Bright Light Therapy for residual daytime symptoms associated with obstructive sleep apnea

NCT04299009

November 11, 2020

VA Pittsburgh Healthcare System

ProSPECT - Protocol Submission Portal and Electronic Communication Tracker

Date: Monday, November 9, 2020 2:28:59 PM

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ID: Pro00003376 View: 0.0 Type of Submission Entry

Study Identification Information

This is the first step in your Human Research Application. You will automatically be guided to the appropriate forms needed to complete your submissions.

1.0 * **Study Name:**
Bright Light Therapy for Residual Daytime Symptoms Associated with Obstructive Sleep Apnea (Bright DayS)

2.0 * **Brief Description (using layman's terms) - 500 words or less:**
Persistent daytime symptoms of sleepiness in individuals with obstructive sleep apnea (OSA) who are using Continuous Positive Airway Pressure (CPAP) are associated with adverse long term medical and functional outcomes. Supplementary exposure to bright light has beneficial effects on sleep quality and daytime vigilance in healthy individuals and it has been increasingly applied in a variety of sleep and neuropsychiatric conditions. This study will explore the role of Bright Light Therapy (BLT), a well-established non-pharmacological intervention for circadian disturbances, for the treatment of residual daytime symptoms of OSA which do not respond to CPAP. BLT will be delivered via therapy glasses in a cross-over design, where each participant will be exposed to active treatment and sham treatment (4 weeks in each arm) in a randomized order. The hypothesis is that participants will demonstrate improvements in the variables of interest during the four-week active treatment portion of the eight-week crossover study, compared to the four-week sham treatment portion. We will collect qualitative data from participants regarding the feasibility and acceptability of BLT to guide future testing and implementation of treatment.

3.0 * **Is this research study a Greater than Minimal Risk Clinical Trial?** ○ Yes ◉ **No**

4.0 * **Is this study a Greater than Minimal Risk Comparative Effectiveness research?** ○ Yes ◉ **No**

5.0 * **Principal Investigator:**
Isabella Soreca

5.1 * **VA hours per week the PI is devoted to project:**
8

5.2 * **Is the PI working with ionizing radiation?** ○ Yes ◉ **No**

5.3 * **Is the PI working with biological hazards?** ○ Yes ◉ **No**

5.4 * **Is the PI shipping biological hazards?** ○ Yes ◉ **No**

A completed and signed Research Financial Conflict of Interest Statement is required for all investigators (including Principal Investigators, Co-Principal Investigators, and Co-Investigators) listed on the study application. **Financial Conflict of Interest Form-Nov. 2013**

5.5 Upload Financial Conflict of Interest Statement:
Soreca FCOI(0.01)

6.0 Research Staff:

Researcher	Role in Project	Hours per Week devoted to project	Administer Informed Consent	Working with Ionizing Radiation	Working with Biologicial Hazards?	Shipping biological hazards?	FCOI Form
Joseph Mikolic	Research Staff	2	no	no	no	no	
Nicole Arnold	Coordinator	10	yes	no	no	no	
Jodilyn Roberts	Coordinator	5	yes	no	no	no	
Hanna Edvardsson	Coordinator	5	yes	no	no	no	
Monique Kelly	Research Staff	2	no	no	no	no	

7.0 Type of Submission:

Description
◉ **This is a new study. This has not previously been submitted to the IRB.**
○ This is a new paper conversion. This study has been previously approved by the IRB.

If this is a 'New Paper Conversion' please include the MIRB Number:

Please upload a letter certifying that you have made no modifications or amendments in converting this research study from paper to electronic:

ID: Pro00003376 View: 1.0 Study Identification Information

Study Identification Information (Continued)

1.0 * **Do you certify that all research staff administering informed consent are knowledgeable about the study?**

yes

2.0 * **To the best of your knowledge do you, or any member of your research staff, have any potential, actual or perceived conflict of interest of a professional or personal nature that may affect any aspect of the research, including, but not limited to, the review and/or conduct of this study?**

○ Yes ◉ **No**

If yes, provide a description, including name of study team member with conflict:

3.0 * **Qualifications of the Investigators:**

Dr Soreca is board certified in Psychiatry and Sleep medicine and has extensive experience in conducting research with OSA patients.

ID: Pro00003376 View: 1.2 VA Involvement

VA Involvement

1.0 **Does the proposed research involve any of the following?:**

	Name
☑	**VA Funding**
☑	**VA Personnel Funded Effort**
☑	**VA Patients or their Private Health Information**
☐	Other VA Resources: Central IRB
☑	**Other VA Resources: VA Equipment**
☑	**Other VA Resources: VA Property (Including space leased to, or used by VA)**
☑	**Other VA Resources: VA Databases**
☐	None of the Above apply to this research

ID: Pro00003376 View: 1.3 Study Funding Information

Study Funding Information

1.0 * **Funding Sources:**

	Funding Source	(Other)	Code
View	Rehabilitation R&D (Prog 822)		9022

2.0 **Upload Grant Application, if applicable (If NIH, VA, voluntary agency, must upload):**

Name	Modified Date
Grant Application proposal	12/16/2019 1:26 PM
DMAP plan	3/26/2020 7:42 AM
Human SUbjects Plan	3/26/2020 7:42 AM

ID: Pro00003376 View: 1.4 Resources

1.0 * **Do you currently have adequate resources (e.g., staff, physical space, information technology, etc.) to protect the safety of participants, staff, and the confidentiality of subjects' data during the conduct of this study?**

(●) **Yes** ( ) No

If yes, include a listing of the VAPHS resources that will be used for this study and are necessary to protect participants.
Letters of support have been requested from the following service lines: Sleep Clinic and StatCore.
Additionally, there is an adequate number of qualified staff - coordinator(s), adequate time for the researcher to conduct and complete the research, access to a population (both the PI's clinic and Sleep Clinic) that will allow recruitment of the necessary number of participants, space and facilities needed to properly conduct the study and data core through StatCore support as applicable.

If no, please describe the resources that will be needed and explain how the resources will be obtained before the study is initiated:

2.0 * **VAPHS requires that either the PI or co-PI have a *physical presence* at VAPHS. Please describe the role the PI and/or co-PI have at VAPHS with respect to clinical responsibilities or in relation to other research activities.**
The PI has a physical presence at VAPHS which includes various clinical duties.
Additionally, there is an adequate number of qualified staff - coordinator(s), adequate time for the researcher to conduct and complete the research, access to a population (both the PI's clinic and Sleep Clinic) that will allow recruitment of the necessary number of participants, space and facilities needed to properly conduct the study and data core through StatCore support as applicable

3.0 * **Will off-site ancillary service facilities (e.g., radiology services, central labs, non VA space, etc) be used for this study?**

( ) Yes (●) **No**

If yes, please provide the location and a brief description of the project activities to be conducted at the off-site ancillary facilities:

4.0 * **Will a firm be contracted to obtain consent from subjects, collect private individually identifiable information from human subjects, or be involved in activities that would institutionally engage the firm in human subjects' research?**

( ) Yes (●) **No**

If yes, please provide a description of the contracted service(s):

* Please specify the IRB that has oversight of the firm's activity(ies):

Name of Site / Institution	IRB Approval Document	FWA Number
There are no items to display		

5.0 **Collaborations**
Please list any non-VAPHS institutions or individuals (i.e. co-authors, mentors, etc.) that you will collaborate with and describe their specific role in the research:
Dr. Helen Burgess, consultant on this study, is an expert in human circadian rhythms and bright light therapy. As a consultant on this study, she will offer guidance to the study staff on

the implementation of all aspects of BLT treatment and treatment adherence tracking.
She is at the University of Michigan and has been PI on studies using the Re-timer glasses. And she will offer technical and scientific guidance, but no access to individual patient data.

5.1 If this is not Multi-Site Research, please upload the appropriate written agreement(s) here:
Name
There are no items to display

ID: Pro00003376 View: 1.5 Project Information

1.0 Does the project involve any of the following (check all that apply):

Type
☐ Biological Hazards (including human biological specimens)
☐ Chemicals
☐ Ionizing radiation or use of radioactive materials
☐ Drug, Biological, or Nutritional (e.g. herbal or dietary) Supplement

2.0 Project Focus (check if applicable):

Type
☐ Traumatic Brain Injury (TBI)
☐ Post Traumatic/Post Deployment Stress Disorder (PTSD/PDSD)
☐ Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF)

3.0 KEYWORDS

Please provide a minimum of 3, maximum of 6 keywords. Please use MeSH terms.

* OSA (obstructive sleep apnea)
* BLT (bright light therapy)
* depression

4.0 * Please describe the type of study:

Randomized, single-blind, crossover, placebo-controlled study of bright light therapy glasses.

5.0 * Will any of the research being conducted as a part of this study be used to fulfill academic requirements (e.g., master's thesis, dissertation, or other academic program requirements necessary to obtain a degree/certification, etc.)? ○ Yes ◉ **No**

ID: Pro00003376 View: 1.6 (CR) Study Locations

Study Locations

1.0 * **Please add the local sites where this study will be conducted:**

	Location
View	VAPHS University Drive Division

If Other, Please Specify:

ID: Pro00003376 View: 1.6.1 (CR) Multi-Site Study

1.6.1 Multi-Site Study

1.0 * **Is this a multi-site study:**

○ Yes ◉ **No**

ID: Pro00003376 View: 1.7 Section Chief and Service Line VP approvals

Please upload the approval of the Section Chief, if applicable and the Service Line VP.

1.0 * **Institutional Approval Document:**
Institutional Approval Page(0.01)

ID: Pro00003376 View: 2 Study Objectives & Design

Study Summary

1.0 Funding End Date:
3/31/2022

2.0

* **Abstract. Please provide a brief description of the study**.

Sleep apnea is one of the most common chronic condition among US military veterans[1], causing sleepiness, reduced psychomotor vigilance and depression, which undermine daytime functioning and quality of life [2 3]. Persistent daytime symptoms of sleepiness in individuals with OSA who are using Continuous Positive Airway Pressure (CPAP) are associated with adverse long term medical and functional outcomes [4 5 6 7 8]. Preliminary studies in humans and animal models have shown persisting alterations of circadian rhythms in OSA patients [12 13], that fail to normalize with CPAP treatment [14]. **CPAP treatment, while effective at correcting respiratory events and night time blood oxygen saturation levels, does not necessarily re-align the circadian system.** Supplementary exposure to bright light has beneficial effects on sleep quality and daytime vigilance in healthy individuals and it has been increasingly applied in a variety of sleep and neuropsychiatric conditions[15 16 17]. However, no study to date has tested the application of BLT to treat daytime symptoms associated with sleep apnea. Our study will be the first to explore the role of Bright Light Therapy (BLT), a well-established non-pharmacological intervention for circadian disturbances, for the treatment of residual daytime symptoms of OSA which do not respond to CPAP.

