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Official Title: Optimizing adherence to the treatment of sleep apnea among patients with stroke undergoing inpatient rehabilitation

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Stroke and CPAP Outcome Study 3 (SCOUTS 3) Protocol

Background and rationale

Stroke is the leading cause of adult, serious long-term disability in the United States.[1] The burden of stroke-related impairments remains unacceptably high and few treatments are proven to improve recovery.[2,3] An estimated 70% to 90% of stroke survivors have obstructive sleep apnea (OSA).[4-6] Compared to those without OSA, stroke patients with OSA have worse recovery after inpatient rehabilitation (IPR),[7,8] 40% longer IPR stays,[8] a 100% increased risk of non-fatal cardiovascular events,[9] particularly recurrent stroke,[9,10] and a 75% increased risk of early death.[11] Observational data suggest that continuous positive airway pressure (CPAP), the first-line treatment for OSA, holds promise to improve stroke recovery and reduce stroke recurrence.[9,12-14] However, poor CPAP adherence has undermined pilot trials, limiting the ability to assess efficacy[4,15,16] and leading multicenter stroke trials to exclude initially poorly adherent participants.[17,18] Individualized and theory-based behavioral interventions to improve CPAP adherence have shown benefits in the general population,[19-25] though have not been rigorously evaluated among stroke patients. Given fundamental differences and worse CPAP adherence in stroke patients compared to general OSA patients, behavioral interventions to increase CPAP use must be adapted for and tested among stroke patients.

Our single arm SCOUTS2 pilot study showed some success of a combination of 1) early CPAP technical support, 2) motivational enhancement therapy (MET) directed toward the patient, and 3) follow-up phone interviews to provide adherence feedback and enhance self-management skills, on CPAP use in post-stroke patients.[26] To maximize adherence and develop a more generalizable protocol, additional work is needed to adapt and supplement these interventions for stroke patients, who often have cognitive, language, and physical dysfunction. The goal of this application is to adapt the three promising and scalable interventions of the SCOUTS2 pilot study[26] for stroke patients with OSA identified in an IPR setting, and to supplement this with MET directed toward a CPAP partner and mobile health (mHealth). Using self-determination theory (SDT), we will adapt these intervention components using a human-centered design approach to create a package of interventions to improve CPAP use. Following adaptation, we will (in a separate, future, IRB application) rigorously test the effectiveness of this multicomponent intervention on CPAP adherence among stroke patients within a randomized controlled trial (RCT).

Goals and objectives

Aim 1a: To adapt and refine the existing SCOUTS2 adherence interventions (CPAP technical support, MET, and phone follow-up) for stroke patients with OSA. Disability related to stroke, including arm/hand, language, and cognitive dysfunction, affects stroke patients' ability to engage in interventions used in the general population to increase CPAP use. We will adapt CPAP adherence interventions iteratively, with input from stroke patients treated with CPAP on IPR, to increase CPAP use.

Aim 1b: To develop theory-driven, tailored mHealth messages to motivate stroke patients to use CPAP. Using SDT, we will develop and adapt a library of tailored messages designed to improve perceived autonomy, relatedness, and competence regarding CPAP use after stroke. Tailored text, e-mail or phone messages, delivered via a web-based application, will be refined after initial pretesting among stroke patients.

Aim 1c: To implement MET to partners of stroke participants treated with CPAP. Using MET counseling sessions during IPR, we will train CPAP partners to deliver autonomy-based support to patients with stroke.

Significance

Aim 1a. Adaptation of existing intervention components

The three existing behavioral interventions in the proposed study have been shown to result in significant improvements in CPAP adherence among the general, non-stroke population with OSA.[20,24,25,27-29] Using a health behavior change framework, we plan to adapt the adherence interventions for stroke patients. The adaptations in content and delivery will optimize the interventions for the unique needs and barriers faced by stroke patients, giving the greatest chance for a potent adherence intervention. The intervention deliverables will be available for immediate application to clinical practice and for future studies testing the benefits of CPAP

on stroke-related outcomes. The lessons from the iterative approach in the proposed human-centered design may also be valuable in developing future stroke interventions in other fields outside of OSA treatment.

Aim 1b. Development of theory-driven, tailored mHealth messages
Interventions with mHealth feedback have been shown to be effective when adapted to stroke patients for other adherence outcomes,[30,31] though have yet to be adapted for post-stroke CPAP adherence. We seek to adapt existing CPAP support messages used for OSA patients non-adherent to CPAP,[32] in content, style and format to be consistent with SDT and be applicable and accessible to the stroke population. The adaption, implementation and refinement through pretesting of a mHealth library of tailored messages intended to motivate CPAP use after stroke will serve as a guide to researchers and clinical providers in this field and potentially in other areas of stroke research.

Aim 1c. Implementation of MET to CPAP partners of study participants
A thematic analysis of data from our pilot study suggests that collaborative CPAP partner support could serve as a facilitator for CPAP adherence,[33] as noted in the general OSA population.[34] The addition of MET sessions with CPAP partners with the goal of empowering the partner to provide sustained autonomy-based support to the stroke patient would provide much-needed evidence for a novel adherence intervention.

Study design and methods

Overview
Stroke patients on Neurology and PM&R will be screened for eligibility and interested eligible patients will be consented. While on either of two IPR units at the University of Washington (UW) or Harborview Medical Center (HMC), consented participants will be tested for OSA, and then, within a single-arm study, exposed to a multicomponent CPAP adherence intervention, beginning during IPR and extending for 3 months. Throughout the intervention exposure, participants' CPAP use will be monitored, and input regarding the intervention will be sought from the participants, CPAP partners (ideally bedpartners, but if not available, then those who can provide support to the patient), and the research team implementing the intervention (sleep technologist, research coordinator, sleep coach, nurses). Semi-structured interviews will take place to obtain formal feedback from participants at three time points during their 3-month intervention. Data will be reviewed in meetings with the study team and a patient advisory board, and adaptations will be devised and then implemented within the next batch of Aim 1 participants. Through this iterative process that includes input from important stakeholders, the behavioral intervention will be adapted for use among stroke patients.

