
  - Complete close-out questionnaire

6.3.6 End of Study and Follow-up

After the end of the study (i.e. at 61 weeks post-randomization), study participants will be asked to complete a close-out questionnaire via Hugo **(see Appendix 5)**. They will also be asked at what health systems or clinicians from whom they received care over the past 61 weeks (including hospitalization, emergency department visit), to assess if all pertinent data were captured in the Hugo platform.

6.3.7 Removal of subjects

Discontinuation of the study intervention will be limited to voluntary patient discontinuation. Patient data will be monitored to watch for gaps in the device data of greater than 7 consecutive days, missed survey responses, as well as portal connection issues. Should an issue be noted, study staff will try to contact patients.

6.4 Statistical Method

6.4.1 Statistical Design

All analyses of results from this RCT will be conducted as intent-to-treat (ITT) to avoid the effects of crossover and dropout.[32] We will report baseline descriptive statistics for the overall study, by site, and for both the control and treatment arms of the study. These will include patient age, sex, race, ethnicity and all co-morbidities, medical history and clinical characteristics. Baseline data will be compared using Pearson Chi Squared tests or Fisher exact test for dichotomous and/or categorical variables and student's t-tests for continuous variables. If variables are deemed as non-parametric, we will use a median test such as a Mann–Whitney *U*-test, where appropriate.

6.4.2 Sample Size Considerations

Analyses solving for minimum detectable effect sizes with 80% power were conducted with PASS software for only the primary outcomes (PASS 15).[33] Because the models assume that each outcome is normally distributed, the outcome effects represent the average amount each outcome is expected to change with incremental shift in any explanatory variable. We will recruit a total of 100 participants and will randomly assign them to treatment and control arms based on a 50% probability of assignment. We also assume a 10% rate of drop-out between baseline and the end of follow-up, resulting in an effective sample size of N=80. Assuming a two-sided alpha threshold of 0.05, for the main outcome (change in ISI from baseline to 9-weeks post-randomization),[34] and a power of 90% this sample size will allow us to detect an effect size of d=0.52 which is ½ to 1/3 of what we have seen previously. Because this effect size is smaller than the levels demonstrated in randomized controlled trials, we are adequately powered to detect changes of interest in the main ISI outcome. We further note that this calculation is conservative because analysis may optionally draw from outcome values recorded at baseline and each follow-up time.

6.4.3 Planned Analysis

6.4.3.1 Primary Analyses

For the primary endpoint analysis, we will use a *t* test to compare the ISI scores[19] for the intervention (PDT + Fitbit) and control group (Fitbit only) at baseline (as this score is a continuous variable). We will then use a 2 (group) × 2 (time) repeated measures analysis of variance (RM ANOVAs) to compare pre to post changes from baseline to 9-weeks across groups.[2,4] Paired sample *t* tests by group will be used to examine time effects within each condition (if the overall interaction effect is significant). At weeks 21, 35, and 61 post randomization we will also perform the same analysis, but this will be as an exploratory secondary endpoint. If a patient drops out, we will carry forward the most recent patient-reported outcome measure response. As this is an RCT, we expect that confounding will be minimal. If patients are missing outcome data, we will use the last observation carried forward for the patient-reported outcome. Missing covariates will be set to missing.

6.4.3.2 Secondary Objectives Analyses

For the secondary endpoint analysis regarding the patient reported outcomes, we will calculate the change in the PHQ-8,[20] ESS,[21] SF-12,[23] PSS-10[22] and the GAD-7[7] scores at baseline and at 9-weeks, 21-weeks, 35-weeks and 61-weeks post randomization (as these are continuous variables) and perform a comparison between patients randomized to the intervention (PDT + Fitbit) and patients randomized to the control (Fitbit only). Based on our prior work using SHUTi,[34] we will examine the change in scores between groups using a mixed model repeated measures ANOVA [35]with an unstructured matrix, and estimated degrees of freedom (df) with Satterthwaite's correction. We will present df alongside F-test statistics and t statistics.

For the secondary clinical/healthcare utilization outcomes we will compare the PDT to the control at all follow-up time points. These outcomes will be defined as: (a) number of outpatient visits per patient with primary care physicians, (b) number of outpatient visits per patient with specialty care, (c) number of medication refills for sleep per patient, and (d) number of medication refills for psychotropic medications per patient. These comparisons will be examined using *t* tests at each time point (as these will be continuous variables).