Background and Significance:

Excessive daytime sleepiness and depression in OSA and the role of CPAP therapy: OSA is characterized by repeated pharyngeal obstruction during sleep, causing airflow cessation or reduction and resulting in fragmented sleep, hypoxia and sympathetic hyperarousal. This constellation of physiological processes often leads to immediate and long term consequences, such as reduced daytime vigilance, sleepiness and fatigue, depressed mood, leading to disability, functional impairment [18], reduced quality of life and increased morbidity and mortality[119 18 20 21]. Although Excessive Daytime Sleepiness (EDS) is considered the cardinal symptom of sleep apnea, it is only weakly associated with other markers of OSA severity, such as Apnea-Hypopnea Index (AHI), nocturnal blood oxygen saturation levels and arousals [22 23 24 25 26]. Several randomized controlled trials have established continuous positive airway pressure (CPAP) efficacy regarding sleepiness in OSA [5 27 28]. However, residual excessive sleepiness (RES) in patients correctly treated with CPAP occurs in more than 12% of patients [4] and is associated with increased risk of depression[29 30], with up 42 % of OSA patients experiencing persistent depressive symptoms after 1 year of CPAP therapy [6] . In summary, sleepiness and depression are clinical indicators of increased risk of adverse health outcomes and diminished quality of life in OSA, their manifestation is weakly correlated with the severity of OSA and they are sometime not resolved by adequate CPAP treatment.

Effects of Bright Light on circadian systems, mood and sleepiness: Environmental light is the strongest synchronizer for the circadian system, and its phase-resetting properties are thought to mediate its biological effects on mood and cognitive functions. These effects are best reproduced by artificial light encompassing the green-blue portion of the spectrum (450-500 nm), which is responsible for the phase-shifting properties on the circadian system [33]. Several studies

have demonstrated that short amounts (30-60 minutes) of daily light therapy in the morning effectively realigns individuals' circadian rhythms, leading to improvements in sleep duration, self-reported sleep quality, insomnia symptoms and fatigue [15]. There is robust evidence that light is effective in acutely decreasing sleepiness and fatigue [34 35] and increasing alertness [36 37 38]. Moreover, light therapy is used alone or as adjuvant therapy in a growing number of psychiatric and neurodegenerative diseases, where alterations of sleep-wake cycles are often observed [39].. Despite the amounting evidence of the benefits of BLT for a number of symptoms and functional domains affected in patients with OSA, no study to date has explored its role for patients with sleep apnea.

Design Overview: This is a feasibility study for a within-subjects cross-over trial: eligible participants will undergo baseline assessments over one week, during which baseline measures, including actigraphy, will be collected. They will subsequently be randomized to one of two treatment sequences Bright Light Therapy-Sham Bright Light Therapy (BLT-sBLT) or sBLT-BLT for the total duration of 9 weeks (4 weeks in each treatment arm, plus one week of "wash-out period in between treatments). To avoid subjects potential awareness of placebo treatment (differences in light intensity between the active and sham treatment cannot be completely eliminated), subjects will be told that the study will test the effects of two different light intensities on the target symptoms. Participants will undergo a further final assessment at week 12, 4 weeks after completion of the treatment.

3.0 * **Describe the study objectives. Please include primary aim and hypothesis, if applicable any secondary aims and hypotheses.**

SA1: to test the feasibility of Bright Light Therapy (BLT) to ameliorate sleep related functional impairment in CPAP-treated individuals with OSA. Hypothesis: BLT, delivered via therapy glasses, will have high rates of acceptance and adherence among Veterans with OSA who still experience residuals symptoms, despite adequate treatment with CPAP. We will use a cross-over design, where each participant will be exposed to active treatment and sham treatment in a randomize order. We will collect qualitative data from participants regarding the feasibility and acceptability of BLT to guide future testing and implementation of treatment. **SA2** (exploratory): to test the effects of bright light therapy on sleep related functional impairment, quality of life and CPAP-resistant symptoms of sleepiness and depression. Hypothesis: participants will demonstrate improvements in the variables o interest during the four-week active treatment portion of the eight-week crossover study, compared to the four-week sham treatment portion. We will also be able to detect potential treatment carryover effects and inform design decisions for a subsequent larger study.**SA3** (exploratory): to test whether the degree of circadian rhythms regularity (marker of re-alignment) during BLT mediates the effects of BLT on CPAP-resistant symptoms. Hypothesis: the effect of BLT on CPAP resistant daytime symptoms will be exerted through increased regularity of circadian rhythms, assessed via actigraphy. At the completion of this project, we will have generated preliminary data critical to the design and implementation of a larger trial investigating the impact of BLT on CPAP-resistant symptoms of sleepiness and depression, leading to increased functional impairment in OSA patients. If proven effective, this intervention has the potential to improve the lives of many Veterans suffering from OSA who do not find full symptomatic relief with CPAP, by offering a non-pharmacological intervention that is safe, relatively inexpensive and whose implementation demands only a minimal degree of behavioral modification on the patient.

4.0

*** Provide a summary of the background of the study, and explain how this research will contribute to existing knowledge. Describe previous studies that provides a basis to show that the proposed research can be carried out without undue risk to human subjects.**

Excessive daytime sleepiness and depression in OSA and the role of CPAP therapy: OSA is characterized by repeated pharyngeal obstruction during sleep, causing airflow cessation or reduction and resulting in fragmented sleep, hypoxia and sympathetic hyperarousal. This constellation of physiological processes often leads to immediate and long term consequences, such as reduced daytime vigilance, sleepiness and fatigue, depressed mood, leading to disability, functional impairment [18], reduced quality of life and increased morbidity and mortality[119 18 20 21]. Although Excessive Daytime Sleepiness (EDS) is considered the cardinal symptom of sleep apnea, it is only weakly associated with other markers of OSA severity, such as Apnea-Hypopnea Index (AHI), nocturnal blood oxygen saturation levels and arousals [22 23 24 25 26]. Several randomized controlled trials have established continuous positive airway pressure (CPAP) efficacy regarding sleepiness in OSA [5 27 28]. However, residual excessive sleepiness (RES) in patients correctly treated with CPAP occurs in more than 12% of patients [4] and is associated with increased risk of depression[29 30], with up 42 % of OSA patients experiencing persistent depressive symptoms after 1 year of CPAP therapy [6] . In summary, sleepiness and depression are clinical indicators of increased risk of adverse health outcomes and diminished quality of life in OSA, their manifestation is weakly correlated with the severity of OSA and they are sometime not resolved by adequate CPAP treatment.

Effects of Bright Light on circadian systems, mood and sleepiness: Environmental light is the strongest synchronizer for the circadian system, and its phase-resetting properties are thought to mediate its biological effects on mood and cognitive functions. These effects are best reproduced by artificial light encompassing the green-blue portion of the spectrum (450-500 nm), which is responsible for the phase-shifting properties on the circadian system [33]. Several studies have demonstrated that short amounts (30-60 minutes) of daily light therapy in the morning effectively realigns individuals' circadian rhythms, leading to improvements in sleep duration, self-reported sleep quality, insomnia symptoms and fatigue [15]. There is robust evidence that light is effective in acutely decreasing sleepiness and fatigue [34 35] and increasing alertness [36 37 38]. Moreover, light therapy is used alone or as adjuvant therapy in a growing number of psychiatric and neurodegenerative diseases, where alterations of sleep-wake cycles are often observed [39].. Despite the amounting evidence of the benefits of BLT for a number of symptoms and functional domains affected in patients with OSA, no study to date has explored its role for patients with sleep apnea.

5.0 * Describe the overall significance of the research in terms of the problem to be studied and potential findings, as well as its relevance to the care of veterans, the VAPHS, and the VHA:

US military service members and veterans have experienced an increased in the prevalence of sleep apnea, recently reaching epidemic proportions [1 40], with rates that exceed those reported for the civilian population. OSA with associated EDS is known to cause significant work disability [41], and EDS contributes to the burden of illness by driving increased rates of depression, lower quality of life and greater impairment in productivity [42]. Failure to achieve symptomatic recovery with current treatments can have detrimental effects on the health and quality of life of our Veterans. The treatment proposed in this pilot study has been showed to be safe, inexpensive, and

potentially effective for the very cluster of symptoms that cause the morbidity and impairment in individuals with OSA

6.0 Please upload any additional documents:

Name	Version
There are no items to display	

ID: Pro00003376 View: 2.1 Required Reviews

Required Reviews

1.0 **Type of Submission:**

New study

If this is a 'New Paper Conversion' please include the MIRB Number:

Please upload a letter certifying that you have made no modifications or amendments in converting this research study from paper to electronic:

2.0 * **Requested Review Type:**

Name
○ Exempt
◉ **Expedited**
○ Full IRB Review
○ Not Human Subject Research

3.0

	Please check which of the following Service Lines/Departments/Entities will be impacted or used in the conduct of this study	**Upload Letter of Support**
☐	Clinical Support	
☑	Medical Specialty	Sleep Clinic LOS (0.01)
☐	Investigational Drug Service	
☐	Imaging	
☐	Community Based Care	
☐	Patient Care Services	
☐	Behavioral Health	
☐	Primary Care	
☐	Surgical Specialty	
☐	Critical Care	
☐	Clinical Trials Center	
	☐ Regulatory Coordinator Support Core	
	☐ Clinical Coordinator Support Core	
	☐ Ancillary Support Core	
	☐ Data Support Core	
☐	Research Registry Registry Number:	
☑	Other	StatCore LOS(0.01)

If Other, please specify:
StatCore

ID: Pro00003376 View: 2.1.1 Expedited Qualification

REQUEST FOR EXPEDITED REVIEW

Minimal risk means that 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

Identification of the subjects and/or their responses would not reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, or reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are minimal.

1.0 * **Please certify that ALL of the following are true:**

Case
Research presents no more than MINIMAL RISK to subjects (considering physical, psychological, social, legal and economic risk)
Identification of the subjects and/or their responses WOULD NOT reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, OR reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are minimal.
The research is not classified.
The research involves only procedures listed in one or more of the categories listed in Section 2.

