STUDY TITLE: A pilot chronotherapeutic intervention to improve sleep following acute coronary syndrome: The SleepWell Study

Principal Investigator: Ari Shechter, PhD (as4874)

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1. Study Purpose and Rationale

The goal of this project is to conduct preliminary testing of a chronotherapeutic intervention targeting disturbed sleep in survivors of acute coronary syndrome (ACS). In Phase A (a single-arm open-label study), we will examine the feasibility of administering the study intervention for 1 month following an ACS event, and specifically, the acceptability, appropriateness, and usability of the intervention. In Phase B, we will conduct a parallel-arm randomized clinical trial (RCT) including active treatment and control arms to examine whether the intervention affects sleep.

Survivors of acute medical events often experience psychological distress including post-traumatic stress disorder (PTSD). Sleep disturbance is also common following acute medical events: our data indicate that short sleep duration occurs in about half of patients, with poor sleep quality seen in about a third of patients, in the month following hospital discharge for ACS. Sleep disturbances are a hallmark of most psychological disorders [1, 2], with up to 70-90% of individuals with PTSD reporting short duration and/or poor quality sleep [3, 4]. Sleep disturbance and psychological distress are likely in a reciprocal relationship. There is evidence for the causal role of sleep in directly influencing psychological symptoms [5, 6]. We have shown that in survivors of ACS, short sleep duration and poor sleep quality in the month following hospital discharge are each associated with subsequent PTSD at 6 months [7].

We will test the feasibility of a "combined chronotherapy" (CC) intervention consisting of morning BLT and evening BLB, administered daily for 4 weeks in patients who experienced ACS. This will be a two-phase pilot study. Phase A of the study will be a single-arm open-label study of the home-based CC intervention in 5 post-ACS patients. Phase B of the study will be a parallel-arm randomized clinical trial (RCT) in which 15 post-ACS patients will be randomized (using a 2:1 allocation) to active CC treatment or sleep hygiene education control group. In Phase A, we are primarily concerned with study feasibility, acceptability, appropriateness, and usability. In Phase B, we will additionally assess whether the intervention engages its proposed proximal target mechanism – sleep. Consenting participants who indicate habitual sleep that is of short duration and/or poor quality after ACS will be eligible for inclusion.

Primary Aim: Determine the feasibility of administering the CC intervention in this population. We will assess a) feasibility, b) acceptability, c) appropriateness, d) usability, and e) adherence of the 4-week CC intervention in ACS survivors with poor sleep.

Primary Aim will be tested by assessing the following measures:

(1) proportion of participants who complete the outcome assessments at study conclusion;

(2) proportion of participants who report scores ≥4 for their final rating of the intervention's feasibility;

(3) proportion of participants who report scores ≥4 for their final rating of the intervention's acceptability;

(4) proportion of participants who report scores ≥4 for their final rating of the intervention's appropriateness for improving sleep;

(5) proportion of participants who report total scores ≥68 for their final rating of the intervention's usability.

(6) proportion of who report administering the intervention (i.e., morning BLT and evening BLB) on ≥50% (and ≥75%) of the days throughout the 4-wk treatment period.

Secondary Aim 1: Determine whether the CC intervention engages its target mechanism: sleep. We will assess insomnia**,** sleep quality, and sleep duration at baseline and at the end of the 4-week intervention period, and will evaluate whether the CC intervention leads to greater changes in sleep-related outcomes relative to the control condition.

