Sleep for Stroke Management And Recovery Trial

NINDS U01NS099043

Protocol training

Study Team

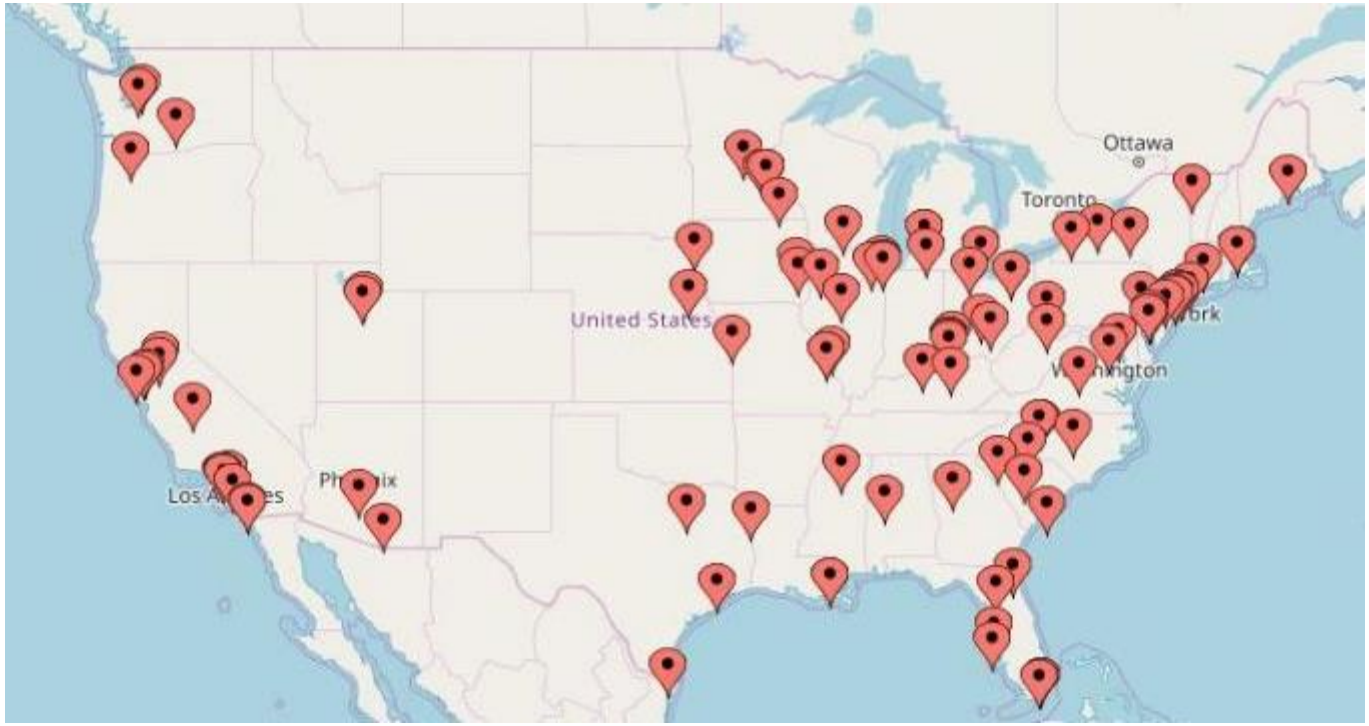
Key roles:

- **Project PIs:** Devin Brown, Ronald Chervin
- **Project managers**: Kayla Novitski (UM), Joelle Sickler (UC)
- **StrokeNet National Data Management Center (NDMC) Project PI**: Valerie Durkalski
- **StrokeNet National Coordinating Center (NCC) PI**: Joseph Broderick
- **StrokeNet NDMC PI**: Jordan Elm, Catherine Dillon, Wenle Zhao
- **Event Adjudicators:** Darin Zahuranec, Deborah Levine
- **Telemedicine partner**: Jeff Durmer (FusionHealth, Chief Medical Officer), Helgi Helgason (Director of Clinical Operations)
- Lewis Morgenstern (Co-I)
- **NCC**: Jamey Frasure, Diane Sparks, Emily Stinson
- **NDMC**: Jessica Griffin, Catherine Dillon, Faria Khattak, Jocelyn Anderson, Katherine Trosclair, Renee Martin, Sherry Livingston, Daniel Huang
- **Consultants**: Craig Anderson, Dawn Bravata, and Klar Yaggi
- **Independent Medical Safety Monitors**: Kingman Strohl, Anna May
- **NINDS**: Robin Conwit, Joanna Vivalda, Scott Janis

Study Organization

- NINDS
- Steering Committee
- Operations Committee
- NCC
  - Project management
  - Central IRB
  - Contracts management
- NDMC
- DSMB/Medical safety monitor
- Fusion Health