2.0 **If you check any of the items below, the study is qualified for EXPEDITED review status under federal guidelines.**

* **Select all that apply:**

	Description
☑	**1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:** **(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.** **(b) Research on medical devices for which an investigational device application (21 CFR 812) is not required OR the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.**
☐	2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: **(a)** From healthy, non-pregnant adults who weigh at least 110 pounds. [not to exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or **(b)** From other adults and children, considering the age, weight and health of the subjects, the collection procedure, the amount of blood to be collected: The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
☐	3. Prospective collection of biological specimens for research purposes by non-invasive means. Examples: **(a)** hair and nail clippings in a nondisfiguring manner; **(b)** deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; **(c)** permanent teeth if routine patient care indicates a need for extraction; **(d)** excreta and external secretions (including sweat);

	Description
	(e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
	(f) placenta removed at delivery;
	(g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
	(h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
	(i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
	(j) sputum collected after saline mist nebulization.
☑	**4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are used, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical devices are not generally eligible for expedited review, including studies of cleared medical devices for new indications)**
☑	**5. This research involves materials (data, documents, records, or specimens) that have been collected for any purpose including previous research or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).**
☐	6. This research involves the collection of data from voice, video, digital, or image recordings made for research purposes.
☑	**7. This research will be performed on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or will employ a survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.**

ID: Pro00003376 View: 3 Research Design

Methods & Procedures

1.0

* **Does this research study involve any of the following:**

Name	
☑	**Deception**
☐	Interview/Focus Groups
☐	Use of Drug, biological, or nutritional (e.g., herbal or dietary) supplement (investigational or FDA approved)?
☑	**Use of medical devices**
☐	Prospective Analysis of Specimens
☐	Banking of Specimens-Data
☐	Retrospective use of specimens
☐	Audio/Video Recordings or Photographs
☐	Honest Broker or other similar service
☐	None of the Above

ID: Pro00003376 View: 3.1 Deception

Deception

1.0 * **Describe the information that will be withheld from, or misinformation that will be provided to subjects, and the justification.**

Participants will be randomized to one of two treatment sequences; Bright Light Therapy-Sham Bright Light Therapy (BLT-sBLT) or sBLT-BLT for the total duration of 9 weeks (4 weeks in each treatment arm, plus one week of "wash-out period in between treatments). To avoid subjects potential awareness of placebo treatment (differences in light intensity between the active and sham treatment cannot be completely eliminated), subjects will be told that the study will test the effects of two different light intensities on the target symptoms.

If they were told that one treatment sequence was a placebo prior to participation, they would certainly notice the difference and likely not evaluate the effects of the two 4-week spectrums objectively.

There is no additional risk in either arm of the study.

2.0 * **Describe the plans for de-briefing the subjects after their participation.**

The plan for debriefing subjects is to do so following their participation. That can be either once they complete the study or if they withdraw prior to full completion. A debriefing statement is written and will be both discussed with the subject and given to them as a hard copy.

3.0 * **Attach Debriefing Statement:**

Debriefing statement(0.01)

ID: Pro00003376 View: 3.4 Use of Medical Devices

Medical Devices

1.0 * **Specify all devices used on this study:**

Device Name	Manufacturer	Use of Device	IDE Number(if Applicable)	Device Brochure	Description of Use	Risk Level Determined by Sponsor
ActiWatch	Respironics	FDA Approved Device used in approved manner		ActiWatch brochure (0.01)	The VA Sleep Clinic has a license for use of this device. The participant will be asked to wear a wrist actigraph. This is a small device that they wear on their wrist like a watch. The actigraph measures body movement, and helps us to see patterns of sleep, wakefulness, and activity. It is to be worn during the entire 9 weeks of the study. It can be worn while they sleep as well as when showering.	Non-Significant Risk
Re-timer bright light therapy glasses	Re-timer	Investigational Device Not Yet Approved for use		ReTimer glasses brochure (0.01)	The FDA has guidelines regarding the use of non-prescription sunglasses available for review. Bearing in mind that the device being used in this study are not sunglasses, we will refer to these guidelines in answering the comment as to why an IDE is not necessary. These glasses are commercially available and in use by the general population. They can be purchased online. This agrees with the guidelines stating that it is "…marketed directly to the end user (i.e., consumer) without the need for a prescription or any other order issued by a licensed eyecare practitioner…." Also that they are"… Nonprescription devices are commonly sold or distributed as "over-the-counter" (OTC) devices." Finally, they meet international UV and blue light safety standards, they are brighter than most	Non-Significant Risk

Device Name	Manufacturer	Use of Device	IDE Number(if Applicable)	Device Brochure	Description of Use	Risk Level Determined by Sponsor
					indoor lighting but dimmer than outdoor light on a bright day."	

2.0 * **Describe your plan for storage and control of devices:**
ActiWatch (actigraphy) will be dispensed following ICF and worn for 1 week.

Following the 1 week assessment period subjects will return actigraph, and received a newly charged actigraph and the BLT glasses. The newly dispensed actigraph will be worn the remainder of the study, i.e. 9 weeks.
The BLT glasses will be worn for 4 weeks followed by a 1-week washout period and then another 4 weeks.

Study Bright light glasses and ActiWatches will be stored in a locked cabinet in the Research Office Building.

ID: Pro00003376 View: 4 Research study methods

Research Study Methods

Describe all study related procedures following enrollment of a subject in this study.

Please see Section 6 for where the study team defines when a subject will be considered enrolled in the study.

1.0

* **Research Procedures/Interventions:**

At the time of the on-site evaluation, a member of the study staff will obtain written informed consent and the study coordinator will administer study questionnaires and instruct subjects to wear the actigraph and complete a sleep diary for one week. If the participant is enrolling remotely, remote consent will be obtained over the phone and study materials, including an information sheet, the actigraph and sleep diary, will be mailed to the participant. At the end of the baseline assessment week, participants will return the actigraph and sleep log and will complete study questionnaires. Research staff will download actigraphy data and determine the time for administration of BLT based on habitual wake up time (average wake up time for baseline week). Participants will then be given a newly charged actigraph to wear for the following 4 weeks and the BLT glasses in person or mailed to them if they are doing visits remotely.

The intervention will consist of four weeks of BLT via therapy glasses (Retimer^{LTD}), and four weeks of sBLT, in randomized order, spaced out by a one-week wash-out (i.e. no treatment) period, to minimize carry-over effects. The sham treatment will be delivered using the same therapy glasses used for active treatment, by applying a neutral density filter film on the LED light, thus blocking 85% of the blue-green wavelength light. To avoid subjects potential awareness of placebo treatment (differences in light intensity between the active and sham treatment cannot be completely eliminated), subjects will be told that the study will test the effects of two different light intensities on the target symptoms. This is "deception" in that if the subjects were told there was a placebo treatment and a study treatment they would be able to discern the difference therefore they are being told there are 2 types of light instead in order to preserve the blind. Subjects will be instructed to self-administer light therapy at home using study-provided BLT glasses for 60 min each morning at the prescribed time (derived from habitual wake up time) during a period of 8 weeks. After the first 4 weeks, they will bring their equipment in and it will be altered to either active or sham treatment. During the light therapy subjects can engage in other activities such as reading or having breakfast, but will be told not to shower with the therapy glasses on. They will also be instructed to remain indoors during the 60-minute treatment. Subjects will be given an alarm which has been pre-programmed to go off at the BLT prescribed time unless they prefer to use their own alarm on their personal alarm clock or phone. Adherence will be monitored by fitting the therapy glasses with a light and motion sensor. They will be instructed to wear the wrist actigraph for the entire duration of the treatment. It will, however, be replaced at intervals along with the glasses to preserve battery life. Participants will undergo a further final assessment at week 13, which is 4 weeks after completion of the treatment.

Please upload a table of procedures if applicable.
The study procedures table must be completed for:
- All Greater than Minimal Risk (GTM) studies; and
- All Minimal Risk studies that use Standard of Care or Usual Care/Interventions.

Name	Modified Date
Table of Procedures	8/7/2020 3:00 PM

2.0 * **Will Usual Care Procedures/Interventions be used?"**

○ Yes ◉ **No**

If yes, please specify and include a description of what the usual care or expected level of care is at VAPHS (e.g., medications, testing, timing, etc.) for patients, similar to those individuals that meet the inclusion/exclusion criteria for this research study:

2.1 If Usual Care Procedures/Interventions will be used, who is the individual or entity responsible for relevant aspects of the usual care (i.e., which of the above usual care activities will the research study team be responsible for)?:

2.2 Does the usual care at VAPHS for the condition of interest in this research study differ from national guidelines/recommendations (i.e. standard of care)?

○ Yes ◉ **No**

If yes, please describe the differences:

2.3 Are any procedures that are considered standard for this patient population performed more frequently than usual care?

○ Yes ◉ **No**

If yes, please indicate which time points are considered usual care and which are considered research.

2.4 If there is more than one standard, does VAPHS limit which one is followed (e.g. warfarin use for atrial fibrillation vs. one of the newer anticoagulants).

○ Yes ◉ **No**

If yes, please explain:

3.0 * **Does clinical expertise need to be enlisted?**

○ Yes ◉ **No**

If yes, please provide the provisions for enlisting the services of a clinician with appropriate expertise and privileges to perform duties, if the investigator is not a clinician [i.e. reviewing the data, adverse events, and new study findings; also making required decisions to protect the health of the subject (e.g., stopping the participant's involvement in the study or determining when to notify the subject or the subject's health care provider of information that may affect the health of the subject)]:

4.0 **Please upload any surveys, questionnaires, and data collection forms.**

	Document	Description	Version Number
View	Demographics basic.docx(0.01)		0.01
View	Epworth Sleepiness scale(0.01)		0.01
View	FOSQ-10(0.01)		0.01

	Document	Description	Version Number
View	HRQOL.docx(0.01)		0.01
View	Inclusion Exclusion Criteria.docx(0.02)		0.02
View	Phone Call - Week 2.docx(0.01)		0.01
View	Phone Call - Week 6.docx(0.01)		0.01
View	QIDS-SR(0.01)		0.01
View	sleepdiary_aasm.pdf(0.01)		0.01
View	Visit 6 - Qualitative Interview Form.docx(0.01)		0.01

ID: Pro00003376 View: 4.1 Research study methods: analysis Plan

1.0 * **Please describe the analysis plan for the study** *(it is acceptable to refer to the sponsor/multi-site protocol for section if applicable):*

Primary Data Analysis: We will use R version 3.4. **SA1**: To assess the feasibility of the current design to measure the effect of BLT on sleep related functional impairment in CPAP-treated individual with OSA. We will describe the following components of feasibility: recruitment and participant flow, adherence, data completeness and participant burden, and time course of treatment effects (e.g. do carry-over effects require a longer wash out period or suggest that a two-arm between-subject RCT design would be more appropriate?). Our main outcome analyses will employ multi-level linear mixed models with sleep related functional impairment and depression as the dependent variable, treatment block (BLT vs. sBLT) as predictor of interest, treatment sequence as a covariate, and subject intercept as a random effect. Bivariate and colinear relationships will be assessed and proxy variables may be created to adjust for variables that are strongly biased (>3 SD from the mean) or highly collinear with a model-pertinent variable. Covariates we will be assessing include demographics (age, sex, race), comorbid conditions, lifestyle behaviors (smoking, alcohol use, substance use), adherence to BLT treatment, adherence to CPAP, medications for treatment of depression, use of hypnotic medications, and healthcare utilization (number of inpatient/ER visits within the past year).