Participants and eligibility criteria
60 adult patients recovering from acute stroke within the past 30 days will be recruited during inpatient acute or IPR (2 IPR units) stroke stays.

Inclusion criteria include:
1. Age 18 years or older

2. Head CT or brain MRI demonstrating an acute ischemic infarction or intraparenchymal hemorrhage within past 30 days
3. Person providing consent (patient or legally authorized representative) able to be consented in English or Spanish.

Exclusion criteria include:
1. Unable to obtain informed consent from participant or surrogate in English or Spanish
2. Incarcerated
3. Known pregnancy
4. Current mechanical ventilation, tracheostomy or supplemental oxygen use > 4L/min
5. Current use of positive airway pressure or use within 14 days prior to stroke
6. History of pneumothorax, bullous emphysema or other serious co-morbid conditions which limit CPAP use
7. Stroke related to tumors, vascular malformations or subarachnoid hemorrhage

8. Active use of sedative drugs that can interfere with testing for obstructive sleep apnea (OSA) including any benzodiazepine, barbiturate, general anesthesia, or conscious sedation within the prior 48 hours of the planned portable sleep apnea study
9. Anticipated inpatient rehabilitation length of stay < 3 nights
10. Co-morbid conditions that limit OSA testing or CPAP use in the judgement of the study team

Recruitment and consent of study participants
Patients: We will review medical records of the acute stroke and/or IPR patients to identify those who may be eligible to participate. We request a HIPAA waiver for this chart review. Patients will be approached in person. The study will be described by a study team member, which may be supplemented by an introductory video (appended). All questions will be answered. Before participation in any study related activity, written informed consent will be obtained from the participant or legally authorized representative (LAR). Assent will be used if appropriate for those who need an LAR. Written documentation of assent will not be collected. eConsent may be used. A copy of the informed consent instrument will be provided to each participant.

CPAP partners: Partners will be selected by participants as the bedpartner or the person most likely to be able to provide support for CPAP use. The purpose of the study will be described to the CPAP partner, in person, by secure video, or by phone. All questions will be answered. Written informed consent will be obtained directly from the partner. eConsent may be used. Not all participants will identify a CPAP partner for participation.

Identification of advisory board members and clinical team members
The advisory board members may include previous participants in the study team's research on CPAP for stroke patients. No advisory board member will be a current participant in one of the study team's studies. CPAP partners of previous study participants may also be included in the advisory board. Advisory board members are not subjects of the proposed research. They will be used for consultation and feedback on study design and implementation issues. Similarly, clinical and research team members will be identified based on their contact with a research subject. They may be asked questions about the implementation of the study procedures but are not research subjects themselves.

Baseline and rehabilitation discharge assessments
After consent, health information including medical history, medications, stroke type (ischemic vs ICH) and severity, and stroke treatments will be obtained. Questionnaires and stroke evaluations will be assessed by a certified investigator, including baseline stroke severity (the NIH Stroke Scale, appended), functional disability (mRS-9Q, appended), pre-stroke symptoms of sleep apnea (the Berlin Questionnaire, appended), questions about CPAP beliefs (Apnea Beliefs Scale, appended), and questions about pre-stroke sleep duration and quality (see below). Near the day of inpatient rehabilitation discharge, study staff will repeat the the NIHSS. In cases of aphasia or cognitive deficits, the participants' proxy, which can include the bedside nurse, may be asked to help complete the assessment. We anticipate the time to complete assessments will be between 10 to 15 minutes.

Sleep duration:
During the month prior to the stroke, excluding naps, how many hours of actual sleep did you get at night (or day, if you work at night) on average?

Sleep quality:
During the month prior to your stroke, how would you rate your sleep quality overall? (Likert scale, with 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor).

Screening for OSA
A single-night portable home sleep apnea test (HSAT) using the Nox T3s sleep apnea test will be obtained in all participants idealy on night 1 after enrollment, assessing for the presence of OSA, defined as a respiratory event index (REI), the number of apneas and hypopneas per hour of recording, ≥ 5 with 3% desaturation criteria for hypopneas,[35,36] and the absence of predominant central sleep apnea (CSA, absence defined as central apnea index < 50% of total REI). The Nox T3s components include the T3s device, a nasal pressure cannula, wrist-based oximeter unit with finger probe, and two respiratory inductance plethysmography (RIP)

belts for the chest and abdomen to assess respiratory effort, as recommended by the AASM.[37] Participants who do not meet criteria for a diagnosis of OSA and those with predominant CSA will be excluded and the results will be given to the study participant and the IPR team caring for the participant. The study may be repeated if necessary to obtain the needed data.

Nox T3s data will be uploaded for review by a scoring team at Elite Sleep Professionals, or similar organization of registered polysomnographic technologists. The sleep apnea tests will not be reviewed by a physician. Study participants who are eligible for the CPAP adherence intervention will not be told of the severity of OSA until completion of study participation so that any decision to adhere to CPAP is not influenced by OSA severity from a single-night HSAT, which typically underestimates the disease severity.[38-40] Nox T3s reports will be provided to the participant and the clinical team at the time the participant exits participation in this study. Based upon prior studies in this population[4-6 17] we anticipate that about 20% of the 60 participants with completed OSA tests may be excluded based on these criteria, yielding approximately 48 participants for the Aim 1 adherence program adaptation.