110 sites



Study Synopsis

- Investigator-initiated, phase 3 multicenter, prospective randomized open-, blinded-endpoint (PROBE) controlled trial
- 110 sites nationwide – recruitment from acute or rehab hospitalization
- ~3000 subjects randomized, 15,000 subjects screened (fewer may be needed if a higher proportion are randomized)
- Enrollment over 4 years

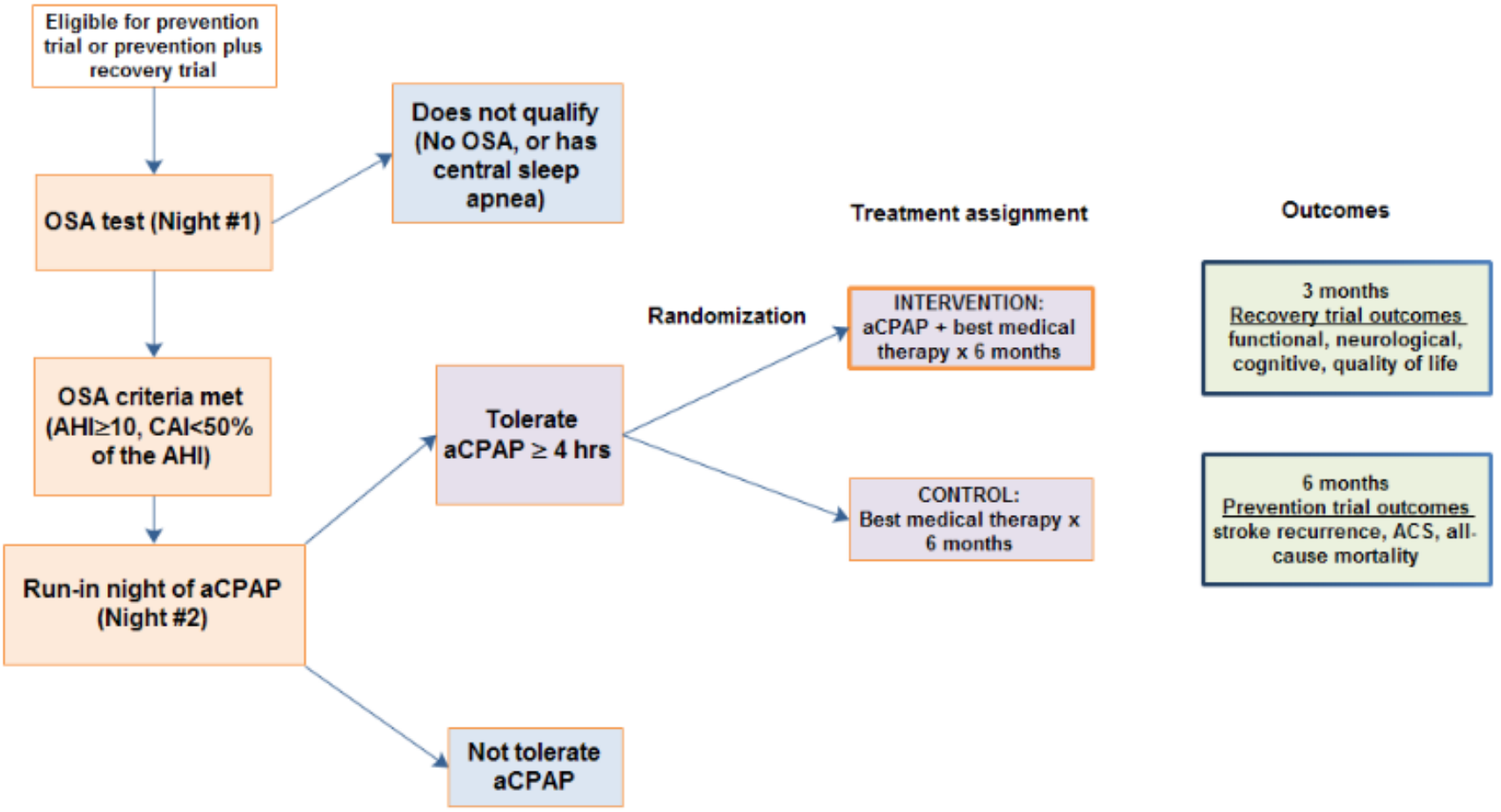
Objectives and Primary Endpoints

Objectives: Determine whether treatment of obstructive sleep apnea (OSA) with positive airway pressure started shortly after acute ischemic stroke or high risk TIA (1) reduces recurrent stroke, acute coronary syndrome, and all-cause mortality 6 months after the event, and (2) improves stroke outcomes at 3 months in patients who experienced an ischemic stroke.

Primary Endpoints: (1) Prevention endpoint: the composite outcome of recurrent stroke, acute coronary syndrome, or all-cause mortality at 6 months, (2) Recovery endpoint: functional outcome at 3 months.

Secondary Endpoints: neurological, cognitive, and quality of life outcomes at 3 months.