Secondary Aim 1 will be tested by assessing the following measures:

(1) Baseline-to-study conclusion change in insomnia severity (measured as the within-person difference in the total score of Insomnia Severity Index);

(2) Baseline-to-study conclusion change in global sleep quality severity (measured as the within-person difference in the total score of Pittsburgh Sleep Quality Index [PSQI]);

(3) Baseline-to-study conclusion change in sleep duration (measured as the within-person difference in the sleep duration subscale of the PSQI and actigraphy);

2. Study Design

To achieve these aims, we propose to enroll a total of 20 patients who have experienced an ACS event into this two-phase study. Phase A will be a single-arm open-label study of the home-based CC intervention in 5 post-ACS patients. Phase A will consist of English-speaking patients only. Phase A will primarily assess feasibility of enrollment and administering the intervention. After all 5 Phase A participants enroll and complete the study procedures, we will implement Phase B of the study. Phase B is an RCT in which 15 post-ACS patients will be enrolled and randomized (using a 2:1 allocation) to active CC treatment or sleep hygiene education control group. Phase B will consist of both English and Spanish-speaking patients. Participants cannot enroll in both Phase A and Phase B of this protocol.

Overview of Phase A Study Design:

Screening and consent:

Our recruitment strategy is multi-faceted and will include recruiting NYP patients who experienced an acute coronary syndrome (ACS) event within the past 3 months.

The study team will first confirm eligibility and obtain approval from the treating clinician as described in the Recruitment and Enrollment section to contact the patient and discuss the study. Patients who are interested and verbally consent to the study will undergo a pre-screening questionnaire to determine eligibility. All study procedures can occur in-person, over the phone, or online via Zoom (a web-based, HIPAA-compliant video-conferencing platform associated with Columbia University Irving Medical Center). Participants will complete a screening questionnaire to collect demographics, contact information, and participant sleep quality and habits. Additional eligibility will be determined during the screening questionnaire. Phase A participants will view two educational videos (~5 minutes each in length) that will provide information about the basics of sleep, the regulation of sleep (including aspects

of how the external light environment impacts sleep), the relationship of sleep with health, function, and well-being and tips for achieving good sleep. Participants will have the option of watching the educational videos during hospitalization or at home for those with internet access and participants will also be given a written summary of the contents of the educational videos.

Phase A participants will then be instructed on how to administer the CC intervention. The CC intervention will consist of a wearable light visor to administer the BLT each morning for 30 minutes after awakening, and the BLB glasses to be worn each night from 8:00pm to bedtime. Instructions on how to use the intervention devices will be offered in person during enrollment, over the phone, or online via Zoom after the participant has returned home.

Visit 1/Baseline: After verbally agreeing to participate and enroll in the study, Phase A participants will be scheduled for Visit 1 (either in person, telephone, or video on Zoom). During Visit 1, participants will complete a questionnaire battery on their sleep, PTSD symptoms, and cardiac anxiety. Participants who were unable to view the educational videos during enrollment will be able to do so during Visit 1.

Phase A participants will receive a wrist-mounted accelerometer (GENEActiv) designed to measure their sleep and physical activity. Coordinators will provide participants with the device and instruct participants to begin wearing it the day following Visit 1. They will be asked to wear this GENEActiv on their wrist for the next 4 weeks. Upon successful completion of Visit 1, Phase A participants will be asked to begin the intervention the following day, starting with BLT in the morning and BLB that night. Use of the intervention will continue daily for the next 4 weeks. Participants will also be asked to complete a paper-based sleep diary/daily-use log, where they will document the times they administered each of the interventions (i.e., time of starting and stopping BLT, time of donning and doffing BLB glasses, and times of going to bed and waking up). Research staff will contact participants weekly to collect the data that were entered in the sleep diary/daily use log, and also to ask about any adverse events or side effects (see below).

Visit 2: At the end of the intervention period (4 weeks after Visit 1), Phase A participants will complete Visit 2 in person, over the phone or via Zoom. During Visit 2, participants will complete measures of their sleep quality, cardiac anxiety, and PTSD symptoms. Additionally, they will complete questionnaires about feasibility, acceptability, appropriateness, and usability of the intervention.

Phase A participants will be provided with a pre-paid envelope which can be used to return the BLT visor, GENEActiv, exit interview, and the sleep diary/daily use log at the end of the study. If the exit interview is not returned, research staff may call the participant to administer the questionnaire over the phone (though this has no bearing on participant compensation).

Participation in Phase A is considered complete after Visit 2 and the return of the BLT visor, GENEActiv, sleep diary/daily use log, and the completion of the exit interview.