Existing SCOUTS2 adherence intervention, implemented for participants
Participants who meet criteria for a diagnosis of OSA will be set up with CPAP on the next available night after the HSAT by study staff led by the study's sleep technologist, who will provide mask fitting and CPAP exposure during the daytime prior to the 1st night of CPAP use. The CPAP device (AirSense™ 11 AutoSet, ResMed) includes an auto-titrator that can adjust the delivered pressure between 4 to 20 cm of water to eliminate obstructive events. Pressure settings may be narrowed. All Aim 1 participants may receive 3 basic supportive treatments to approximate the care provided after a sleep clinic or in-hospital diagnosis of OSA: 1) education on OSA and the importance of CPAP treatment for improved sleep and vascular health; 2) standard inpatient CPAP support from respiratory therapy and IPR nurses for mask placement and adjustments; and 3) outpatient access to a national durable medical equipment (DME) company, for issues that may arise with CPAP at home. Participants may also receive 3 behavioral adherence interventions:

(i) CPAP technical support: Initial mask fitting will be completed by the study's sleep technologist on the IPR unit rather than by respiratory therapists, if possible. The study's sleep technologist will initially ensure adequate mask fit without air leak, trial different CPAP mask interfaces for patient comfort and provide education or adjustments to address adherence issues.[41] A member of the SCOUTS3 team led by the study's sleep technologist may then meet ideally daily with participants over the first three days of initiating CPAP to assess perception of treatment and symptom-related treatment response;[42,43] complete a 7-item questionnaire of common adverse symptoms associated with CPAP (appended);[44] make mask type/size or device adjustments, as needed; and provide training to participants and CPAP partners to improve skills involved with mask placement and device maintenance. For participants with non-acceptance of CPAP over the first night, a standardized desensitization program may be implemented by the sleep technologist. Persistent problems with CPAP use, mask fit, or high residual respiratory events may be discussed between the sleep technologist and Co-I Dr. Billings, a board-certified sleep medicine physician.

(ii) MET with individualized verbal and written feedback: In-person MET sessions during IPR and telephone sessions after IPR discharge will also be completed by a sleep coach. The in-person MET sessions will occur typically within 3 days of starting CPAP and again after about 3 to 5 days if the participant remains on IPR. The 1st in-person MET session will focus on subjective assessment of CPAP use, barriers and facilitators of use, assessment of motivation and confidence for use, decisional balance and feedback. The 2nd MET session will focus on subjective appraisals of CPAP adherence, reinforcement of changes with treatment, and review of treatment goals. The post-discharge MET phone sessions will begin approximately two weeks after discharge, then monthly during the 3 months of CPAP therapy and will last approximately 30-60 minutes. Consistent with prior research in stroke patients on the dose of MET needed, the goal will be to deliver a total of 4 hours of MET counseling over the 3 months of CPAP therapy.[45,46] In the spirit of MET, the participants will dictate the pace of the sessions. We may alter the frequency, duration, and content of the sessions based on participant feedback.

For aphasic participants, the sleep coach will use published recommendations to adapt MET sessions for people with stroke-related aphasia, including strategies to enhance language comprehension and facilitate

expression [47-49] and patient-specific strategies recommended by the study participant's speech-language pathologists on the IPR unit. Patients with more severe aphasia with complete incomprehension are not typically admitted to IPR. The MET for aphasic participants will include two face-to-face sessions during IPR, each lasting about 30 to 60 minutes, and one ~20-minute phone session with inclusion of the CPAP partner, when possible. Face-to-face sessions will incorporate MET components used in non-aphasic participants but will focus on information exchange through visual aids, exploring potential barriers to CPAP use through enhanced communication and goal setting.[50] MET sessions may be bolstered by individualized written and visual feedback regarding the OSA testing, potential vascular consequences, and CPAP download data illustrating the effectiveness of treatment in reducing respiratory events.

Fidelity for the MET sessions will be evaluated in multiple ways. Some MET sessions will be recorded, uploaded for processing, and reviewed via the cloud-based and HIPAA-compliant Lyssn platform, which supports training and quality assurance by providing automated transcription and fidelity feedback from a session recording. The recordings are processed through the system's artificial intelligence analytics tool and automatically transcribed via speech-to-text transcription. The platform will produce reports of each session, including general and specific metrics for MET. The sessions will be evaluated through the Lyssn platform and feedback reports will be provided to the sleep coach. Consultants, Dr. Barbara McCann and Dr. Mark Aloia, may also review ~20% of the counseling sessions for non-aphasic participants utilizing a MET checklist to provide feedback to the sleep coach via quarterly virtual meetings.[20] Co-I Dr. Bombardier, who has adapted motivational counseling to improve adherence to therapy in other populations,[51] may review ~20% of the recordings of aphasic participants utilizing a modified MET checklist.

(iii) Phone follow-up for adherence feedback and self-management skills: The research coordinator will call participants approximately monthly to encourage use and resolve problems with therapy.[21] In an effort to improve CPAP tolerance and minimize side effects, the research coordinator will provide encouragement and basic education, review persistent outpatient CPAP-related issues with co-I Dr. Billings and refer participants toa durable medical equipment (DME) company when needed for device or mask adjustments.

90-day end-of-study assessment
After approximately 90 ± 14 days from enrollment, phone evaluations by study will be obtained by a certified investigator, including the mRS-9Q, questions about sleep duration and quality, and the Zarit Burden Interview. We anticipate the time to complete assessments will be between 10 to 15 minutes.

AIM 1: SCOUTS3 Single-arm study— Research design and methods overview.

Visit 1: (in-hospital and in-person during inpatient rehabilitation)

- Stroke participants will be asked to provide contact information for themselves and their primary caregiver or family member.
- Contact information will be obtained for a "CPAP partner," either a bed partner or caregiver who can assist with CPAP use
- A brief (~10 minutes) set of questionnaires and assessments will be obtained for baseline stroke severity and functional disability by a certified investigator.
- Neck circumference will be measured by a study team investigator.
- The medical record will be reviewed and key data extracted, including medical history, neuroimaging and any note for common implantable devices that can be affected by magnets (pacemakers and intracranial shunt).
- Participants will be screened for any personal or bed-partner medical implants that can be affected by magnets (i.e., pacemakers, implantable cardioverter defibrillators (ICD), neurostimulators, cerebrospinal fluid (CSF) shunts, insulin/infusion pumps) or metallic implants/objects containing ferromagnetic material (i.e., aneurysm clips/flow disruption devices, embolic coils, stents, valves, electrodes, implants to restore hearing or balance with implanted magnets, hearing implants, metallic splinters in the eye). If participant has any such medical implants or metallic implants/objects, a note will be made in the database to

refrain from using magnet-containing masks.