Sleep SMART flow



Before study enrollment starts

- Talk with your hospital biomedical engineering unit about possible need to have equipment inspected and stickered
- Work out logistics of subject payments
- Create a relationship with RT (there is $ for RT)/sleep tech
- Educate inpatient nursing staff about the trial
  - Try to generate enthusiasm
- Take appropriate Sleep SMART quizzes after training
- KOEO KIT installation on computer
- ****Push forward execution of FusionHealth DUA and Consignment Agreements****

Inclusion criteria

- Inpatient at an enrolling site
- ≥ 18 years old
- Ischemic stroke, or TIA with $ABCD^2 \geq 4$ within the prior 14 days
  - Prevention analysis: all subjects
  - Recovery analysis: NIHSS ≥1, consented within 7 days

Exclusion Criteria

- Pre-event inability to perform all of own basic ADLs
- Unable to obtain informed consent from subject or legally authorized representative
- Incarcerated
- Known pregnancy
- Current mechanical ventilation (can enroll later if this resolves) or tracheostomy
- Current use of PAP, or use within one month prior to stroke
- Anatomical or dermatologic anomaly that makes use of CPAP interface unfeasible
- Severe bullous lung disease
- Prior or current spontaneous pneumothorax

Exclusion criteria (2)

- Hypotension requiring current treatment with pressors (can enroll later if this resolves)
- Other specific medical circumstances that could, in the opinion of the site PI, render the patient at risk of harm from use of CPAP
- Previous or current massive epistaxis
- Cranial surgery or head trauma within the past 6 months, with known or possible CSF leak or pneumocephalus
- Recent hemicraniectomy or suboccipital craniectomy (i.e. those whose bone has not yet been replaced), or any other recent bone removal procedure for relief of intracranial pressure
- Current receipt of O_2 supplementation >4 liters per minute
- Current contact, droplet, or respiratory/airborne precautions

Eligibility

- Determined to be eligible for consent if eligibility met at any time within the first 14 days of stroke symptom onset
  - Exclusions may resolve
  - If a contraindication to CPAP develops during the pre-randomization phase, the subject should be withdrawn and end of study paperwork completed.

Who’s not eligible

- Venous infarction from DVST
- Primary ICH

Who is eligible (these are not exclusionary)

- Any amount of hemorrhagic conversion into ischemic infarction
- Prior diagnosis of OSA
- Supplemental O_2 (≤4 liters)
- Those with aphasia, cognitive dysfunction, altered LOC

Questions about eligibility of specific patient

Email: sleepsmart@umich.edu

*Please do not include any PHI

Patient approach

- Apply eligibility criteria
- Study team approach (use script)
- Use recruitment video to introduce study
- Informed consent process – use mandatory checklist (upload with consent for randomized subjects)

Informed Consent Process Checklist

☐ Person who obtained consent has been assigned this responsibility on the DOA
☐ Most recently CIRB-approved and stamped consent document used
☐ Patient or LAR personally signed and dated document, in all the correct spots
☐ If the patient lacked cognitive capacity to consent for him or herself, the appropriate LAR was used
☐ If an LAR was used, the reason for using an LAR was documented in the subject's medical or research record (as per local procedures) and on the informed consent CRF in WebDCU
☐ An impartial witness (of consent process and signature) was used, and documented appropriately, if any of the following situations apply:
- ☐ Short form consent used
- ☐ Patient physically incapable of signature
- ☐ Patient is illiterate
- ☐ Patient is visually impaired

☐ Assent obtained if appropriate
☐ If patient/LAR is not English-speaking, then the following were performed:
- ☐ the consent conversation was conducted in the patient/LAR's primary language (either the person obtaining consent was fluent or a formal interpreter was used), **AND**
- ☐ a fully translated ICF (CIRB-approved) was used, **OR**
- ☐ a translated CIRB-approved short form was used, the process was witnessed (translator may perform), and a fully translated consent was provided within 30 days

☐ If faxed consent procedure was available locally and used, a signed and dated ICF was returned to the site prior to performing any study procedure
☐ Copy of signed/dated consent given to patient/LAR for his/her records
☐ Consent process documented per institutional process
☐ Re-consent performed if a change in consent capacity occurred during the study

Rah, rah, rah, sis, boom, bah!

- Why might patients be excited about Sleep SMART?
  - Altruism – sense of purpose – improve health of stroke patients, advance medical science
  - Opportunity for OSA screening – no charge to patient or insurance company
  - State-of-the-art, treatment (for half of subjects) of OSA via telemedicine – convenience
  - No risky activities in trial – FDA-approved treatment
- We have de-emphasized:
  - Monetary incentives to compensate for time and travel
  - Subjects randomized to aCPAP group able to keep their aCPAP machine and supplies at the end of the trial
- Once the **scripts** are acknowledged by your site's IRB (if needed), please use these to communicate with patients/subjects at each stage of the process.