BLT Intervention: For Phase A participants, BLT will occur each morning throughout the 4-week intervention period starting after awakening and will last for 30 minutes. BLT will be administered via a Luminette 3 light therapy visor. The Luminette 3 is a visor worn above the eyes containing light emitting diode (LEDs) emitting a blue-enriched white light reflecting to the retina at 1,000 lux via a holographic system in order to ensure correct penetration into the eye without impeding vision. This range of light and intensity is sufficient to synchronize the circadian clock. Participants can engage in other activities (e.g., reading, getting dressed, eating) while the visor is worn.

BLB Intervention: For Phase A participants, BLB glasses (LowBlueLights Zzz Fitover Sleep glasses) will be worn each night throughout the 4-week intervention period, starting at 8:00 pm and removing the glasses immediately prior to going to sleep. This time corresponds with the onset of nocturnal melatonin

secretion and is therefore likely to encourage physiological mechanisms favoring sleep initiation and circadian stabilization. Participants will also wear the glasses during any nocturnal awakenings in which a light is turned on, an electronic device is used in bed, etc. Polycarbonate lenses of different colors selectively absorb wavelengths of visible light. Depending on the color of lenses used, this results in distinctive filtration of visible wavelengths that are further transmitted along the retinohypothalamic tract. The BLB lenses are orange lenses that filter out short-wavelength blue light, while allowing the other visible spectrum light to pass. The BLB lenses result in a reduction in melanopic irradiance (i.e., the light that affects sleep) of about 85%. The BLB lenses only make the overall light environment about 30% dimmer. Therefore, the BLB lenses are effective in blocking out most of the blue light in the visible environment that impacts sleep, but do not result in drastic overall dimming/darkening of the light environment.

Overview of Phase B Study Design:
Screening and consent:

Our recruitment strategy is multi-faceted and will include recruiting NYP patients who experienced an acute coronary syndrome (ACS) event within the past 3 months.

The study team will first confirm eligibility and obtain approval from the treating clinician as described in the Recruitment and Enrollment section to contact the patient and discuss the study. Patients who are interested and verbally consent to the study will undergo a pre-screening questionnaire to determine eligibility. All study procedures can occur in-person, over the phone, or online via Zoom (a web-based, HIPAA-compliant video-conferencing platform associated with Columbia University Irving Medical Center). Participants will complete a screening questionnaire to collect demographics, contact information, and participant sleep quality and habits. Additional eligibility will be determined during the screening questionnaire. After completing the screening questionnaire, Phase B participants will be randomized to either the CC intervention arm or sleep hygiene education control group (in a 2:1 ratio). All participants will view two educational videos (~5 minutes each in length) that will provide information about the basics of sleep, the regulation of sleep (including aspects of how the external light environment impacts sleep), the relationship of sleep with health, function, and well-being and tips for achieving good sleep. Participants will have the option of watching the educational videos during hospitalization or at home for those with internet access and participants will also be given a written summary of the contents of the educational videos.

Phase B participants randomized to the active CC arm will then be instructed on how to administer the CC intervention. The CC intervention will consist of a wearable light visor to administer the BLT each morning for 30 minutes after awakening, and the BLB glasses to be worn each night from 8:00pm to bedtime. Instructions on how to use the intervention devices will be offered in person during enrollment, over the phone, or online via Zoom after the participant has returned home.

Visit 1/Baseline: After verbally agreeing to participate and enroll in the study, Phase B participants will be scheduled for Visit 1 (either in person, telephone, or video on Zoom). During Visit 1, participants will complete a questionnaire battery on their sleep, PTSD symptoms, and cardiac anxiety. Participants who were unable to view the education videos during enrollment will be able to do so during Visit 1.