Visit 2: (in-hospital and in-person during inpatient rehabilitation)

- The participant will be set-up by a study team member with a single-night sleep test on night 1 after enrollment to assess for the presence of OSA using the Nox T3 or T3s™ portable home sleep apnea test monitor (includes the T3/T3s device, a nasal pressure cannula, wrist-based oximeter unit with finger probe, and two respiratory inductance plethysmography belts for the chest and abdomen). The Nox T3 may be repeated up to 2 times in the rare cases of failed recordings or self-reported poor sleep if the participant is willing to repeat the study.

Visit 3: (in-hospital and in-person during inpatient rehabilitation)

- Participants will be informed of their eligibility in the study approximately 1 day after the sleep apnea study (if the respiratory event index or REI, the number of apneas and hypopneas per hour of recording, ≥ 5 with 3% desaturation criteria for hypopneas, and the absence of predominant central sleep apnea, defined as central apnea index < 50% of total REI).
- Study participants will be informed the day after the testing but will not be told of the severity of OSA until completion of study participation so that any decision to adhere to CPAP is not influenced by OSA severity.

Visit 4: (in-hospital and in-person during inpatient rehabilitation)

- Participants with a diagnosis of OSA will be set up with CPAP on the next available night after the sleep apnea test by the study's sleep team led by the study's sleep technologist, who will provide mask fitting and CPAP exposure during the daytime prior to the 1st night of CPAP use.
- Magnetic masks will not be used in participants with implantable devices or metallic objects affected by magnets.
- The CPAP device (AirSense™ 11 AutoSet, ResMed) includes an auto-titrator that adjusts the delivered pressure between 4 to 20 cm of water to eliminate obstructive events.

Visits 5-7 (in-hospital and in-person during inpatient rehabilitation)

- Study's sleep team will meet daily with participants over the first three days of initiating CPAP to assess perception of treatment and symptom-related treatment response; complete a 7-item questionnaire of common adverse symptoms associated with CPAP; make mask type/size or device adjustments, as needed; and provide training to participants and CPAP partners to improve skills involved with mask placement and device maintenance.

Visit 8 (in-hospital and in-person during inpatient rehabilitation)

- Interview with participants and, if available, CPAP partners after 3 days to evaluate impressions of CPAP technical support
- Interviews will last approximately 30 minutes

Visit 9 (in-hospital and in-person during inpatient rehabilitation)

- An in-person Motivational Enhancement Therapy (MET) session will occur by a trained sleep coach within the first the first week of starting CPAP and again within a week if the participant remains on IPR. Initial session will last approximately 60 minutes for non-aphasic participants.
- For aphasic participants, the sleep coach will use published recommendations to adapt MET sessions for people with stroke-related aphasia, including strategies to enhance language comprehension and facilitate expression and patient-specific strategies recommended by the study participant's speech-language pathologists on the IPR unit. These sessions will focus on information exchange through visual aids, exploring potential barriers to CPAP use through enhanced communication and goal setting and will last 30-60 minutes
- An in-person or phone MET session will also be conducted with a CPAP partner, when available. With participant permission, MET sessions for CPAP partners will focuse on the OSA diagnosis, standard therapy for OSA and ways the CPAP partner can provide support for the participant

Visit 10 (in-hospital and in-person during inpatient rehabilitation)

- A second in-person Motivational Enhancement Therapy (MET) session will occur within a week if the participant remains on inpatient rehabilitation.

Visit 11 (in-hospital and in-person during inpatient rehabilitation)

- The research coordinator will meet with participants to assist in registering for the mobile health (mHealth) ResMed myAir app, demonstrate use of the app, and provide increased support to participants if needed, including those with deficits related to dexterity, aphasia and cognition. Increased efforts will be made with aphasic participants or those with other cognitive or dexterity deficits, including frequent coaching during IPR, utilizing patient-specific strategies recommended by the IPR unit's speech-language pathologists and working with caregivers when possible.
- Participants limited by dexterity issues will be trained to use a stylus. Screen zoom features will be implemented if the participant has difficulty seeing due to presbyopia. Tablets or internet card-enabled devices will be provided to those without access to smartphone, tablet or home internet service.

Visit 12 (in-hospital during inpatient rehabilitation)

- At the end of inpatient rehabilitation, a brief (~10 minutes) set of questionnaires and assessments will be repeated for baseline stroke severity and functional disability by a certified investigator.
- Interview with participants and, if available, CPAP partners will be conducted to evaluate impressions of the inpatient MET sessions and mHealth interventions

Visit 13-14 (by phone to participant's home or other facility after discharge from inpatient rehabilitation)

- A post-discharge MET phone sessions will occur approximately two weeks after discharge from the inpatient rehabilitation unit and last approximately 30-60 minutes.
- A repeat and final MET phone session will occur approximately 1 months after the prior one and will last approximately 30-60 minutes

Visit 15-16 (by phone to participant's home or other facility after discharge from inpatient rehabilitation)

- The research coordinator will call participants approximately monthly after discharge from the inpatient rehabilitation unit (on 2 occasions over the 3-month study treatment period) to encourage use and resolve problems with therapy.