For the sleep outcomes,[2] we will calculate the change in each sleep outcome from baseline to 9-weeks, 21-weeks, 35-weeks, and 61-weeks post randomization comparing PDT to the control based on sleep diaries. These outcomes will be defined as: (a) sleep efficiency; (2) sleep onset latency [SOL], (3) number of awakenings, (4) sleep quality, and (5) total sleep time (minutes) (6) waking after sleep onset [WASO], (7) time in bed. We will examine the change in scores between groups using a mixed model repeated measures ANOVA.[35] Paired-sample *t* tests will be used to examine time effects within each condition if the overall interaction effect is significant.

For the secondary health utilities outcome, we will calculate the change in health utilities scores from baseline to 9-weeks, 21-weeks, 35-weeks and 61-weeks post randomization (as these are continuous variables) and perform a comparison between patients randomized to the intervention (PDT + Fitbit) and patients randomized to the control (Fitbit only). Health utilities scores are derived from the SF-6D algorithm as applied to the SF-12 data[36].

For the secondary engagement outcome, we will examine the relationship between engagement with PDT and clinical outcomes in the PDT arm at all follow up time points. Correlations between engagement and clinical outcomes will be evaluated using both Pearson's correlation coefficient and Spearman's rank correlation as follows. Change from baseline (Follow up – baseline) will be calculated for ISI, sleep diary-derived metrics of SOL and WASO, and PHQ-8, at both the end of treatment and the end of all follow-ups. These will be correlated with core completion rates, sleep diary completion rate, and the number of times the PDT is opened. In addition, clinical outcomes among those who complete all six cores of treatment will also be examined.

Lastly, the exploratory physical and sleep activity outcomes (measured using Fitbit) will again be compared from baseline to 9-weeks, 21-weeks, 35-weeks, and 61-weeks comparing PDT to control. These outcomes will be defined as: (a) number of steps per day; (b) sleep [total sleep time in minutes], and (c) self-reported metrics such as weight, height, and BMI). We will examine the change in scores between groups using a mixed model repeated measures ANOVA.[35] Paired-sample *t* tests will be used to examine time effects within each condition if the overall interaction effect is significant.

6.4.3.3 Safety

N/A.

6.4.3.4 Analysis of Subject Characteristics

We will report baseline descriptive statistics for the overall study, by site, and for both the control and treatment arms of the study. These will include patient age, sex, race, ethnicity and all co-morbidities, medical history and clinical characteristics specified in Section 6.4.4 **(Appendix 6)**. Baseline data will be compared using Pearson Chi Squared tests or Fisher exact test for dichotomous and/or categorical variables and student's t-tests for continuous variables. If variables are deemed as non-parametric, we will use a median test such as a Mann–Whitney *U*-test, where appropriate.

6.4.3.5 Interim Analysis (if applicable)

N/A

6.4.3.6 Health economic evaluation

N/A

6.4.3.7 Other

N/A

6.4.4 Subsets and Covariates

Covariates will include socio-demographic, socio-economic variables and clinical comorbidities such as age, sex, ethnicity, marital status, working status, level of education, weight, height and BMI (through patient self-report). Patients will also self-report if they have any of the following co-morbidities: hypertension, diabetes mellitus, high cholesterol, smoking history, alcohol use, sleep apnea, coronary artery disease (including myocardial infarction/heart attack), cancer, PTSD, or generalized anxiety disorder.

6.4.5 Handling of Missing Data

If patients are missing outcome data, we will use the last observation carried forward for the patient-reported outcome. Missing covariates will be set to missing.

7 Trial Administration

7.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

Compensation: Patients will receive a stipend for their time contributed as part of this study. Estimated hourly stipend based on the average minimum wage in Connecticut and Minnesota ($10) will be provided. This stipend will cover the consent process, initial set up and baseline questionnaire (3 hrs), questionnaires provided at 9, 21, 35 and 61 weeks post-randomization and time it takes to sync and use the provided devices (3 hours per timepoint). The total estimated maximum time is 15 hours, for a total of $150.00.