Phase B participants will receive a wrist-mounted accelerometer (GENEActiv) designed to measure their sleep and physical activity. Coordinators will provide participants with the device and instruct participants to begin wearing it the day following Visit 1. They will be asked to wear this GENEActiv on their wrist for the next 4 weeks. Upon successful completion of Visit 1, Phase B participants randomized to the active CC intervention will be asked to begin the intervention the following day, starting with BLT in the morning and BLB that night. Use of the intervention will continue daily for the next 4 weeks. Participants will also

be asked to complete a paper-based sleep diary/daily-use log, where they will document the times they administered each of the interventions (i.e., time of starting and stopping BLT, time of donning and doffing BLB glasses, and times of going to bed and waking up). Phase B participants randomized to the sleep hygiene education control arm will also be asked to wear a GENEActiv for 4 weeks and complete the sleep diary (indicating times of going to bed and waking up) each day. Research staff will contact all Phase B participants weekly to collect the data that were entered in the sleep diary/daily use log, and also ask the participants randomized to the active CC intervention about any adverse events or side effects (see below).

After enrollment, participants will be provided with a pre-paid package which can be used to return the BLT visor, GENEActiv, the sleep diary/daily use log, and the exit interview at the conclusion of Visit 2.

Visit 2: At the end of the intervention period (4 weeks after Visit 1), all Phase B participants (intervention and control arm) will complete Visit 2 in person, over the phone or via Zoom. During Visit 2, participants will complete measures of sleep quality, cardiac anxiety, and PTSD symptoms. Additionally, participants in the active CC intervention group will complete questionnaires about feasibility, acceptability, appropriateness, and usability of the intervention.

Phase B participants will be provided with a pre-paid envelope which can be used to return the study devices, the exit interview, and the sleep diary/daily use log after Visit 2. If the exit interview is not returned, research staff may call the participant to administer the questionnaire over the phone (though this has no bearing on participant compensation).

BLT Intervention: For all Phase B participants randomized to the active CC group, BLT will occur each morning throughout the 4-week intervention period starting after awakening and will last for 30 minutes. BLT will be administered via a Luminette 3 light therapy visor. The Luminette 3 is a visor worn above the eyes containing light emitting diode (LEDs) emitting a blue-enriched white light reflecting to the retina at 1,000 lux via a holographic system in order to ensure correct penetration into the eye without impeding vision. This range of light and intensity is sufficient to synchronize the circadian clock. Participants can engage in other activities (e.g., reading, getting dressed, eating) while the visor is worn.

BLB Intervention: For all Phase B participants randomized to the active CC group, BLB glasses (LowBlueLights Zzz Fitover Sleep glasses) will be worn each night throughout the 4-week intervention period, starting at 8:00 pm and removing the glasses immediately prior to going to sleep. This time corresponds with the onset of nocturnal melatonin secretion and is therefore likely to encourage physiological mechanisms favoring sleep initiation and circadian stabilization. Participants will also wear the glasses during any nocturnal awakenings in which a light is turned on, an electronic device is used in bed, etc. Polycarbonate lenses of different colors selectively absorb wavelengths of visible light. Depending on the color of lenses used, this results in distinctive filtration of visible wavelengths that are further transmitted along the retinohypothalamic tract. The BLB lenses are orange lenses that filter out short-wavelength blue light, while allowing the other visible spectrum light to pass. The BLB lenses result in a reduction in melanopic irradiance (i.e., the light that affects sleep) of about 85%. The BLB lenses only make the overall light environment about 30% dimmer. Therefore, the BLB lenses are effective in blocking out most of the blue light in the visible environment that impacts sleep, but do not result in drastic overall dimming/darkening of the light environment.

3. Study Procedures

Eligibility Criteria: A total of 20 ACS patients who report some degree of sleep disturbance (either insomnia symptoms or short sleep duration) will be offered an opportunity to enroll in the study. 5 ACS patients will be enrolled into Phase A and 15 ACS patients will be enrolled into Phase B.

Patients will be eligible for Phase A if they meet the following criteria: (1) 18 years of age or older, (2) can write, speak and read English, (3) provider and patient confirmed ACS, (4) ACS event occurred within the past 3 months, and (4) presence of insomnia symptoms based on the Insomnia Symptoms Questionnaire, or frequently (3-4 times per week) or always (5-7 times per week) experiencing short sleep duration of 6 hours or less per night.