Visit 17 (by phone to participant's home or other facility after discharge from inpatient rehabilitation)

- After approximately 90 ± 14 days from enrollment, a certified investigator will repeat questionnaires and assessments (~10 minutes) for baseline stroke severity and functional disability.
- At the end of the 3-month treatment period, a repeat interview with participants and, if available, CPAP partners will be conducted to evaluate impressions of the outpatient MET sessions and mHealth interventions

Between visits at 11 and 16, participants will continue to receive messages through the ResMed myAir app (11 messages over the first 60 days of use that are time-based and designed to provide education to make CPAP more comfortable and build confidence). These messages are presented by email, but texting can be selected by the participant. Supplemental to myAir, the research team will also send CPAP support messages using simple language (8th grade level) which will be tailored to the participant's current CPAP use. Message delivery will be implemented through a web-based program designed to deliver CPAP care management, via the participant's preferred mode of delivery (text, email, or automated phone messages).

MET sessions recordings will be uploaded into the HIPAA compliant Lyssn platform for evaluation.

If any component of the adherence intervention is not delivered, it will not be reported as a protocol violation/deviation as this is an expected part of this project which is designed to adapt the intervention protocol.

Adaptation and refinement

Our adaptation approach will be guided by the simple and iterative Discover, Design and Build, and Test (DDBT) framework for psychosocial and health behavior change intervention development and adaptation stemming from a human-centered design perspective.[52] The DDBT approach aims to maintain the core components of interventions while improving usability for specific populations (here, stroke patients with OSA) and implementation outcomes in specific settings (here, acute IPR and in the home).[53-59] (i) The **Discovery** phase seeks to identify facilitators and barriers of contextual usability among stakeholders. This phase will initially involve interviews of participants, their CPAP partners, when available, and intervention staff (sleep technologist, sleep coach, and research coordinator) to explore CPAP barriers and facilitators through structured and open-ended feedback opportunities. Interviews with participants and CPAP partners lasting approximately 30 minutes will occur typically after the first 3 days of CPAP technical support, at the end of IPR to evaluate the MET and mHealth interventions and at the end of the 3-month treatment period to assess outpatient and prior IPR treatments. Interviews with the intervention staff, occurring quarterly from the beginning to the end of aim 1 and lasting approximately 20 minutes, will focus on feedback about the content, process and feasibility of each intervention.[60] The study team will analyze after about 6 months of recruitment the participant interviews and adherence patterns after completion of an estimated 15 of the 3-day interviews, 13 of the end-of-IPR interviews and 8 of the 3-month interviews. Analysis of participant, CPAP partner and staff interviews along with adherence and engagement data will feed Discovery. (ii) The **Design and Build** phase uses the Discovery information to iteratively refine the intervention and implement strategies to address the unique barriers faced by stroke IPR patients as they work to engage with the intervention components to successfully and consistently use CPAP. Refinements in Aim 1 will involve iterative and collaborative content and delivery adaptation by the study team based on the Discovery data above. The study team will present adaptation proposals to a stroke patient advisory board. This may be repeated as needed. After approximately 6 months of recruitment, researchers will review interview feedback with the patient advisory board and present proposed adaptations to the interventions. The patient advisory board will review these proposals and make recommendations for adapting the behavioral interventions. (iii) The **Test** phase evaluates the intervention's user experience, satisfaction, and implementation outcomes. The adapted intervention will be tested on the next 12 participants over an estimated 4 months. The iterative DDBT cycle will be repeated, with results being presented again to the patient advisory board with additional adaptation feedback, as needed. We will conduct 'think-aloud' cognitive interviews with the next approximately 5 participants while they interact with the intervention components to elicit organic reactions to the intervention and reveal any final needed adaptations.[61,62]

mHealth component of the intervention

In the proposed study, mHealth support will include two key features: implementation of the ResMed myAir app and implementation of tailored and targeted messages for participants.

myAir: The myAir app, free of charge to patients with the AirSense 11 CPAP device, allows self-tracking of adherence and participation in decision making and problem solving[63,64] through three integrated services: (1) self-tracking of CPAP use: participant's data from the prior night's use including hours used, mask seal, residual AHI, mask on/off events, and a summary score based on these metrics (0-100 scale). (2) Coaching and reinforcement messages: 11 messages over the first 60 days of use that are time-based and designed to provide education to make CPAP more comfortable and build confidence. Additionally, myAir provides event-based messages including the following: praise message (based on hourly usage), alert messages (based on low use), leak alerts and suggestions (based on mask leaks), AHI alerts (based on high residual AHI), no data alerts (for no data during 5 of 7 days), and badges (awards for reaching usage milestones). These messages are presented by email, but texting additionally can be selected by the participant. (3) Educational tools: the myAir sleep library provides instructions and videos to assist with therapy. Participants will be encouraged to use the app during IPR. Research coordinators will assist in registering for myAir, demonstrate use of the app, and allow participants to practice accessing data through the app and messages through their email. Increased efforts will be made with aphasic participants or those with other cognitive or dexterity deficits, including frequent coaching during IPR, utilizing patient-specific strategies recommended by the IPR unit's speech-language pathologists and working with caregivers when possible. Participants limited by dexterity issues may be trained to use a stylus. Tablets or internet card-enabled devices will be loaned to those without access to smartphone, tablet or home internet service.

Tailored messages: Supplemental to myAir, we will again use DDBT to adapt, implement, and refine through pretesting the use of mHealth messages designed to motivate CPAP use specifically in stroke patients. A library of CPAP support messages using simple language will be created and/or adapted from a prior intervention,[32] to be consistent with SDT, targeted to stroke patients, and tailored to current CPAP use. Message delivery will be implemented through a web-based program to deliver CPAP care management, via the participant's preferred mode of delivery (text, email, or automated phone messages). CPAP data will be provided by ResMed and integrated within REDCap. Message logic will be programmed into REDCap. REDCap will be integrated with the Mosio platform which will be used to send the text messages. Two-way texting will also be possible through Mosio's platform for communication between study staff and participants. Mosio is HIPAA-compliant and compliant with FDA 21 CFR PART 11.