Learned with experience: recruitment barriers and possible response

- Review Recruitment challenges and responses on our website
- Feeling overwhelmed: better sleep at night could leave you better able to deal with challenges during the day
- Didn't like CPAP in the past: technology has evolved; new equipment may make easier to use; careful assistance from sleep coach to optimize changes CPAP will work for you
- Not able to return in person for outcome assessments: can be done by phone when needed
- I don't have sleep issues: most stroke patients with sleep apnea don't know they have sleep apnea because they don't all snore, feel tired, or have know sleep trouble

Consent issues

- LAR consent allowed when appropriate
- Assent when appropriate (not documented)
- eConsent via REDCap is available (once set up by NCC)
- Faxed consent approved by CIRB, may use if ok with local IRB
  - Telephone consent conversation
  - IC sent to LAR by fax or email – opportunity for questions
  - Signed IC returned by fax
- Language of choice
  - language ≥10% of the patient population, full-version provided
  - language <10%, short form with translator for conversation/full IC translation, provide a translated copy of the full consent to the subject/LAR within 30 days

Consent (2)

- Keep original signed/dated copy place another signed/dated copy in the medical record (if allowed by institutional standards), and a copy to the subject/LAR
- If change in capacity, need to reconsent
  - Originally subject consented, now lacks capacity: consent LAR +/- assent
  - Originally LAR consent, but capacity regained: consent subject
- At the time of consent, sign local medical record release
  - Facilitates acquisition of records if SAE occurs

Learned with experience: IC process

- Do not use LAR if subject able to consent for self
- Make sure to use approved, stamped (pdf) current consent version
- Use impartial witness (to process and signature) if subject unable to sign, illiterate, visually impaired, or used short form
- Use consent process checklist to “stay out of trouble”
- Use assent process