Participants will be excluded if they have any of the following: (1) severe disabling chronic medical and/or psychiatric comorbidities determined on a case-by-case basis that prevent safe or adequate participation; (2) deemed unable to comply with the protocol (either self-selected or indicated during screening that s/he/they could not complete all requested tasks). This includes, but is not limited to, patients with a level of cognitive impairment indicative of dementia, patients with current alcohol or substance abuse, and patients with severe mental illness (e.g., schizophrenia); (3) unavailable for follow-up for reasons such as terminal illness and imminent plans to leave the United States (as we have migrant or mobile patients due to their citizenship and work issues); (4) Non-English speaking; (5) Lack of reliable phone or e-mail access; (6) History of bipolar disorder (manic episode can be triggered by BLT) or positive screen for bipolar disorder based on the Mood Disorder Questionnaire; (7) Eye disease including glaucoma or retinopathy (BLT contraindications); (8) Blindness; (9) Night shift work schedules; (10) taking any anti-depressant or anti-anxiety medications; (11) taking other medications that increase sensitivity to light (by self-report).

Please note, as of 7/25/2023, Phase A of the study is closed to enrollment. All participant follow-up is complete however, the study team will mail and/or email the Phase A PayCard Addendum letter to ensure they utilize any remaining study funds before the PayCard expires.

Patients will be eligible for Phase B if they meet the following criteria: (1) 18 years of age or older, (2) can write, speak and read English or Spanish, (3) provider and patient confirmed ACS, (4) ACS event occurred within the past 3 months, and (4) presence of insomnia symptoms based on the Insomnia Symptoms Questionnaire, or frequently (3-4 times per week) or always (5-7 times per week) experiencing short sleep duration of 6 hours or less per night.

Participants will be excluded if they have any of the following: (1) severe disabling chronic medical and/or psychiatric comorbidities determined on a case-by-case basis that prevent safe or adequate participation; (2) deemed unable to comply with the protocol (either self-selected or indicated during screening that s/he/they could not complete all requested tasks). This includes, but is not limited to, patients with a level of cognitive impairment indicative of dementia, patients with current alcohol or substance abuse, and patients with severe mental illness (e.g., schizophrenia); (3) unavailable for follow-up for reasons such as terminal illness and imminent plans to leave the United States (as we have migrant or mobile patients due to their citizenship and work issues); (4) Non-English and non-Spanish speaking; (5) Lack of reliable phone or e-mail access; (6) History of bipolar disorder (manic episode can be triggered by BLT) or positive screen for bipolar disorder based on the Mood Disorder Questionnaire; (7) Eye disease including glaucoma or retinopathy (BLT contraindications); (8) Blindness; (9) Night shift work schedules; (10) taking any anti-depressant or anti-anxiety medications; (11) taking other medications that increase sensitivity to light (by self-report).

After agreeing to participate in the study, participants will complete questionnaires to determine eligibility and collect sociodemographic factors (including age, gender, race, ethnicity, height, weight, partner status, education, work history, phone number, internet access, and home/mailing address). Further questionnaires specific to this study eligibility for the sleep complaint will assess presence of insomnia symptoms and/or short sleep duration. Insomnia is determined with a positive screen on the Insomnia

Symptoms Questionnaire. Habitual short sleep duration is determined by asking participants if they have slept 6 hours or less per night on any nights during the past month and if so, how often. Choices will include don't know, never (0 times per week), rarely (less than 1 time per week), sometimes (1-2 times per month), frequently (3-4 times per week) and always (5-7 times per week). Those indicating a positive screen for insomnia or "frequent" or "always" experiencing habitual short sleep duration will be eligible. Participants will also complete the Mood Disorder Questionnaire to screen for bipolar disorder (a contraindication for BLT), which will be an exclusion criterion.