Implementation of MET to CPAP partners of participants with stroke. We plan to implement MET for CPAP partners. Partners will be selected by participants as the bedpartner or the person most likely to be able to provide support for CPAP use. MET sessions for CPAP partners will take place in-person during IPR visits, or by phone or secure video. The initial session will focus on background information, including (with participant permission) the OSA diagnosis, standard therapy for OSA and ways the CPAP partner can provide autonomy support for the participant.[50] Not all participants will identify a CPAP partner. Partners will be taught to deliver autonomy support to the stroke participant to help support his/her CPAP use.

Data collection

Study personnel will enter data into a UW REDCap database. REDCap is a HIPAA-compliant, secure, easy to use online data capture platform. The REDCap platform can support processes that are 21 CFR part 11 compliant. Data integrity and completeness are monitored by REDCap and enhanced by flags for missing data, range checks, and frequent quality control reports. Paper documents will be kept in a locked office.

Human subjects

Potential Risks to participants

The Nox T3s portable sleep apnea test used to identify those with qualifying sleep apnea is FDA cleared (K082113) for evaluation of adults for sleep-disordered breathing and is intended for hospital or home use. The components include a nasal cannula, thoracic and abdominal Respiratory Inductance Plethysmograph (RIP) belts, and wrist oximeter unit with finger probe. We will upload sleep apnea test data from the Nox T3s device Elite Sleep Professionals, or similar company, to provide rapid scoring and reporting of study results along with data storage during and after the trial. Study data will be shared with the scorer via a HIPAA-compliant means. The studies will contain embedded study date, but otherwise should not contain PHI. Potential risks to participants include the loss of privacy and confidentiality from data gathered from the Nox T3s, CPAP device, and the recordings of the MET interviews. Data from the CPAP devices automatically upload via modem to ResMed AirView™ cloud application, a secure CPAP adherence monitoring program that is typically used by home medical equipment companies and sleep medicine clinics to ensure patients meet insurance company requirements for adherence. ResMed's AirView will also be used to track CPAP use. ResMed's privacy policy can be found here: https://www.resmed.com/en-us/privacy/ The MET interviews are also recorded and analyzed by Lyssn, a HIPAA-compliant, cloud-based software platform that supports training and quality assurance through automated transcription of counseling session recordings. Other risks of study participation include stress or anxiety related to completing health questionnaires. Information from surveys or the sleep apnea test (in instances of predominant central sleep apnea) may be shared with IPR care providers to assist in treatment.

The use of CPAP for treatment of OSA should be exempt from the requirements of 21 CFR Part 812 because this represents a medically cleared device (ResMed AirSense 11 AutoSet: K203126), used for its labeled indication (i.e., treatment of OSA). The UW Institutional Review Board (IRB) has assigned a no more than minimal risk status in similar studies.[26,65,66] CPAP is a safe treatment. The most common side effects of CPAP include mask-related discomfort; dry eyes, nose, mouth and/or throat; nasal congestion; stomach bloating; and difficulty falling or staying asleep. These are all non-serious. Skin irritation related to the mask interface, or rarely skin allergy can occur. We will minimize these risks by having a variety of mask and nasal pillow interfaces, and offering multiple options. Respiratory therapists and sleep technicians will assist with mask fit and troubleshoot any discomfort during the IPR hospitalization. For all participants, we will make use of

respiratory therapy expertise during IPR and provide information for DME-support after IPR discharge to make CPAP as comfortable as possible, which would be covered by the study. For persistent issues related to CPAP, the study team may ask the participant if he/she would like a referral to the local sleep medicine clinic, that would not be covered by the study.

Protection Against Risk
Patients will be excluded from the study after enrollment if they are found to have central sleep apnea (≥ 50% of apneas related to central events) or no evidence of OSA (respiratory event index < 5 per hour) on the Nox T3s sleep recording. In such case, the results of the sleep apnea testing will be given to the participant and the IPR clinical team caring for the patient. Either a sleep technologist or respiratory therapist, depending on randomization assignment, will be involved in mask fitting to assure appropriate size selection. For all participants, the respiratory therapists or sleep tech will troubleshoot any CPAP issues during ideally each night of inpatient use. Participants will also be offered a variety of masks/interfaces to facilitate comfort. Heated humidification will be used to reduce mucosal dryness and maximize adherence. The consent form provides information about withdrawal of study participants for pregnancy and the need to discuss this topic, should it arise, with study staff and the participant's physician. This should be rare given our stroke population. Participants will be cautioned not to drive when sleepy, though sleepiness is not a prominent feature of post-stroke OSA.[67-69]

Regarding loss of privacy or confidentiality from data gathered from the Nox T3s sleep apnea test, CPAP use or MET interviews, all participant health information and personal identifiable information is kept confidential on ResMed AirView, ResMed myAir and Lyssn cloud-based applications. Also, the privacy policy from ResMed, and Lyssn will be provided to participants at the time of enrollment. The informed consent document will outline the use of these applications including the need to share identifiers with ResMed as part of this use - a procedure often done as part of routine medical care related to CPAP. Regarding risks of the questionnaires or MET counseling sessions, participants will be given the option to stop answering questionnaires or counseling or to take a break if they become physically tired or emotionally upset. No particularly sensitive topics are planned for discussion. Participants will be assured that they are not required to answer a question if a particular question makes them uncomfortable and can also withdraw their study participation at any time.

The data collection process or MET session will be postponed and rescheduled at another time if needed and if agreeable to the participant. Our study staff will undergo strict training in the proper way to conduct interviews with personal health information, including HIPAA and Good Clinical Practice (GCP) training. We protect Protected Health Information (PHI) with all of our efforts. Study participants' identification numbers will be used on forms rather than names.

Vulnerable Subjects
No prisoners, children, or pregnant women will be enrolled. Pregnancy is an exclusion criterion because of potential safety concerns for the fetus and mother related to untreated OSA. Women of child-bearing potential will be included. Participants who become pregnant will be withdrawn from the study. This should be uncommon given the stroke population. Pregnancy testing is considered part of routine care for stroke patients.