SA2: to test the effects of bright light therapy on sleep related functional impairment, quality of life and CPAP-resistant symptoms of sleepiness and depression during the four-week active treatment portion of the eight-week crossover study, compared to the four-week sham treatment portion. These exploratory analyses will include bivariate analyses comparing patient outcomes between treatment and sham time periods by utilizing repeated measures ANOVA for quality of life and the Friedman test for categorical variables. We will conduct multi-level mixed effects models of each outcome while adjusting for covariates as listed in the primary aim.

SA3: to test the effect of BLT on CPAP resistant daytime symptoms through **reduced variability of circadian rhythms,** assessed via actigraphy. In order to test this, we will first generate relevant rest-activity rhythms (RAR) measures from minute by minute actigraphy measurements collected over seven days: *RAR height (amplitude, mesor), timing (up-mesor , acrophase, down-mesor). RAR parameters will be modelled from minute-to-minute actigraphy count data using a five-parameter extended sigmoidally transformed cosine model with an anti-logistic function. This model has been shown to fit human RAR data more effectively than a standard cosine curve*[49]*. The extended cosine model also provides a measure of how well the observed activity data are fitted by the 24-h rhythm model known as the pseudo-F statistic; lower values indicate poorer model fit and suggest an erratic or variable rhythm*[50]. Bivariate analyses of the effect of BLT on variability of circadian rhythms parameters will be compared using repeated measures ANOVA. We will conduct multi-level mixed effects models of each outcome while adjusting for covariates as listed in the primary aim.

ID: Pro00003376 View: 5 Sub-Studies

1.0 * **Is there a sub-study or are there sub-studies associated with this study?**
There is no sub-study associated with this study.

ID: Pro00003376 View: 6 Study Population Summary

Study Population Summary

1.0 * **What is the maximum number of subjects you plan to enroll at VAPHS?**
25

2.0 * **Do you plan on enrolling patients into different categories:**
(●) **Yes** ( ) No

If yes, please explain:
This is a 2-arm cross-over study with each participant receiving both arms of treatment for 4 weeks each separated by one week of wash-out period to minimize carry over effects. The order of treatment is randomly assigned.

3.0 **If this is a multi-site study, indicate the projected total subject accrual:**
N/A

4.0 * **Please provide a justification for the sample size:**
Sample size strictly based on statistical power is not applicable in the proposed pilot trial. This study is mainly aimed at testing feasibility of the proposed design and intervention, rather than hypothesis testing through inferential statistics. The statistics and qualitative data obtained from the proposed pilot trial will be used to inform design adjustments in the subsequent large trial.

ID: Pro00003376 View: 6.1 Study Population

Study Population

1.0 * **Check all that apply to describe your study population:**

Study Population
☐ Non-Veterans
☑ **Special Populations**
☑ **Veterans**
☐ Vulnerable populations
☐ Other

2.0 * **Indicate the inclusion criteria for enrollment:**

1) Male or female veterans aged 45-65
2) Documented diagnosis of OSA, currently on CPAP or BiPAP with documented adherence (defined as wearing CPAP/BiPAP for >4h/ night on at least 75% of nights)
3) Excessive residual daytime sleepiness (Epworth score >/= 10)
4) Minimal sleep time, i.e. average total sleep time (TST)≥6 hours

3.0 * **Indicate exclusion criteria for enrollment:**

1) shift work
2) Travel across time zones in past month
3) Narcolepsy
4) Decompensated congestive heart failure (CHF)
5) Dementia, or bipolar disorder
6) Macular degeneration
7) Recent (within 3 months) lasik surgery or planned lasik surgery in the next 3 months
8) Taking medication that will cause photosensitivity to blue-green light spectrum wavelength
9) Poorly controlled diabetes (HgA1c>8%)
10) Active substance use disorder
11) Currently taking alertness-promoting agents such as Modafinil or stimulants
12) Current enrollment in another Greater than minimal risk study

4.0 **If there are any age, ethnic, language, or gender-based exclusion criteria, including the exclusion of any pregnant or lactating women, or those of child-bearing potential, please provide justification:**

N/A

5.0 **Please specify why vulnerable subjects and/or special populations will not be enrolled:**

6.0 **With some exceptions as listed in VHA Handbook 1200.05, incompetent subjects cannot be enrolled in VAPHS approved research. Specify that you will not enroll incompetent subjects and the general rules to be used in making that determination:**

Incompetent subjects will not be enrolled.

ID: Pro00003376 View: 6.3 Study Population- Special Populations

Study Population

1.0 * **Check all that apply to describe your study population:**

Name
☐ Employee and Student Subjects
☑ **Investigators Clinical Population**

2.0 * **Provide a justification for including these subjects:**

Dr. Soreca is a sleep provider clinician so she will recruit from her patients when appropriate. Some may be her own patients, but the majority will be other provider's patients. We have selected special populations in the event that any subject is from her own case load.

ID: Pro00003376 View: 6.3.2 Investigators clinical population

Investigators clinical population

1.0 * **Please indicate how you will minimize the potential for them to feel coerced to participate. Discuss how the potential confusion in roles will be addressed:**
The informed consent document emphasizes the investigator's conflict of interest and voluntary participation of the patient. Dr. Soreca will emphasize that fact to the patient when they are potentially eligible to participate in this study.

ID: Pro00003376 View: 7 Risk/Benefit Assessment-Risks

Risk/Benefit Assessment-Risks

1.0 * **Risk classification for this study (select one).**

Name
◉ **Minimal Risk**
○ Greater than Minimal Risk

2.0 * **Basis for making the above recommendation:**

The device used in this study, the Re-timer® glasses, is commercially available and in use by the general population, and is available without a prescription and individuals are not prevented from buying it, hence the level of risk incurred by the participant is not greater than what they may incur in daily life, as they could go online and buy it.
The light intensities used in this study are greater than most indoor light, but much dimmer than sunlight on a bright day.
The Re-timer® device is commercially available and not FDA-regulated because it is considered a minimal risk system, and is currently being used in a Michigan Medicine study in patients with postpartum depression.

3.0 * **Describe the safety precautions that will be taken to minimize risks/harms:**

Education about use of the study equipment. Instruction on proper home use for the BLT glasses will be provided by study staff.
Any issues will be addressed at each of the scheduled study visits.
In addition there will be a phone call to each subject 1 week after receiving the study glasses to address compliance and any issues they may be having.
During the assessments (both phone and in person), the participant will be directed to verbalize to the PI or research staff if they are having any discomfort and all research activity will be stopped if necessary.
Additionally, any issues will be addressed at each of the scheduled study visits.
If a participant responds to the questionnaires indicating that they are at risk for suicidality, the physician investigator will be consulted. Based on the information obtained, the PI or co-investigators will evaluate suicide risk and decide what level of care is sufficient in conjunction with participants' behavioral health clinician. If the participant does not have a behavioral health clinician, they will be referred to behavioral health for evaluation and treatment.

4.0 * **Provide details regarding the nature of each risk using the area provided below:**

Risk Name
View wearing bright light therapy glasses
View Privacy and confidentiality
View Wearing ActiWatch

5.0 * **Do you plan on using the research answering service:** ○ Yes ◉ **No**

If yes, please Upload the research answering service form:

6.0 **If your study involves a treatment or intervention, please upload the Patient ID Card:**

Patient ID card (0.01)

ID: Pro00003376 View: 7.1 Risk/Benefit Analysis-Potential Benefits and Alternatives

Risk/Benefit Analysis-Potential Benefits and Alternatives

Describe any potential for direct benefits to participants in this study:

1.0 * **Benefit to Subjects:**

Hypothesis: The effect of BLT on CPAP resistant daytime symptoms will be exerted through increased regularity of circadian rhythms, assessed via actigraphy. At the completion of this project, we will have generated preliminary data critical to the design and implementation of a larger trial investigating the impact of BLT on CPAP-resistant symptoms of sleepiness and depression, leading to increased functional impairment in OSA patients. If proven effective, this intervention has the potential to improve the lives of many Veterans suffering from OSA who do not find full symptomatic relief with CPAP, by offering a non-pharmacological intervention that is safe, relatively inexpensive and whose implementation demands only a minimal degree of behavioral modification on the patient.

2.0 * **Describe alternatives (research or non-research) that are available to subjects if they choose not to participate in this study:**

not participate
other research opportunities
VAPHS Standard of Care (patient dependent)

ID: Pro00003376 View: 8 Methods of Recruitment and Retention

Recruitment Methods and Materials used for Retention

1.0 * **Select recruitment methods used on this study:**

Name	
☐	Mail Campaign
☐	Referral by independent source
☐	Advertising such as fliers, letters, or ads (newspaper, TV, radio)
☐	Web Site
☐	Research registry
☑	**Selected from pre-existing records**
☑	**Pre-existing relationship with participants**
☐	Other

If Other Methods Specify:

2.0 * **Specify how subjects will be identified and how study eligibility will be determined:**
We will request a waiver of HIPAA to review the CPRS records of veterans coming for a follow up appointment at the VAPHS Sleep Center. Those that are age 45-65 with a documented diagnosis of OSA and have a documented adherence to CPAP/BiPAP of at least 75% of nights and Epworth score > 10 according to their medical record, will be considered for screening. The clinician seeing (in person or by tele visit) the patient will be contacted by encrypted email asking if they agree to suggest to their patient that they may be eligible to participate in a research study. They can hand the patient (or mention) a brochure describing the study (IRB-approved). If (s)he is interested in participating, (s)he will have the option to undergo an in-person meeting or call the study research coordinator, whose contact information will be provided in the brochure, at another time so the research coordinator can answer any questions the subject may have about the study. There will be no cold calling of veterans who do not express interest in participating. Those who choose to meet in person will sign an informed consent. Those who would like to participate in the study will undergo remote consent over the phone.