These payments will be made via a Visa pre-paid card from a rewards platform called Tremendous, which is linked to the Hugo platform. Hugo contracts with Tremendous to manage payments to patients as they are earned. As surveys are completed, the balance will be automatically credited to the patient's Hugo rewards account which is linked to the email address they used to set up their Hugo account. Patients will receive payments when they respond to the study surveys. When these payments are ready, patients will receive an email with instructions on how to redeem their payment. The Visa card will then be sent to their email as a digital ecard from Tremendous. Patients may redeem their payments at any time once they have accrued a balance. Patients will be given the necessary syncable devices to keep as well. Fair market value of the Fitbit Inspire 2 is $99.95.

Please see the attached Informed Consent in the IRB submission.

7.2 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.

The IRB will conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year.

A study closure report will be submitted to the IRB after all research activities have been completed.

Other study events (e.g. data breaches, protocol deviations) will be submitted per IRB's policies.

7.3 Subject Confidentiality

Subject confidentiality is held in strict trust by the research team. Subject medical record review will be limited to the just the elements needed to complete the study. The RA will also access the patient's full medical record, with read-only access, within the YNHH Epic electronic medical record (EMR) system. These data will not leave the Epic EMR system in any way, and are only being used to verify baseline eligibility. Data access to the YNHH Epic EMR will only be granted after all necessary trainings are complete and sign off is received from the Yale IRB and YNHH medical records department using the Yale New Haven Health System's Research Request for Medical Records Access form.

Each subject will be assigned a unique study number. A master list linking the unique study number to the human subject will be maintained in a secure encrypted folder on a password protected file.

All patient data will be collected, handled, and stored according the most rigorous accepted standards. Staff involved in the study will be appropriately trained to maximize data security and technical systems will meet or exceed requirements imposed by HIPAA. Sensitive information will always be encrypted in transit and at rest.

7.4 Deviations/Unanticipated Problems

We do not expect protocol deviations. As noted above in section 6.3.5, we will make significant efforts to reduce non-compliance or participant withdrawal through reminders and contact with patients. If the study team becomes aware of an anticipated problem arise, the event will be reported to the IRB by the RA.

7.5 Data Collection

Age, gender, date of birth and several categories of health information (provider encounters, notes – if available, medication lists, problem lists, family history, allergies, laboratory findings, procedures, immunizations, vital signs, and medical record numbers) will be collected via the Hugo platform. Patients will also be asked to self-report race, ethnicity, weight and co-morbidities/pre-existing conditions, in addition to pre-existing conditions pulled into Hugo from the EHR. We will also be collecting data provided and synced to the Hugo platform from the and Fitbit.

Patient self-reported data collected via Hugo will include insomnia severity using the self-reported ISI scale,[19] and depression using the PHQ-8.[20] These measures will be used to track sleep and depression improvement progress over the 63-week study period. We will also collect data on daytime sleepiness (using the ESS),[21] stress (measured using PSS-10),[22] health-related quality of life (measured using the SF-12)[23] and anxiety (measured GAD-7).[24] Please see section 6.3.5 for the timing of collection. All patient data will be collected, handled, and stored according the most rigorous accepted standards. Staff involved in the study will be appropriately trained to maximize data security and technical systems will meet or exceed requirements imposed by HIPAA. Sensitive information will always be encrypted in transit and at rest.

7.6 Data Quality Assurance

The Principal Investigator and research team will ensure all trial data are generated, documented, and reported in accordance with the Good Clinical Practice (GCP) guidelines. There will be regular team-wide meetings that will seek to ensure that GCP guidelines are being met. This study is not being conducted to meet regulatory requirements.

7.7 Study Records

Study records include: regulatory documents, protocols, consent forms, surveys.