Potential Benefits
Potential direct benefits to research study participants include sleep apnea testing using a portable device, education regarding OSA after stroke, and CPAP therapy for all those who meet the study's OSA treatment criteria. Both the screening sleep apnea study and the initiation of CPAP are rarely performed in the inpatient stroke setting due to logistic challenges and clinical equipoise related to the potential benefits of early CPAP treatment. Benefits to the intervention may include improved adherence to CPAP therapy, improved stroke recovery or secondary stroke prevention and better overall health outcomes. In regards to indirect benefits, the project has the potential to generate important new and much-needed information about improving adherence to CPAP therapy and the treatment of post-stroke OSA. The no more than minimal risks associated with this study are reasonable considering the significant potential direct and indirect benefits.

Enrolled stroke participants will be compensated for their time with $25 for completion of the outcome assessment at 3 months.

AE monitoring and reporting
Given the no more than minimal risk nature of the study, Dr. Khot will be responsible for monitoring the safety of participants. Given the risks, only serious adverse events that are definitely, possibly, or have a reasonable possibility of being related to a study procedure will be reported to the IRB. Standard definitions of serious adverse events, relatedness, and seriousness will be used. Standard reporting scheduled will be applied.

Statistical analysis

The primary endpoint is the themes related to acceptability, feasibility, and appropriateness of the behavioral adherence intervention based upon participant and CPAP partner feedback during the semi-structured interviews. The secondary endpoint is 3-month average nightly CPAP usage.

Demographic and stroke- or sleep-related factors associated with mean CPAP use will be assessed using t-tests for dichotomous variables and linear regression for continuous variables. Additional post-hoc analysis of race/ethnicity may be completed.

Introductory Pamphlet (to be edited)

NIH Stroke Scale

NIH Stroke Scale Item	Function	Scores	Score
1a. Level of Consciousness (Alert, Drowsy, etc.)	Alert Drowsy Stuporous (requires repeated stimuli) Comatose (reflex responses only)	0 1 2 3	
1b. LOC Questions (**Ask** month, age)	Both correct One Correct Both Incorrect, unable to answer·	0 1 2'	
1c. LOC Commands (Open, close eyes, make fist, let go}	Obeys both correctly Obeys one correctly Both Incorrect, unable to perform•	0 1 2'	
2. Best Gaze (Eyes open-patient follows examiner's finaer or racel	Normal Partial gaze palsy (for coma see Forced deviation Note 2 below)	0 1 2	
3. Visual (Introduce visual stimulus hreat to patient's visual field quadrants)	No loss Partial hemianopia (for coma see Complete hemianopia Note 3 below) Bilateral hemianopia	0 1 2 3	
4. Facial Palsy (Show teeth, raise eyebrows and squeeze eyes shut)	Normal Minor asymmetry Partial (lower face paralysis) Comolete•	0 1 2 3•	
5a. Motor Arm-Left (Elevate extremity 90 degrees When sitting and score drift/movement}	No drift Drift Some effort against gravity No effort against gravity No movement"	0 1 2 3 4"	
5b. Motor Leg-Left (Elevate extremity 30 degrees When lying down and score drift/movement)	No drift Drift Some effort against gravity No effort against gravity No movement•	0 1 2 3 4'	
6a. Motor Arm-Right (Elevate extremity 90 degrees When sitting and score drift/movement)	No drift Drift Some effort against gravity No effort against gravity No movement'	0 1 2 3 4'	
6b. Motor Leg-Right (Elevate extremity 30 degrees When lying down and score drift/movement)	No drift Drift Some effort against gravity No effort against gravity No movement·	0 1 2 3 4•	
7. limb Ataxia (Finger-Nose, heel down shin)	Absent' Present in upper or lower Present in both	0· 1 2	
8. Sensory (Pin prick to face, arm, trunk, and leg comoare side to sidel	Normal Partial Loss Dense Loss•	0 1 2'	
9. Best Language (Name items, describe picture and read sentences)	No aphasia Mild-moderate aphasia Severe aphasia (see Intubated Mute• and Alert notes	0 1 2 3·	
10. Dysarthria (Evaluate speech darity by patient repeatina listed words)	Normal articulation if appropnate) Mild-moderate slurring Severe. nearly unintelliaible or worse·	0 1 2·	
11. Extinction and Inattention (Use information from prior testing to identify nealect or double simultaneous stimuli testinal	No neglect Partial neglect Profound Neolecr	0 1 2·	
		NIH Stroke Scale Total	

·assign this score 1f patient comatose or unresponsive
Note 2: perform oculocephalic testing to determine score if comatose, absent oculocephalic reflex leads to score of 2
Note 3: determine via visual threat if comatose, no response leads to score of 3
Intubated and Alert: for item 9, make best guess and score; for item 10, untestable so score O

MRS-9Q

Question 1: Do you have any symptoms that are bothering you? YES | NO

Question 2: Are you able to do the same work as before? YES | NO

Question 3: Are you able to keep up with your hobbies? YES | NO

Question 4: Have you maintained your ties to friends and family? YES | NO

Question 5: Do you need help making a simple meal, doing household chores, or balancing a checkbook? YES | NO

Question 6: Do you need help with shopping or traveling close to home? YES | NO

Question 7: Do you need another person to help you walk? YES | NO

Question 8: Do you need help with eating, going to the toilet, or bathing? YES | NO

Question 9: Do you stay in bed most of the day and need constant nursing care? YES | NO

Pre-stroke Berlin (baseline only) – 10 items

Read to participant: "Please answer the following set of questions as you would have BEFORE your recent stroke."