Screening Procedures: Participant eligibility (see inclusion/exclusion criteria above) will be initially determined by the Inclusion and Exclusion Criteria document based on CPRS records. If there is criteria unable to be answered during the pre-screening process, this does not eliminate the potential participant. If eligible or potentially eligible based on the pre-screen, the participant will be invited to come in for on-site evaluation. After being consented, any unanswered questions from the Inclusion and Exclusion Criteria document will be asked. If confirmed to be eligible, the patient will continue. If not, the subject will be considered a screen fail and participation in the study will end.

3.0 * **Provide the location (or locations) of the sites where participants will be recruited:**
VAPHS sleep clinic

4.0 **Please include information regarding any advertisements (print, TV, radio, etc) that will be used to recruit subjects including a general description of where this information will be posted:**
Approved brochure located in VAPHS Sleep Clinic

5.0 **Please UPLOAD the documents that will be used for recruitment and an introductory statement or letter to accompany consent for those studies obtaining written informed consent using methods such as fax, email or mail (if applicable). Please also upload any**

screening/recruitment questions that will be verbally asked of potential research subjects. Also, if you will be providing any retention materials, please upload them here.

Name	Reviewer	Modified Date	Version Number
APPROVAL RE_ Review_ Bright Light Therapy study brochure.pdf	Roberts, Jodilyn	2/26/2020 1:33 PM	0.01
Bright-Light-Therapy_Research-study_brochure2.pdf	Roberts, Jodilyn	2/26/2020 1:33 PM	0.01

ID: Pro00003376 View: 9 Informed Consent

Informed Consent

1.0

* **Indicate the types of consent that will be involved in this study (check any or all that apply):**

Informed Consent Category
Written/signed consent by subject
Waivers are being requested.

2.0 * **Waivers: If you are applying for any waivers of consent (check any or all that apply):**

	Name
☐	Waiver of Informed Consent
☑	**Waiver of HIPAA Authorization**
☑	**Waiver of Documentation of Informed Consent (telephone consent, verbal script)**
☐	No Waiver at all

3.0 * **Will this study include non-English speaking participants?**

○ Yes ◉ **No**

ID: Pro00003376 View: 9.1 Waiver of HIPAA

You have indicated you are requesting a waiver of HIPAA.

1.0 * **Is the request only for Screening/Recruitment purposes?**

○ Yes ◉ **No**

If yes, please describe your screening/recruitment method:

If no, the request is for the full study (e.g. retrospective chart reviews and certain observational studies)

Please describe the types of records and/or databases to be accessed:
VAPHS Sleep Clinic scheduled patients' CPRS records to identify potential subjects.
The request reflects the need to potentially perform the entire study remotely with those participants that request to do so.

THE IDENTIFIABLE INFORMATION BEING REQUESTED:
Note: If participants will be receiving payment and HIPAA Authorization is not being obtained, you must select Names, Addresses and Social Security Numbers as that information will be disclosed for payment purposes.

2.0 * **Identifiable Information per HIPAA Definition**

Name
☐ None
☐ Account numbers
☐ Biometric identifiers, including finger and voice prints
☐ Certificate/license numbers
☐ Device identifiers and serial numbers
☑ **Elements of dates (except year, for example, date of birth, admission date, discharge date, date of death, date of procedures; and all ages over 89)**
☐ Email Address
☐ Fax Numbers
☐ Full-face photographic images or any comparable images
☑ **Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)**
☐ Health plan beneficiary numbers
☐ Internet Protocol (IP) address numbers
☐ Medical Record Numbers
☑ **Name or any derivative of name such as initials**
☑ **Social Security Numbers**
☑ **Telephone Numbers**
☐ URLs (Web Universal Resource Locators)
☐ Vehicle identifiers and serial numbers, including license plate numbers
☐ Any other unique identifying number, characteristic, or code (Note: The study ID number, code or other means of record identification is not considered one of the identifiers that must be excluded for de-identification)

3.0 * **Patient Protected Health Information:**

Name

Name	
☑	**Demographic Information (e.g., Name, Address, Phone Number, Social Security Number**
☐	Billing and Payment Information
☑	**Hospital or Medical Records**
☑	**History and Physical Exam Notes**
☐	Mental Health Records
☐	Data Previously Collected for Research Purposes
☑	**Progress Notes**
☑	**Consultation Reports**
☐	Laboratory Test Results
☐	Operative Reports
☐	Other

Please indicate the 'Other' Patient Protected Health Information:

4.0 **Other Health Information:**

Name

There are no items to display

ID: Pro00003376 View: 9.1.1 Waiver of HIPAA - More Information

Waiver of HIPAA- More Information

1.0 * **Describe how the identifiable information is to be used and/or disclosed only by members of the research team and the following persons *(identify with specificity and justify the need to disclose the information to anyone outside the VHA.)* Note: If participants will be receiving payment and HIPAA Authorization is not being obtained, you must also describe this disclosure to representatives of the VA for administrative purposes here.**

Also describe how this activity meets the "minimum necessary standard" described in the HIPAA Privacy Rule:
The identifiable information (patient name and social security number) will be used by the study team members to access potential subjects electronic medical records for pre-screening to assess study eligibility and also to submit study payments. The information will not be disclosed to anyone outside the VHA.
By being able to pre-screen the charts in CPRS this will allow for the maximum patient enrollment with minimal amount of confusion and post-consent screen failures.

It is anticipated that not all patients in the Sleep Clinic will meet initial eligibility criteria and therefore it would require contact with a large number of patients who would likely subsequently screen negative, making the conduct of the study prohibitive. This would be a better use of time to pre-screen scheduled patients.

The proposed study poses minimal risk to the privacy of the subjects because...

2.0 * **Describe how the identifiable information will be protected from improper use or disclosure by (detail how this will be accomplished including the limitations of physical or electronic access to the information and other protections):**
The identifiable information will only be used by the study team member conducting the pre-screening chart review and will not be disclosed to anyone outside of the study or outside of the VHA. CPRS review will be limited to review of the primary care history, and physical exam notes and progress notes, for the purpose of determining if the potential participant meets inclusion and exclusion criteria.

3.0 * **Describe how the identifiers will be destroyed at the earliest opportunity consistent with the research (discuss the timeframe or the reasons the identifiers must be retained, including health or research justifications or any legal requirement to retain them) (Note: At this time, identifiers used for research screening and all other screening records must be retained indefinitely and this must be documented by checking "Other" below):**
Screening is only to identify potential subjects. Once study accrual is completed, all research records will be maintained in accordance with the Veterans Health Administration (VHA) Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS Privacy Officer, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.

* **When will screening data be de-identified or destroyed:**
Name

Other
If Other, please describe:
All research records will be maintained in accordance with the Veterans Health Administration (VHA) Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS Privacy Officer, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.

4.0 * **Describe how the identifiable information will not be reused or disclosed to any other person or entity outside the VHA other than the manner described in the protocol, except as a required by law, for authorized oversight of this research study, or as specifically approved for used in another study by an IRB:**

The identifiable information will not be reused or disclosed to any person or entity outside the VHA, except as required by law, for authorized oversight of this research study.

5.0 * **Describe why the proposed study cannot be practicably conducted without a waiver of authorization: (discuss reasons why it would not be possible to obtain authorization from individual subjects. Time constraints themselves are generally not considered adequate for this justification:**

By being able to pre-screen the charts in CPRS this will allow for the maximum patient enrollment with minimal amount of confusion and post-consent screen failures.

It is anticipated that not all patients in the Sleep Clinic will meet initial eligibility criteria and therefore it would require contact with a large number of patients who would likely subsequently screen negative, making the conduct of the study prohibitive.

6.0 * **Describe why the proposed study cannot be done without the specified identifiable information: Discuss reasons why it would not be possible to conduct the research without the identifiable information being collected.**

The specified identifiable information is necessary to adequately pre-screen potential participants for the study. The identifiable information is necessary to access the electronic medical record of the potential participant in order to review their medical history to determine study eligibility.

Many patients in the Sleep Clinic will not meet initial eligibility criteria given the exclusion criteria. Without pre-screening, a large number of patients would have to be contacted and would likely subsequently screen negative, making the conduct of the study prohibitive.

ID: Pro00003376 View: 9.3 Waiver of Documentation of Informed Consent

Waiver of Documentation of Informed Consent

You have selected a waiver of Documentation of Informed Consent

1.0 **This is a request for Waiver of Documentation of Informed Consent because this research study conforms to either A and/or B (Check if 'yes' and provide the verifying information requested):**

* A: The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. ◉ **Yes** ○ No

AND/OR

* B: The proposed study poses minimal risk to the subjects. ◉ **Yes** ○ No

If yes, please explain why the proposed study poses minimal risks to the subjects. (Outline the subject's involvement in the project and why the study poses minimal risk) :
The questionnaires done with the subject are for collection of data through this non-invasive process. Subjects do not have to answer any questions that make them uncomfortable.
The paper sleep diary serves the purpose of providing data which is used to proceed in determining current sleep patterns. This is needed to set the start time for wearing the Re-Timer glasses for 60 minutes daily.
The Actiwatch is worn like a wristwatch and can be removed if the subject experiences any irritation. These all have non-significant risk.
Since we are in a time where it is often safer for participants to communicate from home, this study is offering them the ability to do so. Because all of these procedures and devices do not have significant risk, we are asking for the Waiver of Documentation of Informed Consent.

2.0 * **The research involves no procedures for which written consent is normally required outside of the research context. Research procedures include:**
Questionnaires, a sleep diary, wearing Re-Timer glasses and an actigraphy. These activities are all deemed minimal risk and thus do not require written consent.

3.0 * **Explain how whenever appropriate, the subjects will be provided with additional pertinent information (e.g. an information sheet):**
Subjects will be initially supplied with an information sheet detailing the timeline of the study as well as descriptions of each visit/study activity that they will be asked to do. They will also receive contact information for each study staff member and receive information sheets on each study device that they are provided.