After a participant's eligibility is confirmed, the research coordinator will schedule Visit 1 with the participant. Visit 1 can occur either via Zoom Video, telephone, or in person according to participant preference and in consideration of the current institution guidelines related to COVID-19 and social distancing. The research coordinator may provide study devices and materials (e.g., GENEActiv, BLT visor, BLB glasses, and device instructions) while they are still in the hospital, within the next 1-2 weeks post-discharge or at Visit 1 if in person. If Visit 1 is conducted remotely, study devices and materials will be sent to the participant's home address. Participants will view the educational videos (~5 minutes each in length) during the enrollment visit. Participants will also have the option of watching the educational videos at home if they have internet access.

Visit 1: A member of the research team (coordinator or PI) will meet with the participant via Zoom Video, in person, or over the phone to conduct a series of pre-intervention preparation components, which includes a set of baseline questionnaires on sleep, a questionnaire on PTSD symptoms, and a questionnaire on cardiac anxiety. They will then conduct the intervention setup. If participants were unable to watch the educational videos during the enrollment visit, they will have the opportunity to view the video during Visit 1.

Baseline Questionnaires (20 mins): Participants will complete a set of questionnaires to obtain the following measures: severity of insomnia symptoms (7-item Insomnia Severity Index, ISI), self-reported global sleep quality and sleep duration (9-item Pittsburgh Sleep Quality Index, PSQI), PTSD symptoms (17-item PTSD Checklist – Specific, PCL-5), cardiac anxiety symptoms (18-item Cardiac Anxiety Questionnaire, CAQ). Note: These assessments will be completed at baseline (i.e., before intervention begins), 4 weeks later at the end of the intervention period, and in participants who are in Phase B, 3 months after the end of the intervention period.

Between Visit 1 and Visit 2: For the 4 weeks between Visit 1 and Visit 2, participants in Phase A and participants in the active CC arm group of Phase B, will be instructed to wear the BLT visor for 30 minutes each morning starting after awakening, and to record the time they put them on and remove them each day in their sleep diary/use log. These participants will also be instructed to wear their BLB glasses beginning at 8:00PM each night until they go to sleep, and to record the time they put them on and remove them each day in their sleep diary/use log. Participants will also wear the glasses during any nocturnal awakenings in which a light is turned on, a light-emitting electronic device is used in bed, etc. All participants (in both arms) will also be instructed to record in their sleep diary/use log when they go to sleep and wake up each day. There will be weekly check-ins via telephone call by the research team to remind participants to use the devices and continue to complete the sleep diary/use log. During the check-ins, research staff will collect the data that has been entered in the sleep diary/use log. Additionally, research staff will ask on a weekly basis during the check-in call if the participant has experienced any adverse events or side effects. The research staff will ask "Over the past week, have you experienced any side effects from either of the treatments? If so, please tell us what you experienced. If possible, please tell us which portion of the intervention (light visor or orange-tinted glasses) you believe may have caused this side effect." Any reported adverse events or side effects will be reported to the study PI (Shechter), the study physician (Kronish) and the study safety officer (Sethi).

Visit 2: Post-Intervention Questionnaires (20 min): A member of the research team (coordinator or PI) will meet with the participant over the phone, via Zoom or in person to administer a series of questionnaires. All participants will complete the same set of baseline questionnaires and only the active CC intervention participants will complete valid, reliable, and pragmatic 4-item surveys on the acceptability, appropriateness, and feasibility of the intervention: (1) Acceptability of Intervention Measure (AIM), (2) Intervention Appropriateness Measure (IAM), and (3) Feasibility of Intervention Measure (FIM).[18] They will also complete the System Usability Scale to assess the intervention usability. The participant will return study devices and materials (in person, if this visit is conducted as such) or will be instructed to return these items by mail using a pre-paid envelope. The items which will be returned include the BLT visor, the GENEActiv, the sleep diary/use logs, and the exit interview.

3. Compensation

Participants will be reimbursed for their time participating in the study in the form of PayCards.