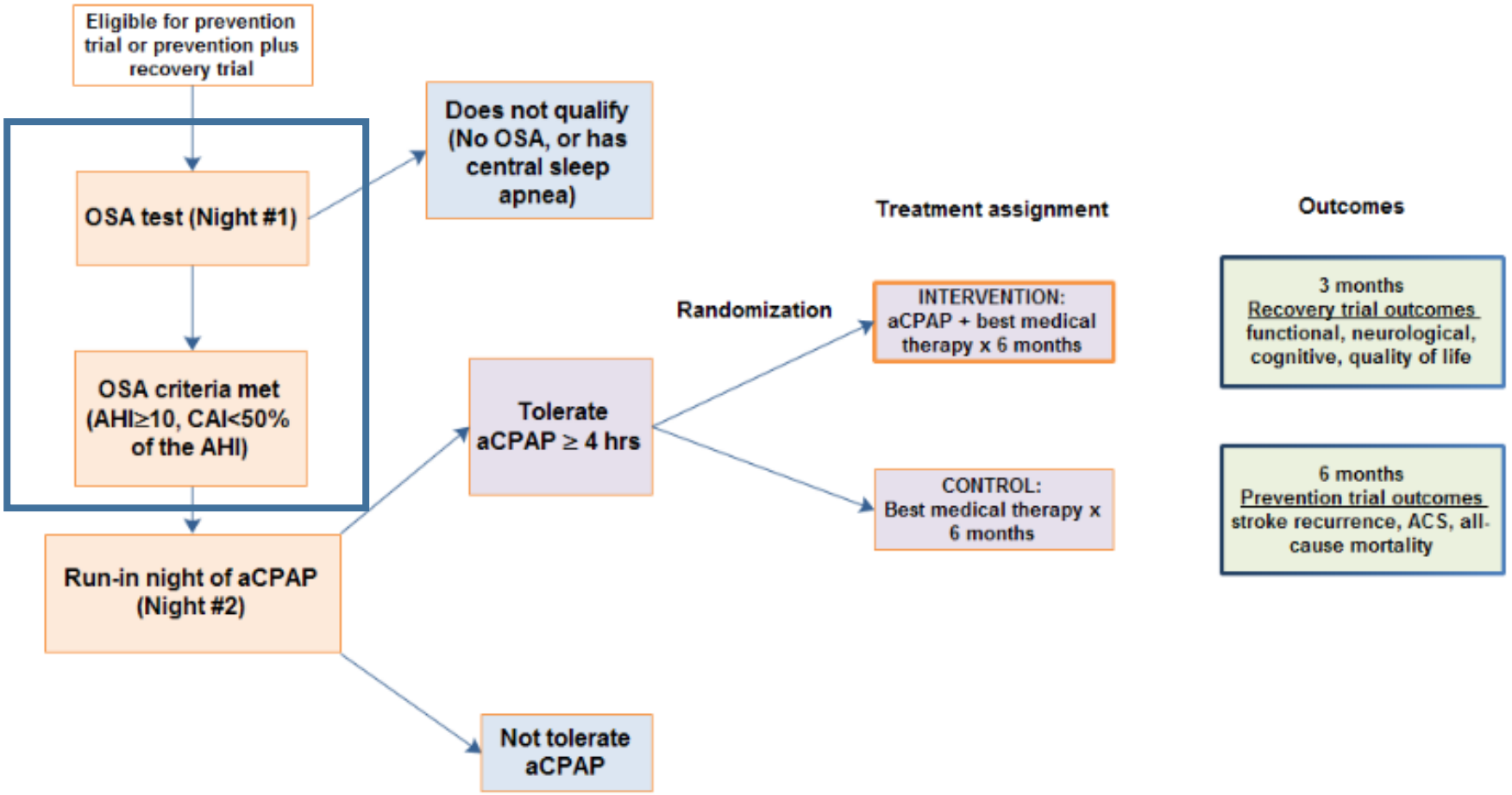
Eligible patients who do not consent

- Document in screen failure log: only for those who appear eligible but decline consent. Collect:
  - Age
  - Sex
  - Race/ethnicity
  - Reason not consent
  - Date consent declined

Baseline information – collect prior to OSA testing

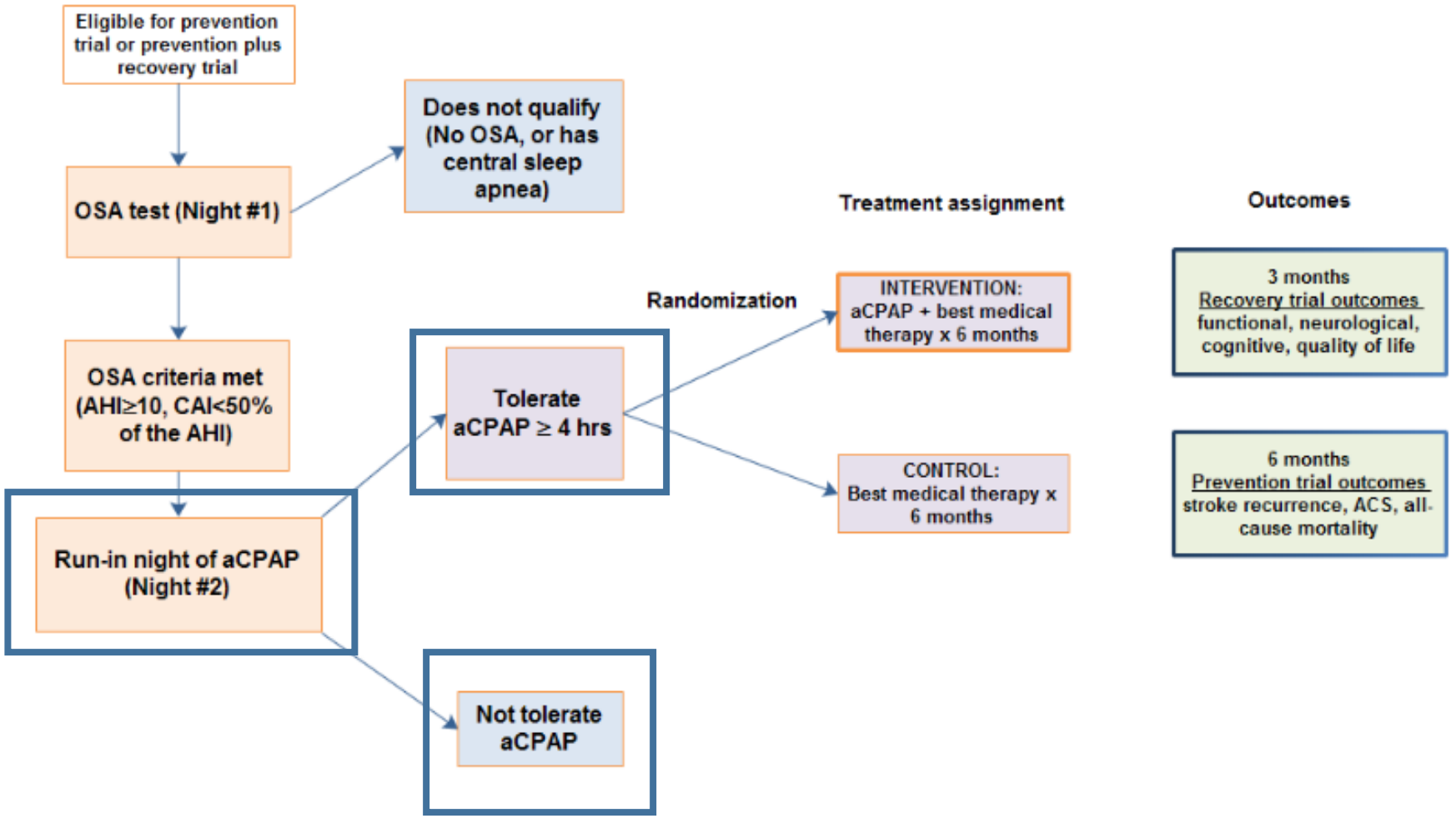
- Obtain baseline information on all consented subjects
- Medical history (risk factors, etc), blood pressure
- Pre-stroke modified Rankin
- Pre-stroke depression, sleep apnea, sleep duration, sleepiness questions
- Informant based cognitive status assessment – from person who knows subject best