4.0 **Please upload SCRIPT here:**
CLEAN- Bright DayS Consent Script_10_8_2020(0.05)

ID: Pro00003376 View: 9.4 Consent Forms & Process of Consent

Consent Forms & Process of Consent

1.0 Upload the completed forms into the correct lists below.

1.1 **Informed Consent Form (clean copy):**

	Document	Modified Date	Version Number
View	CLEAN-SPIRE Consent 10.8.2020.doc(0.02)	10/8/2020 12:00 AM	0.02

1.2 **Provider Behavior Informed Consent Form (clean copy):**

Document	Modified Date	Version Number
There are no items to display		

1.3 **Screening Informed Consent Form (clean copy):**

Document	Modified Date	Version Number
There are no items to display		

2.0 **Consent Forms (modified copy):**

	Document	Modified Date	Version Number
View	TRACKED-SPIRE Consent 10.8.2020.doc(0.02)	10/8/2020 12:51 PM	0.02

3.0 * **Describe how, where, when, and by whom the consent process will be initiated:**

The Sleep Clinic schedule will be reviewed by both the PI and study coordinator to identify potential patients. Subjects will be identified by the study staff or may be referred by clinical staff in the Sleep Clinic. The PI will also recruit patients from her clinic. The PI will discuss the study with the clinical providers and staff and ask them to let her know of any patients who may qualify. Those patient's charts will then be pre-screened in CPRS to see if they may be eligible. If the coordinator finds a patient that may be eligible, the coordinator will contact a member of the patient's clinical care team. The patient will be approached by a member of the research team who is also part of the clinical care team to see if they are interested in participating in research opportunities. If the patient expresses interest, the consent will be provided to the patient. If there is no member of the research team who is also part of the clinical team, the clinical team will inform the patient about the study and pass along the patient's information to the research team if the patient expresses interest in the study and agrees to have their information forwarded to the research team for contact. If the clinical coordinator is available, she will come to speak with the patient. If the patient is ambulatory this will be done in an empty conference room or empty exam room. If the patient is not ambulatory, the curtain will be drawn, and the discussion will be kept quiet to ensure patient confidentiality. The patient may take time to review this with family. Once the patient has reviewed the consent and had all questions answered the consent process will be completed in the Sleep clinic by the Principal Investigator.

4.0 * **Will you be maintaining a Master List of Subjects?**

Yes

5.0 * **Describe when the subject's name will be added to the master list and how the list will be maintained in a secure fashion.**

Once the patient is enrolled in the study, they will be added to the master list of subjects. This will be maintained in CPRS on a personal list and on a VAPHS shared drive; \\vhapthmul6 \Pro3286_Soreca, that only study team will have access to.

ID: Pro00003376 View: 10.0.0 Data Security and Privacy: Data Types Storing

10.0 Data Types Collecting and Storing

1.0 **Click the add button (below) to open an entry form to indicate the types and/or sources of the data that will be collected/stored as part of the project.**

Instructions: **For each type/source of data that will be collected as part of the project, this includes screening data, click the add button to open an entry form that lists the types and/or sources of data. Select a source/type of the data that will be collected/stored. Then indicate what, if any, identifiers or sensitive information will be collected/stored from the source/type (None is an option). To add another source/type click "OK Add Another" button to open up a new entry form to repeat the process.**

Example 1: You are collecting data from VA Medical records including names, last 4 of SSN, and addresses. Therefore, you would select "VA medical record data" as the source, and then select in the identifiers: "Name or any derivative of name, such as initials," "Social Security Numbers," and "Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)" as the identifiers being collected.

Example 2: You are screening VA Medical Records and recording the information you use to screen (i.e.: names, last 4 of SSN, and addresses, etc.) Note: This information must be treated as a Source document, please select "Screening" as the source and then select the identifiers "Name or any derivative of name, such as initials," "Social Security Numbers,", as applicable.

*

	Data Type/Source	Collection Details	Identifiers
View	Questionnaires/Surveys, paper	Any data will be collected by approved member of the research study team. It will be recorded on paper. Questionnaires response will be recorded on paper and then transferred to VA REDCap electronic data capture for analysis. Paper is stored in the locked Research Office Building in a locked cabinet accessible only by the study staff. Electronic data is saved on the study shared drive, again only accessible by the study staff.	Elements of dates (except year, for example, date of birth, admission date, discharge date, date of death, date of procedures; and all ages over 89) Telephone Numbers Social Security Numbers Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)

	Data Type/Source	Collection Details	Identifiers
			Name or any derivative of name such as initials
			Device identifiers and serial numbers
View	Other *Actigraph*	The Actigraph system comes with an Actigraphy (watch), charger and software. There is a USB in the device that is removed and the data then transferred to a computer with the software. The data is scored and saved to the study drive and recorded in the study specific RedCAP database. The data is then erased from the computer.	Device identifiers and serial numbers
View	VA medical record data (i.e., diagnoses, procedures, visits) via **chart review**	Using the waiver of HIPAA, study staff will pre-screen VAPHS Sleep clinic scheduled patients for potential participants based on general inclusion and exclusion criteria. This information will be stored on paper charts by subject and kept in a locked cabinet in a locked building (ROB).	Elements of dates (except year, for example, date of birth, admission date, discharge date, date of death, date of procedures; and all ages over 89)
			Social Security Numbers
			Name or any derivative of name such as initials

ID: Pro00003376 View: 10.0.1 Data Security and Privacy: Social Security Numbers

10.0.1 Data Security and Privacy: Social Security Numbers

1.0 You indicated that you will be using all or some part of the research subjects' SSNs as part of this study. Which of the following will you be using:

Real Social Security numbers	*	(●) **Yes** ( ) No
Scrambled Social Security numbers	*	( ) Yes (●) **No**
Last 4 digits of Social Security Number	*	(●) **Yes** ( ) No
Other (some derivation of the SSN)	*	( ) Yes (●) **No**

If other, please explain:

2.0 * Please describe how subjects' Social Security numbers will be used in this study:
Full social security number is required to submit reimbursement request.
Last 4 of the social security number is used to access the subject's medical record.

3.0 * Please describe the security measures that will be taken to protect SSNs.
SSNs will be used for participant payments and will be on the 10-7078 form and will be kept in a binder in a locked cabinet in the study coordinator's office in the Research Office Building.

ID: Pro00003376 View: 10.1.0 Data Security and Privacy: Incoming Data

10.1.0 Incoming Data

1.0 * **Will data be transferred into VAPHS?**

No. Data is not being transferred into this facility

ID: Pro00003376 View: 10.2.0 Data Security and Privacy: Outgoing Data

10.2.0 Outgoing Data

1.0 * **Will any of the data being collected/stored be transferred outside of VAPHS?**

No. The data is not being transferred outside of this facility.

ID: Pro00003376 View: 10.3.0 Data Security and Privacy: Local Data Storage Types

10.3.0 Local Data Storage Types

1.0 * **How will data be stored on this project? (Select all that apply)**

On Paper

Electronically

ID: Pro00003376 View: 10.3.1 Data Security and Privacy: Local Data Storage Types - Paper

10.3.1 Local Data Storage Types - Paper

1.0 * **All VA research data collected in paper must be stored in a locked room at VAPHS. List the room number(s) and the campus(es) where data will be stored in the text box below.**

Study staff will maintain the data in the Research Office Building (which is locked) in a locked cabinet at the study coordinators cube, 1-27.

ID: Pro00003376 View: 10.3.2 Data Security and Privacy: Local Data Storage Types - Electronic

10.3.2 Local Data Storage Types - Electronic

1.0 * **Where is the electronic data being stored? Select all that apply.**

VAPHS Network (shared drive)

Other

If "Other" please describe OR if you would like to provide additional information for clarification, please elaborate in the text box below.

VA RedCap

If you selected VAPHS or VA Network (Shared Drive), please provide the name of the drive (i.e. "MySharedDriveName (\\vapthshsare) (X:)"):

(Z:)Pro3286_Soreca(\\vhapthmul6)

ID: Pro00003376 View: 10.4.0 Data Security and Privacy: Reusing Data

10.4.0 Data Security and Privacy: Reusing Data

1.0 * **Will the data collected in this study be reused in other studies?** (●) **Yes** ( ) No

If yes, please describe where the data to be reused will be stored and how access to that data will be provided and monitored:

Access to the data will be limited to the individuals named in the informed consent document and HIPAA Authorization signed by the study subjects.

The data will be used in future studies as this is a pilot and feasibility study.

2.0 **If this research is part of a grant, please upload the Data Management Access Plan (DMAP) or Resource Sharing Plan for this study.**

Name	Modified Date
There are no items to display	

The DMAP is uploaded with the grant in Section 1.3".

ID: Pro00003376 View: 10.6.0 Data Security and Privacy: HIPAA

10.6.0 Data Security and Privacy: HIPAA

The Healthcare Insurance Portability and Accountability Act(HIPAA) prohibits the use of a person's Protected Health Information without a valid authorization.

1.0 * **Select the option which fits this study:**

Name
○ Not applicable: No PHI is being used or disclosed by VAPHS
○ Not applicable: Waiver has been requested
◉ **HIPAA Authorization**

Upload HIPAA authorization (clean copy) here:

	Document	Modified Date	Version Number
View	HIPPA Combined With Consent Clean.docx(0.01)	1/10/2020 9:18 AM	0.01

Upload HIPAA authorization (tracked changes) here:

	Document	Modified Date	Version Number
View	HIPPA Combined With Consent Tracked.docx(0.01)	1/10/2020 9:18 AM	0.01

2.0 **At screening will clinical personnel be asked to share potential participants PHI:**

○ Yes ◉ **No**

If yes, please upload the 10-5345:

ID: Pro00003376 View: 10.7.0 Data Security and Privacy: Additional Information

10.7.0 Data Security and Privacy: Additional Information

1.0 **Does this research involve...**

* **...specially obtained software?** (●) **Yes** ( ) No

If yes, please describe the software and what it is being used for:
Data will be analyzed with Actiware 6.0.9 software (Philips Respironics), using the medium sensitivity setting. A validated algorithm for sleep scoring each 30 second epoch will be used. These data will be used to characterize habitual sleep and establish a stable index of mid-sleep time (MST), which is needed for calculation of circadian outcomes.
The VA Sleep Clinic has a license for the Actiware 6.0.9 software (Philips Respironics). This software is VA TRM approved and all constraints will be followed.

* **...one or more Web-based applications?** (●) **Yes** ( ) No

If yes, please describe the application and what it is being used for:
VA RedCAP is the web-based application used to record participant data. The data stored will be from surveys, demographics, screening and eligibility data. Information will be de-identified other than dates of specific assessments.

* **...mobile devices?** (●) **Yes** ( ) No

If yes, please describe:
The Phillips Respironics Actiwatch 2 will be used. The participants will start to wear it following consent and continue to wear it for the entire 9 weeks of the study.
The device does not have wireless capability. No data will be transmitted to the cloud. The devices come with a charger and software. It has a small USB which is used to transfer the data to a computer. The data is then scored and transferred to the study data base and entered into RedCAP. The data is then erased from the original computer.