Phase A: Participants in Phase A will receive $40 for successful completion of Visit 1. They will receive a second payment of $40 for completion of Visit 2. They will receive a third payment of $50 for returning the GENEActiv, sleep diary/use log and the BLT visor. All 3 items must be returned in order to be compensated. Compensation for completing all study procedures in Phase A is up to $130 (including participation and returning study materials/devices).

Phase B: Participants in Phase B will receive $40 for successful completion of Visit 1. They will receive a second payment of $40 for completion of Visit 2. They will receive a third payment of $50 for returning the GENEActiv, sleep diary/use log and the BLT visor. Please note, the BLT visor return is only applicable to the intervention group but additional compensation is not provided for the return of the visor. Participants will receive $20 for completing the 3-month follow-up assessment (PCL-5 and PSQI questionnaires). Compensation for completing all study procedures in Phase B is up to $150 (including participation and returning study materials/devices).

All Phase A and Phase B participants will be permitted to keep the study-provided BLB glasses.

Please note, participants who are determined to be ineligible at any time during the screening questionnaire will not be compensated.

Please note, due to the change in vendor for Columbia University PayCards, current and past participants of both Phase A and Phase B who receive(d) a Bank of America PayCard, will receive a PayCard addendum letter by email and/or mail to ensure they are aware of the card expiration date.

4. Risks

Bright light therapy (BLT): Although extremely unlikely, participants may encounter risks that any person may encounter when engaging in treatment with BLT. BLT side effects can rarely include eye strain, headache, nausea, irritability or agitation. These side-effects are expected to be mild, and to be reversible with cessation of therapy.

Participants are encouraged to stop or reduce their use of light therapy if they experience any side-effect that they perceive as severe. A study physician and a sleep expert (the study PI) will be available by email for questions about side-effects during business hours and participants will also be able to contact

their personal physicians as they would in clinical practice if any questions pertaining to study light therapy arise. Research coordinators will review phone calls and emails at least twice per day and will relay any questions that could relate to patient safety to the study physicians. The presence of adverse events or side effects related to treatment will be assessed on a weekly basis, via phone calls made to participants by research staff.

Blue light blocking (BLB): The lenses in the glasses to be used are non-significant risk. Lenses are available in a variety of tints to reduce glare, screen hazardous radiation, or to provide other task specific filtration. The BLB lenses are orange lenses that filter out short-wavelength blue light, while allowing the other visible spectrum light to pass. The BLB lenses result in a reduction in melanopic irradiance (i.e., the light that affects sleep) of about 85%. The BLB lenses only make the overall light environment about 30% dimmer. Therefore, the BLB lenses are effective in blocking out most of the blue light in the visible environment that impacts sleep, but do not result in drastic overall dimming/darkening of the light environment. The lenses are commercially available in the United States. All participants in Study 1 as well as the active CC group in Study 2 will use the BLB glasses each night throughout the 4-week intervention period, starting at 8:00pm and removing the glasses immediately prior to going to sleep. This time corresponds with the onset of nocturnal melatonin secretion, and is therefore likely to encourage physiological mechanisms favoring sleep initiation and circadian stabilization. Patients will also wear the glasses during any nocturnal awakenings in which a light is turned on, a light-emitting electronic device is used in bed, etc. We have conducted pilot studies with this same intervention and there have been no adverse events or harms reported by participants. There are no known risks associated with use of BLB lenses during the night. Since the amber BLB lenses do not produce a substantial dimming/darkening of the environment they are unlikely to increase risk of accidents or falls.

Other potential risks/difficulties with this protocol:

Questionnaires: The proposed questionnaires have been extensively used in clinical research and during routine clinical practice, and pose no risk to the subjects. The questions asked and the thoughts evoked during the course of this research study pose minimal risk of psychological discomfort. Participants will be made aware of these risks, and will be assured they can terminate their participation in the study at any time without penalty.

Confidentiality: A potential risk from this study is the violation of the participant's privacy, since patient medical information will be used as a source of data. Special protections against this risk be provided.

There are no known long-term risks from any study activities.

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