	Baseline with reference to pre-stroke period	**Baseline**
Stroke risk factors		X
Medical history (height, weight, etc)		X
Sleep duration/sleep apnea symptoms (STOP-BANG)	X	
Informant-based prestroke cognitive status (IQCODE)	X	
Pre-stroke modified Rankin Scale (mRS)	X	
Depression (Hospital Anxiety and Depression Scale (HADS-D))	X	
Blood pressure		X
Epworth Sleepiness Scale	X	


Eligible for prevention trial or prevention plus recovery trial
OSA test (Night #1)
Does not qualify (No OSA, or has central sleep apnea)
OSA criteria met (AHI≥10, CAI<50% of the AHI)
Run-in night of aCPAP (Night #2)
Tolerate aCPAP ≥ 4 hrs
Not tolerate aCPAP
Randomization
Treatment assignment
INTERVENTION: aCPAP + best medical therapy x 6 months
CONTROL: Best medical therapy x 6 months
Outcomes
3 months
Recovery trial outcomes
functional, neurological, cognitive, quality of life
6 months
Prevention trial outcomes
stroke recurrence, ACS, all-cause mortality

Night of consent (ideally)

- Screen for sleep apnea with Nox T3 device
- Consult the Nox T3 KOEO and T3 MOPs (https://www.nihstrokenet.org/sleep-smart-trial/research-team)
- Set up device within the FusionHealth system (to associated with subject)
- Apply device at night (start shortly before anticipated sleep)
- Collect in AM
- Upload to FusionHealth
- Data processed that day (10am/2pm eastern) to determine eligibility
- If indicates subject eligible for run-in night, that means:
  - AHI_{T3} ≥10 (some significant sleep apnea)
  - Central apnea index <50% of total AHI_{T3} (mostly obstructive)
- No sleep apnea or too much central sleep apnea: provide T3 results; participation complete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Next night (ideally): aCPAP run-in night

- Consult the aCPAP MOP (https://www.nihstrokenet.org/sleep-smart-trial/research-team)
- Fit subject with appropriately sized mask during the day - RT
- Have subject practice place and remove mask many times
- Have subject use aCPAP while awake for 15-20 minutes to help get used to it
- aCPAP run-in night
  - Apply aCPAP overnight for one night to determine randomization eligibility
  - Have RT check on subject during night and troubleshoot any issues
  - Document aCPAP results (read from device) in WebDCU
- Use scripts to communicate results
- Randomization criteria:
  - Used aCPAP for ≥4.0 hours (read off device)
  - aCPAP CAI <10 (read off device)
  - Subject willingness to continue with Sleep SMART (must ask subject)
- Does not meet randomization criteria: provide T3 results; participation complete

Repeat T3?

- T3: up to 2 additional nights if the testing failed to provide sufficient information from which to determine OSA status. Examples include:
  - test fails for technical reasons
  - the subject does not tolerate the Nox T3
  - assessment is interrupted for clinical testing
  - any issue arises that the study team believes is not likely to recur but results in testing inadequate to make a determination about OSA