7.8 Access to Source

This study seeks to leverage a combination of EHR and patient-reported outcome data collected using Hugo, as well as patient-generated health data from the Fitbit. These data will be made available to our research team via enrolled patients electing to connect their specific portals within the Hugo platform and share them with our research team. The NESTcc Data Quality

Framework states that to be useful, the data must possess 4 characteristics: high quality; relevant to purpose and context; amendable to the application of appropriate analytic methods; and interpretable using clinical and scientific judgment. First, the data must be high quality, focused on completeness, accuracy, and timeliness. In a recent study published in April 2020 in *npj Digital Medicine*, we demonstrated that the Hugo platform had high levels of completeness and accuracy (all >90%). We also found that the data were available in near real-time, therefor being timely. However, at baseline, these are EHR data and, thus, will be subject to the limitations of EHR data (e.g. these are not designed specifically for research purposes). That said, the clinical outcomes that we seek to ascertain via EHR data are focused on healthcare utilization, which we think should be accurate (e.g. if a patient had an encounter in an Emergency Department). It is likely that some study participants will link data from multiple EHRs, and we will seek to understand clinical utilization using the dates of different encounters.

7.9 Data or Specimen Storage/Security

All patient data will be collected, handled, and stored according the most rigorous accepted standards. Staff involved in the study will be appropriately trained to maximize data security and technical systems will meet or exceed requirements imposed by HIPAA. Patient's Hugo health records will be linked to the study over SSL with a minimum of 128 bit encryption. These data will initially be transferred to Mayo Clinic to a data analyst associated with this project for cleaning. Access to these data will only by available to study personnel at Yale and Mayo Clinic (collaborators at the Mayo Clinic will receive their own IRB approval), and Pear Therapeutics.

7.10 Retention of Records

Primary study records will be maintained on secure, encrypted servers at Mayo Clinic after completion of the research study for a minimum of 5 years after publication of our findings in a peer-reviewed journal (in such case as there is a need to return to the original data source to validate a finding or respond to a question).

7.11 Study Monitoring

The Research Associate will monitor the study.

7.12 Data Safety Monitoring Plan

This study has been deemed minimal risk because the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests and will therefore not be required to be reviewed by a data safety monitoring committee. Information about the minimal risks for this study can be found in Section 3.2.1.

PROMs and syncable data received will not be reviewed by researchers, and this fact will be made clear to study participants at enrollment. Patients will be informed that symptoms reported in this study are not being monitored or evaluated for any clinical purposes or in any timely manner and that any adverse or severe symptoms should be reported directly to their physician(s), or emergency room physicians as they would have in the normal course of their care.

The study coordinators will regularly monitor the status of the portal data (MyChart/pharmacy/Fitbit) coming into the Hugo platform using the Hugo study dashboard only available to research staff listed on the IRB. Within this dashboard, the research staff will be able to review the connection status of all portals connected to each patient's Hugo account. Should a connectivity issue be noticed by research staff, they will note the connection issue reported by the dashboard and determine if the issue is limited to one participant, or if multiple participants are experiencing the same problem. The research staff will then follow up directly with the Hugo support team.

Once the source of the issue is identified, research staff will follow up with the affected patients as needed to correct the issue in a timely fashion.

Research staff will also keep track of any technical issues reported by patients during their follow-up period. If the technical issues are not able to be resolved by the research staff, or if multiple patients report the same problem, the research staff will forward the issue to the Hugo support team to identify and correct the issue and in order to follow-up with those patients affected.

7.13 Study Modification

We do not foresee any study modifications beyond IRB approval beyond potential changes in personnel.

7.14 Study Discontinuation

Given the track-record of conducting high-quality research at YNHH and Mayo Clinic, as well as the collaborative relationships between the investigators, we do not anticipate that any site will be discontinued for any reason. If this becomes necessary for any reason, even though we maintain near certainty that it will not, then we will cease enrollment at that site and shift to other sites.

7.15 Study Completion

Expected completion date is 10/31/2022.

7.16 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.

All investigators will follow the applicable conflict of interest policies.

7.17 Funding Source

This study is funded by the Medical Device Innovation Consortium.

7.18 Publication Plan

The PI holds the primary responsibility for publishing the study results through Yale's publication policy.

8 Appendices

Appendix #	Title	Section	Topic
1	Patient Education	6.3.4	Enrollment
2	Study Questionnaires	6.3.4	Enrollment
3	Fitbit SOP	6.3.4	Enrollment
4	Participant Declined Questionnaire	6.3.4	Enrollment
5	End of Study Questionnaire	6.3.6	End of Study Follow-up
6	Baseline Questionnaire	6.4.3.4	Analysis of Subject Characteristics
7	Study Flyer	6.3.3	Screening
8	Wallet Card	6.3.4	Enrollment

9 List of Tables

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