1. Do you snore?
   0 = No (Go to 6.2)
   1 = Yes
   80 = Don't know (Go to 6.2)

   1a. Would you say your snoring is:
      1 = Slightly louder than breathing
      2 = As loud as talking
      3 = Louder than talking
      4 = Very loud; can be heard in adjacent room
      80 = Don't know

   1b. How often do you snore?
      1 = Nearly every day
      2 = 3-4 nights per week
      3 = 1-2 nights per week
      4 = 1-2 nights per month
      5 = Never/nearly never
      80 = Don't know

   1c. Has your snoring ever bothered other people?

      0 = No
      1 = Yes
      80 = Don't know

2. Has anyone noticed that you quit breathing during your sleep?
   0 = No (Go to 6.3)
   1 = Yes
   80 = Don't know (Go to 6.3)

   2a. How often would you say you quit breathing during your sleep?
      1 = Nearly every day
      2 = 3-4 times a week
      3 = 1-2 times a week
      4 = 1-2 times a month
      5 = Never/nearly never
      80 = Don't know

3. How often do you feel tired or fatigued after your sleep?
      1 = Nearly every day
      2 = 3-4 times a week
      3 = 1-2 times a week
      4 = 1-2 times a month

5 = Never/nearly never
80 = Don't know

4. During your wake time, how often do you feel tired, fatigued, or not up to par?
1 = Nearly every day
2 = 3-4 times a week
3 = 1-2 times a week
4 = 1-2 times a month
5 = Never/nearly never
80 = Don't know

5. Have you ever nodded off or fallen asleep while driving a vehicle?
0 = No (Go to 6.6)
1 = Yes
80 = Don't know (Go to 6.6)

5a. How often would you say you nod off or fall asleep while driving a vehicle?
1 = Nearly every day
2 = 3-4 times a week
3 = 1-2 times a week
4 = 1-2 times a month
5 = Never/nearly never
80 = Don't know

6. What is your height?
___feet ____inches

7. What is your weight?
_____lbs
8. Do you have high blood pressure?

RESPONSE OPTIONS: yes, no, don't know

Motivation to Use CPAP Scale **(baseline only) – 9 items -** visit 8 (Day 5-7 and after 3-day ST visits)

Now I'm going to ask you 9 questions about what motivates you to use CPAP.

1. I use the CPAP treatment because it makes me feel good.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
2. I use the CPAP treatment because I want to avoid having apneas.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
3. I use the CPAP treatment because I want to feel more alert.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
4. I use the CPAP treatment because it feels important to use the CPAP.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
5. I use the CPAP treatment because my health is important to me.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
6. I use the CPAP treatment because it feels good to use CPAP.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
7. I use the CPAP treatment because other people say I have to.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
8. I use the CPAP treatment because the personnel say I have to.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1
9. I use the CPAP treatment because I have to.	Strongly agree 5	Agree 4	Undecided 3	Disagree 2	Strongly disagree 1

Prestroke sleep duration & Quality (baseline in reference to pre-stroke state)

Sleep duration:

During the month prior to the stroke, excluding naps, how many hours of actual sleep did you get at night (or day, if you work at night) on average?

RESPONSE OPTIONS: < 6 hours per night, 6-8 hours per night, > 8 hours per night

Sleep quality:

During the month prior to your stroke, how would you rate your sleep quality overall?

RESPONSE OPTIONS: 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor

Prestroke sleep duration & Quality (90 day)

Sleep duration:

During the past month, excluding naps, how many hours of actual sleep did you get at night (or day, if you work at night) on average?

RESPONSE OPTIONS: < 6 hours per night, 6-8 hours per night, > 8 hours per night

Sleep quality:

During the past month, how would you rate your sleep quality overall?

RESPONSE OPTIONS: 1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor

After Nox T3 sleep apnea test

Was the T3 qualifying for CPAP treatment (REI ≥5 and CAI was <50% of REI)?

RESPONSE OPTIONS: yes, no, sufficient data not obtained

If yes,

Did the participant try CPAP for at least one night?

RESPONSE OPTIONS: yes, no

Participant phone number:

Participant email:

Participant address:

Did the participant identify a CPAP partner?

RESPONSE OPTIONS: yes, no

If yes,

CPAP partner name

CPAP partner phone number

7 adverse symptoms of CPAP (after night 1, night 2 and night 3 of using CPAP)

"Did you have problems with CPAP last night?" ☐ **No** ☐ **Yes**

"We would like you to answer yes or no to some **side effects** of CPAP that people may experience."

List of 7 adverse events or problems associated with CPAP use

Patient receives a score of one point for the presence of any complaints within each category, producing a total possible side effect score of seven points.

Mouth dryness

Nasal symptoms

Eye problems

Claustrophobia

Noise problems

Facial soreness or skin irritation from the mask

Mask fit or leak problems (i.e. trouble keeping mask in place, air leaks or difficulty putting the mask on)

"Some other side effects that people may experience include: dry nose or throat, headache, sore throat, jaw pain, waking up frequently, stomach upset, or increased saliva. Have you had any of these side effects?"

Asked of CPAP Partner

Short-form 7-item Zarit Burden Interview (discharge, 90 day) measured on a 5-point Likert scale from 0 (never) to 4 (nearly always)

INSTRUCTIONS: The following is a list of statements, which reflect how people sometimes feel when taking care of another person. After each statement, indicate how often you feel that way; never, rarely, sometimes, quite frequently, or nearly always. There are no right or wrong answers.

1. Do you feel you do not have enough time for yourself?
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

2. Do you feel stressed between caring and meeting other responsibilities?
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

3. Do you feel your relative affects your relationship with others in a negative way
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

4. Do you feel strained when are around your relative?
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

5. Do you feel your health has suffered because of your involvement with your relative?
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

6. Do you feel you have lost control of your life since your relative's illness?
RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

7. Overall, how burdened do you feel in caring for your relative?

RESPONES OPTIONS: 0: NEVER 1: RARELY 2: SOMETIMES 3: QUITE FREQUENTLY 4: NEARLY ALWAYS

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