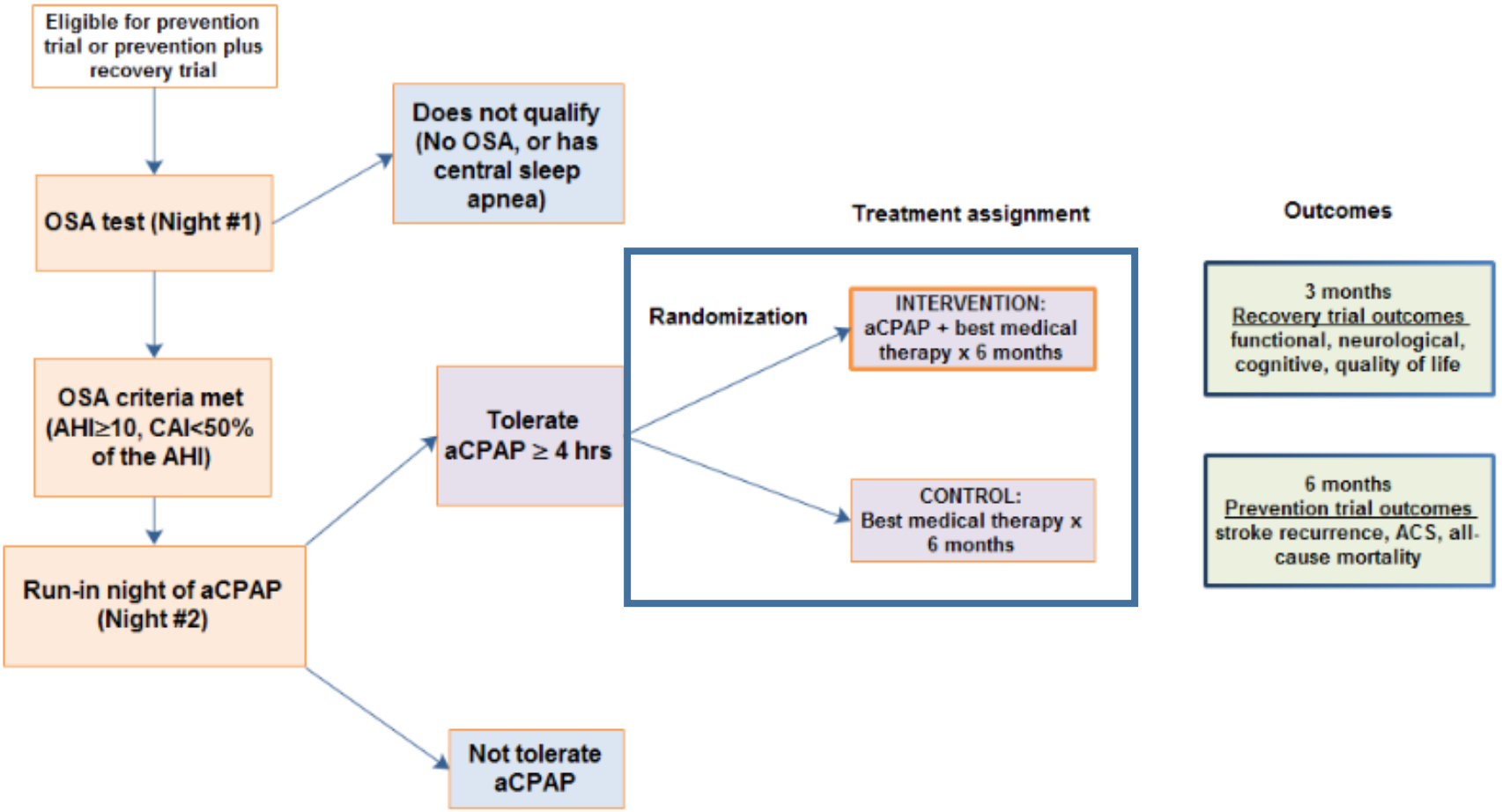
- The Nox T3 testing may also be repeated (up to two times for a total of 3) if it fails to show OSA and there is reason to suspect that the subject's OSA status is not accurately reflected by the study. For example:
  - subject receives supplemental O2 during the study
  - subject reports not sleeping for at least 4 hours during the recording
  - study likely captured hours of wakefulness

Repeat aCPAP run-in night

- aCPAP: up to 2 additional night
  - If use <4 hours and interrupted/limited due to clinical activity, or other external interruptions
  - Poorly tolerated due to specific situation not likely to recur (e.g. failure to use humidifier)

T3 results

- Provide to subject and study team
- At conclusion of study participation:
  - After non qualifying T3
  - After failed run-in night
  - At time of withdrawal
  - After 6-month visit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stroke recurrence, ACS, all-cause mortality

Randomization

- If run-in night qualifies
- Log into WebDCU, randomize subject – covered in WebDCU presentation
- Enter data into Fusion Health's KOEO system
  - Patient identifiers
  - Equipment provided
  - Run-in night results
  - Randomization assignment

Recruitment/retention

- Recruitment video
- Recruitment script
- Study brochures
- Compensation (paid by site)
  - Baseline info + T3: $25
  - Run-in night: $25
  - 3-month outcomes: $75
  - 6-month outcomes: $75
- aCPAP use monitored remotely; state-of-the-art telemedicine-based CPAP management by sleep coach
- Outcomes: Provision for home visits or as last resort telephone follow-up
- At baseline, obtain at least 3 phone numbers/texting/email/alternative contact info to aid in outcome scheduling

aCPAP arm

- 6 months of aCPAP + guideline concordant care
- Assistance with aCPAP by RT during hospitalization
- Show subject and caregiver aCPAP video, provide written materials
- Check in with subject each day about CPAP
- Telemedicine-based care management after discharge
  - Remote monitoring of use, residual AHI, mask leak
  - Proactive management and troubleshooting (including send new equipment directly to subject)
    - technology team
    - respiratory therapy team
    - sleep medicine physicians
- Bilevel PAP by Fusion Health
- Possible further escalation to sleep medicine clinical care (outside that provide through the trial)

aCPAP arm

- Use the scripts to communicate with subject about recruitment, Nox T3 set up, Nox T3 results, run-in night results, after randomization
- Script provides language to let subject know about myAir app for self-tracking
- Show the care management video to intervention subjects
- Provide written CPAP order (template on website) if discharge location not home

Inpatient CPAP use – Useful strategies

- Subjects' experience in the first couple days may determine their use for months to come
  - Inpatient assistance, encouragement, and troubleshooting is key
- Daily check-ins with intervention subject
  - Ask about any difficulties
  - Check front panel of PAP machine for usage hours, and offer positive feedback to subject
  - Engage the RT or sleep tech for answers or solutions
- FusionHealth Care Team is available to discuss any problems and help troubleshoot, so feel free to reach out! Phone: 470-655-6688
- Praise the subject for small improvements
- Offer to help subject or LAR enroll in MyAir (myair.resmed.com) so he or she can track PAP use independently

aCPAP group

- If contraindication arises, aCPAP must be held until it resolves
- Subject remains in original treatment assignment

Facilitate contact with FH Sleep SMART Care Team!