2.0 * **Will a Certificate of Confidentiality be obtained for this study?** ( ) Yes (●) **No**

If yes, please attach the Certificate of Confidentiality:

3.0 * **Will VA sensitive information be transported and utilized outside protected environments?** ( ) Yes (●) **No**

If you answered yes above, please upload a fully executed VAPHS Memo to Take VA Sensitive Information Outside a Protected Environment by following **these instructions** .

ID: Pro00003376 View: 10.8.0 Data Security and Privacy: Certifications

10.8.0 Certifications

1.0 * **I certify that all study staff are up-to-date and will remain up-to-date with Information Security Awareness Training, Rules of Behavior, and VHA Privacy Training.**
(●) **Yes** ( ) No

2.0 * **I also certify that when an individual is no longer part of the study team, access will be removed to research study data.** (●) **Yes** ( ) No

3.0 * **I certify that all research records will be maintained in accordance with the Veterans Health Administration (VHA)Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS Privacy Officer, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.** (●) **Yes** ( ) No

4.0 * **I certify that any loss or compromise of any VA sensitive information (including research data), VA equipment or device, or any non-VA equipment or device that is used to transport, access, or store VA information will be reported in accordance with the reporting requirements outlined in VA Handbook 6500.** (●) **Yes** ( ) No

5.0 * **I certify that, in accordance with VA Handbook 6500, no personal laptops will be used for official VA business in conjunction with this study.** (●) **Yes** ( ) No

ID: Pro00003376 View: 11 Local Data Safety Monitoring Plan

Local Data Safety Monitoring Plan

For local studies, a data and safety monitoring plan (DSMP) must be established.

1.0 * **Please describe how the study procedures and data being collected will be continuously monitored so that changes in the risk/benefit ratio can be determined in a timely fashion during the course of the study:**

The data monitoring plan will ensure that there is no change to the risk/benefit ratio during the course of the study and that confidentiality of research data is protected. The principal investigator, Dr. Soreca, and study personnel will meet at 1 month intervals and additional check-ins as needed to re-evaluate study goals, subject recruitment and retention, data coding and analysis, documentation and identification of adverse events, complaints, protocol deviations, and violations of confidentiality. Modifications to the protocol and to the consent document will be recommended as determined by the Data Monitoring Plan. Adverse events will be reported to the IRB. Study renewals will include a summary report and interpretation of the findings of the Data Monitoring Plan for the previous years.

2.0 * **Describe how frequently Investigators, study personnel, and the clinical coordinators involved in the study will meet and/or review study data.**

Investigators, study personnel, and the clinical coordinators involved in the study will meet monthly to discuss the study goals, progress, modifications, documentation, recruitment, retention, data analysis and confidentiality and address any concerns or issues at the time. These meetings will be overseen by Dr. Soreca. Any instances of adverse events, protocol deviations, or other problems identified during the meetings will be reported as soon as possible within the required reporting timeframes using the standard forms and/or procedures set forth by the IRB. In addition, clinical coordinators may review study documentation and/or consent forms to ensure that subject's confidentiality is maintained.

3.0 * **Will this study use a Data Safety Monitoring Board or Data Monitoring committee?**

○ Yes ◉ **No**

4.0 * **Will this study use a Medical Monitor?**

○ Yes ◉ **No**

ID: Pro00003376 View: 12 Costs and Payments

Costs and Payments

1.0 * **Does this study have a budget?:**

(●) **Yes** ( ) No

If yes, please upload the current budget:

SPIRE budget(0.01)

2.0 * **Will patients receive payments for this study?**

(●) **Yes** ( ) No

If yes, please upload the financial letter of support (either from the Business Service line or the Veterans Research Foundation of Pittsburgh) or documentation waiving the requirement of a letter of support:

ALL SIGNED LOS memo - VA Financial _v3_Sept2018.soreca.jra.pdf 0.01

3.0 * **Are you paying patients using the WePay system?**

no

ID: Pro00003376 View: 12.1 Costs

Costs

1.0 * **Will subjects be required to pay for any services outside of the VHA that may be required as part of participating in this research study?**
no

ID: Pro00003376 View: 12.2 Participant Payments

Participant Payments

1.0 * **Please explain how the proposed payments are reasonable and commensurate with the expected contributions of the subject:**
Subjects are only being paid $25 per visit (Baseline(Visit 2), Visits 3, 5 & 6) to compensate them for their time and travel.

2.0 * **Please provide information on how the subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in, the research study. In additional the payments do not constitute (or appear to constitute) coercion to participate in, or continue to participate in, the research study:**
The payments for this study are only $25 a visit in order to help cover the costs of transportation and their time for participating in this study. The payment does not reflect undue pressure or influence on these patients.

3.0 * **Specify the amount, form of payment and the specific disbursement schedule of payments:**
Participants will be paid $25 for their participation in each assessment (Baseline(Visit 2), Visits 3, 5 & 6) that they complete to pay for their time and travel. Payment will go by direct deposit into their checking account through EFT or onto a Direct Express card issued by Comerica.

4.0 * **Are the subjects being paid employees?**
no
If yes, please describe how it will be in accordance with the SOP:

ID: Pro00003376 View: 14 References

References:

1.0 * **Please provide a list of references** *(Multi-site protocols: You may reference the page numbers in the original protocol):*

Bibliographic References

1 Alexander M, Ray MA, Hébert JR, et al: The National Veteran Sleep Disorder Study: Descriptive Epidemiology and Secular Trends, 2000-2010. Sleep 2016; 39(7): 1399–410. Doi: 10.5665/sleep.5972.

2 Baniak LM, Chasens ER, Luyster FS, Strollo PJ, Thunström E, Peker Y: Obstructive sleep apnea and self-reported functional impairment in revascularized patients with coronary artery disease in the RICCADSA trial. Sleep Breath Schlaf Atm 2018; 22(4): 1169–77. Doi: 10.1007/s11325-018-1733-4.

3 Vijayan VK: Morbidities associated with obstructive sleep apnea. Expert Rev Respir Med 2012; 6 (5): 557–66. Doi: 10.1586/ers.12.44.

4 Pépin J-L, Viot-Blanc V, Escourrou P, et al: Prevalence of residual excessive sleepiness in CPAP-treated sleep apnoea patients: the French multicentre study. Eur Respir J 2009; 33(5): 1062–7. Doi: 10.1183/09031936.00016808.

5 Giles TL, Lasserson TJ, Smith BJ, White J, Wright J, Cates CJ: Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database Syst Rev 2006; (1): CD001106. Doi: 10.1002/14651858.CD001106.pub2.

6 Gagnadoux F, Le Vaillant M, Goupil F, et al: Depressive symptoms before and after long-term CPAP therapy in patients with sleep apnea. Chest 2014; 145(5): 1025–31. Doi: 10.1378/chest.13-2373.

7 Mulgrew AT, Ryan CF, Fleetham JA, et al: The impact of obstructive sleep apnea and daytime sleepiness on work limitation. Sleep Med 2007; 9(1): 42–53. Doi: 10.1016/j.sleep.2007.01.009.

8 Pagel JF: The burden of obstructive sleep apnea and associated excessive sleepiness. J Fam Pract 2008; 57(8 Suppl): S3-8.

9 Tranah GJ, Blackwell T, Stone KL, et al: Circadian activity rhythms and risk of incident dementia and mild cognitive impairment in older women. Ann Neurol 2011; 70(5): 722–32. Doi: 10.1002/ana.22468.

10 Guo VY, Cao B, Wong CKH, Yu EYT: The association between daytime napping and risk of diabetes: a systematic review and meta-analysis of observational studies. Sleep Med 2017; 37: 105–12. Doi: 10.1016/j.sleep.2017.01.018.

11 Groeger JA, Lo JCY, Burns CG, Dijk D-J: Effects of sleep inertia after daytime naps vary with executive load and time of day. Behav Neurosci 2011; 125(2): 252–60. Doi: 10.1037/a0022692.

12 Moreira S, Rodrigues R, Barros AB, et al: Changes in Expression of the CLOCK Gene in Obstructive Sleep Apnea Syndrome Patients Are Not Reverted by Continuous Positive Airway Pressure Treatment. Front Med 2017; 4: 187. Doi: 10.3389/fmed.2017.00187.

13 Burioka N, Koyanagi S, Endo M, et al: Clock gene dysfunction in patients with obstructive sleep apnoea syndrome. Eur Respir J 2008; 32(1): 105–12. Doi: 10.1183/09031936.00138207.

14 Hernández C, Abreu J, Abreu P, Castro A, Jiménez A: Nocturnal melatonin plasma levels in patients with OSAS: the effect of CPAP. Eur Respir J 2007; 30(3): 496–500. Doi: 10.1183/09031936.00051906.

15 van Maanen A, Meijer AM, van der Heijden KB, Oort FJ: The effects of light therapy on sleep problems: A systematic review and meta-analysis. Sleep Med Rev 2016; 29: 52–62. Doi: 10.1016/j.smrv.2015.08.009.

16 Mårtensson B, Pettersson A, Berglund L, Ekselius L: Bright white light therapy in depression: A critical review of the evidence. J Affect Disord 2015; 182: 1–7. Doi: 10.1016/j.jad.2015.04.013.

17 Ancoli-Israel S, Rissling M, Neikrug A, et al: Light Treatment Prevents Fatigue in Women Undergoing Chemotherapy for Breast Cancer. Support Care Cancer 2012; 20(6): 1211–9. Doi:

10.1007/s00520-011-1203-z.
18 Rod NH, Kjeldgård L, Åkerstedt T, et al: Sleep Apnea, Disability Pensions, and Cause-Specific Mortality: A Swedish Nationwide Register Linkage Study. Am J Epidemiol 2017; 186(6): 709–18. Doi: 10.1093/aje/kwx138.
19 Zhao Y, Yu BY-M, Liu Y, Liu Y: Meta-Analysis of the Effect of Obstructive Sleep Apnea on Cardiovascular Events After Percutaneous Coronary Intervention. Am J Cardiol 2017; 120(6): 1026–30. Doi: 10.1016/j.amjcard.2017.06.035.
20 Ruel G, Martin SA, Lévesque J-F, et al: Association between multimorbidity and undiagnosed obstructive sleep apnea severity and their impact on quality of life in men over 40 years old. Glob Health Epidemiol Genomics 2018; 3: e10. Doi: 10.1017/gheg.2018.9.
21 Vinnikov D, Blanc PD, Alilin A, Zutler M, Holty J-EC: Fatigue and sleepiness determine respiratory quality of life among veterans evaluated for sleep apnea. Health Qual Life Outcomes 2017; 15(1): 48. Doi: 10.1186/s12955-017-0624-x.
22 Roure N, Gomez S, Mediano O, et al: Daytime sleepiness and polysomnography in obstructive sleep apnea patients. Sleep Med 2008; 9(7): 727–31. Doi: 10.1016/j.sleep.2008.02.006.
23 Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D, Kales A: Sleep apnea and sleep disruption in obese patients. Arch Intern Med 1994; 154(15): 1705–11.
24 Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S: The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328(17): 1230–5. Doi: 10.1056/NEJM199304293281704.
25 Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A: Effects of age on sleep apnea in men: I. Prevalence and severity. Am J Respir Crit Care Med 1998; 157(1): 144–8. Doi: 10.1164/ajrccm.157.1.9706079.
26 Bixler EO, Vgontzas AN, Lin HM, et al: Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001; 163(3 Pt 1): 608–13. Doi: 10.1164/ajrccm.163.3.9911064.
27 Marshall NS, Barnes M, Travier N, et al: Continuous positive airway pressure reduces daytime sleepiness in mild to moderate obstructive sleep apnoea: a meta-analysis. Thorax 2006; 61(5): 430–4. Doi: 10.1136/thx.2005.050583.
28 Patel SR, White DP, Malhotra A, Stanchina ML, Ayas NT: Continuous positive airway pressure therapy for treating sleepiness in a diverse population with obstructive sleep apnea: results of a meta-analysis. Arch Intern Med 2003; 163(5): 565–71.
29 LaGrotte C, Fernandez-Mendoza J, Calhoun SL, Liao D, Bixler EO, Vgontzas AN: The relative association of obstructive sleep apnea, obesity and excessive daytime sleepiness with incident depression: a longitudinal, population-based study. Int J Obes 2005 2016; 40(9): 1397–404. Doi: 10.1038/ijo.2016.87.
30 Björnsdóttir E, Benediktsdóttir B, Pack AI, et al: The Prevalence of Depression among Untreated Obstructive Sleep Apnea Patients Using a Standardized Psychiatric Interview. J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med 2016; 12(1): 105–12. Doi: 10.5664/jcsm.5406.
31 Meijer JH, Colwell CS, Rohling JHT, Houben T, Michel S: Dynamic neuronal network organization of the circadian clock and possible deterioration in disease. Prog Brain Res 2012; 199: 143–62. Doi: 10.1016/B978-0-444-59427-3.00009-5.
32 Abbott SM, Zee PC: Circadian Rhythms: Implications for Health and Disease. Neurol Clin 2019; 37(3): 601–13. Doi: 10.1016/j.ncl.2019.04.004.
33 Duffy JF, Czeisler CA: Effect of Light on Human Circadian Physiology. Sleep Med Clin 2009; 4 (2): 165–77. Doi: 10.1016/j.jsmc.2009.01.004.
34 Phipps-Nelson J, Redman JR, Dijk D-J, Rajaratnam SMW: Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. Sleep 2003; 26(6): 695–700.
35 Viola AU, James LM, Schlangen LJM, Dijk D-J: Blue-enriched white light in the workplace

improves self-reported alertness, performance and sleep quality. Scand J Work Environ Health 2008; 34(4): 297–306.
36 Lockley SW, Evans EE, Scheer FAJL, Brainard GC, Czeisler CA, Aeschbach D: Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. Sleep 2006; 29(2): 161–8.
37 Beaven CM, Ekström J: A comparison of blue light and caffeine effects on cognitive function and alertness in humans. PloS One 2013; 8(10): e76707. Doi: 10.1371/journal.pone.0076707.
38 Smolders KCHJ, de Kort Y a W, Cluitmans PJM: A higher illuminance induces alertness even during office hours: findings on subjective measures, task performance and heart rate measures. Physiol Behav 2012; 107(1): 7–16. Doi: 10.1016/j.physbeh.2012.04.028.
39 Wulff K, Gatti S, Wettstein JG, Foster RG: Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. Nat Rev Neurosci 2010; 11(8): 589–99. Doi: 10.1038/nrn2868.
40 Caldwell JA, Knapik JJ, Lieberman HR: Trends and factors associated with insomnia and sleep apnea in all United States military service members from 2005 to 2014. J Sleep Res 2017; 26(5): 665–70. Doi: 10.1111/jsr.12543.
41 Omachi TA, Claman DM, Blanc PD, Eisner MD: Obstructive Sleep Apnea: A Risk Factor for Work Disability. Sleep 2009; 32(6): 791–8.
42 Stepnowsky C, Sarmiento KF, Bujanover S, Villa KF, Li VW, Flores NM: Comorbidities, Health-Related Quality of Life, and Work Productivity Among People With Obstructive Sleep Apnea With Excessive Sleepiness: Findings From the 2016 US National Health and Wellness Survey. J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med 2019.
43 Fischer D, Lombardi DA, Marucci-Wellman H, Roenneberg T: Chronotypes in the US - Influence of age and sex. PloS One 2017; 12(6): e0178782. Doi: 10.1371/journal.pone.0178782.
44 Zhu L, Zee PC: Circadian Rhythm Sleep Disorders. Neurol Clin 2012; 30(4): 1167–91. Doi: 10.1016/j.ncl.2012.08.011.
45 Burgess HJ, Rizvydeen M, Kimura M, et al: An Open Trial of Morning Bright Light Treatment Among US Military Veterans with Chronic Low Back Pain: A Pilot Study. Pain Med Malden Mass 2018. Doi: 10.1093/pm/pny174.
46 Weaver TE, Laizner AM, Evans LK, et al: An instrument to measure functional status outcomes for disorders of excessive sleepiness. Sleep 1997; 20(10): 835–43.
47 Burgess HJ, Savic N, Sletten T, Roach G, Gilbert SS, Dawson D: The relationship between the dim light melatonin onset and sleep on a regular schedule in young healthy adults. Behav Sleep Med 2003; 1(2): 102–14. Doi: 10.1207/S15402010BSM0102_3.
48 Kantermann T, Burgess HJ: Average mid-sleep time as a proxy for circadian phase. PsyCh J 2017; 6(4): 290–1. Doi: 10.1002/pchj.182.
49 Marler MR, Gehrman P, Martin JL, Ancoli-Israel S: The sigmoidally transformed cosine curve: a mathematical model for circadian rhythms with symmetric non-sinusoidal shapes. Stat Med 2006; 25(22): 3893–904. Doi: 10.1002/sim.2466.
50 Smagula SF, Boudreau RM, Stone K, et al: Latent activity rhythm disturbance sub-groups and longitudinal change in depression symptoms among older men. Chronobiol Int 2015; 32(10): 1427–37. Doi: 10.3109/07420528.2015.1102925.

ID: Pro00003376 View: 15 Miscellaneous Documents

Miscellaneous Documents

If you have any documents that need to be included in this submission, but do not fit in any of the previous sections please upload them here.

	Document	Description	Version Number
View	BrightDayS Info Sheet v1.2_072720-CLEAN.irb (1).doc(0.01)		0.01
View	Pro 3376 DSMB comment 5_4_2020.pdf(0.01)		0.01
View	Pro 3376_Investigator COVID Risk Assessment v8.7.6.2020. IS SIGNED_Soreca_FC.pdf(0.01)		0.01
View	TRACKED- Bright DayS Remote Consent Script 10.8.2020.docx (0.01)		0.01

ID: Pro00003376 View: SF - Final Page

Final Page

You have completed your application!

Please hit "Finish" to save and exit the application. Doing so will NOT submit the application for review.

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must press the "SUBMIT STUDY" button in My Activities for this Study ID:Pro00003376.

You can track the ongoing status of your submission by logging into the study workspace.

Please feel free to contact the IRB with any questions or concerns.

ID: Pro00003376 View: Create/Edit

Study Funding Source

1.0 * **Funding Source Name:**
Rehabilitation R&D (Prog 822)
If you can't find the Funding Source above, choose "Other" and enter it here:

ID: Pro00003376 View: VA Create-Edit

* **Device Name:**	ActiWatch
* **Use of Device:**	FDA Approved Device used in approved manner
Manufacturer:	Respironics
IDE Class:	
IDE Number(if Applicable):	
Risk Level Determined by Sponsor:	Non-Significant Risk
Upload Device Brochure	ActiWatch brochure(0.01)

Provide any other notes about how this device will be used or justification for lack of IDE number
The VA Sleep Clinic has a license for use of this device. The participant will be asked to wear a wrist actigraph. This is a small device that they wear on their wrist like a watch. The actigraph measures body movement, and helps us to see patterns of sleep, wakefulness, and activity. It is to be worn during the entire 9 weeks of the study. It can be worn while they sleep as well as when showering.

Is the investigator hold the IDE for this device?

○ Yes ◉ **No**

If yes please provide a basis for risk level.

ID: Pro00003376 View: VA Create-Edit

* **Device Name:**	Re-timer bright light therapy glasses
* **Use of Device:**	Investigational Device Not Yet Approved for use
Manufacturer:	Re-timer
IDE Class:	
IDE Number(if Applicable):	
Risk Level Determined by Sponsor:	Non-Significant Risk
Upload Device Brochure	ReTimer glasses brochure(0.01)

Provide any other notes about how this device will be used or justification for lack of IDE number

The FDA has guidelines regarding the use of non-prescription sunglasses available for review. Bearing in mind that the device being used in this study are not sunglasses, we will refer to these guidelines in answering the comment as to why an IDE is not necessary.
These glasses are commercially available and in use by the general population. They can be purchased online. This agrees with the guidelines stating that it is "…marketed directly to the end user (i.e., consumer) without the need for a prescription or any other order issued by a licensed eyecare practitioner…."
Also that they are"… Nonprescription devices are commonly sold or distributed as "over-the-counter" (OTC) devices."
Finally, they meet international UV and blue light safety standards, they are brighter than most indoor lighting but dimmer than outdoor light on a bright day."

Is the investigator hold the IDE for this device?

○ Yes ◉ **No**

If yes please provide a basis for risk level.

ID: Pro00003376 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
wearing bright light therapy glasses

Common Risks:

Infrequent Risks:
headache, eyestrain

Other Risks:
discomfort

ID: Pro00003376 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Privacy and confidentiality

Common Risks:

Infrequent Risks:

Other Risks:
As a part of this study, private information is being collected; for that reason there is a risk to the subject's privacy and confidentiality. The research staff will take every precaution to protect the subject's identity and the confidentiality of the information collected.

ID: Pro00003376 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Wearing ActiWatch

Common Risks:

Infrequent Risks:
skin irritation

Other Risks:
discomfort