(Warm transition – from inpatient to Care Team)

- With permission, store the Fusion sleep coach team number in the intervention subject's/partner's cell phone (470-655-6688).
- Before discharge, help facilitate a call between intervention subject and sleep coach at Fusion to initiate contact. (Leave a message if a person does not answer.) This call can be scheduled ahead of time if you prefer.
- Remind intervention subject that if another call is completed with the Care Team within 7 days of discharge, he/she will receive a $10 Amazon gift card as a thank you. (This is managed by UM team.)

Usual care arm

- 6 months of guideline concordant care
- No aCPAP (if clinical team orders this, it will just be a protocol violation, intention to treat analysis)

Both arms

- Site PI to assure guideline concordant care during hospitalization
- Site PI (or stroke provider) to send letter to PCP at discharge to provide recommendation about secondary prevention
- Subjects should be counseled about healthy lifestyle recommendations from AHA for secondary prevention

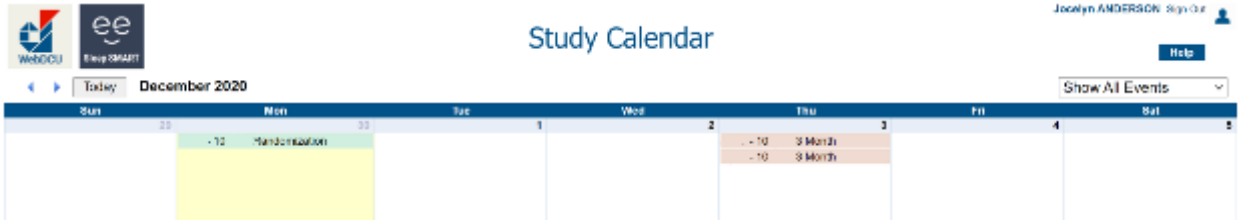
Outcomes - blinded

- Remind subject not to disclose treatment assignment
- 3 months (-4wks +4 wks), 6 months (-2wks +8 wks) post randomization
  - In person, if not possible then home visit. If not possible, then by telephone as last resort. Less compensation to study sites for telephone outcomes.

	3 months	**6 months**
Depression (Hospital Anxiety and Depression Scale (HADS-D))	X	X
Blood pressure	X	X
Epworth Sleepiness Scale	X	X
Generic quality of life (Global PROMIS 10)	X	X
Medication Adherence	X	X
10-meter walk test	X	
Functional outcome (mRS)	**X**	X
Neurological outcome (NIHSS)	X	X
Cognitive outcome (short MoCA)	X	X
Stroke-specific quality of life (short SSQOL)	X	X
Assessment for recurrent stroke, ACS, death	X	**X**

Schedule the assessment before discharge

- Determine window by using www.timeanddate.com/date/dateadd.html or the WebDCU Study Calendar. This calendar will display both completed and projected visits. This is a great way to find upcoming visits!



- Schedule the assessment before subject leaves the hospital – have placed in discharge paperwork
- Schedule it early in the window in case it's missed
- Send 'Follow-up visit reminder letter'
- Options include: subject returns for visit, study team performs home visit, telephone (not video)

Follow-up visit reminder letter

Sleep SMART

Sleep for Stroke Management and Recovery Trial

Date: _____

Dear _____
(Participant's name)

This is a reminder about your upcoming follow-up visit for the Sleep SMART trial.
Your Sleep SMART follow up appointment with _____at
(Trial staff name)

_____
(Location)
is scheduled on _____at _____.
(Date) (Time)

The address and directions are attached to this letter.

Call our office at _____ if you have any questions or if you
(Phone number for trial staff)
need to reschedule this visit.

Sincerely,

Name of PI or Research Coordinator

I can’t reach my subject for the 3- or 6- mos outcome

- Hierarchy:
  - Call subject at telephone number listed on consent or other known number
  - Text or email, if ok with subject (check back of consent)
  - Send message through patient portal
  - Alternative contact number on back of consent
  - Alternative contact person (back of consent)
  - If at facility, contact facility
  - Send letter (‘Unable to reach letter template’)
  - Check medical record or local obituary
  - If for 6-month assessment and unable to reach, use ‘Lost to follow-up letter’ template

In attempt to avoid problem:

- Obtain medical record release at time of consent
- Schedule follow-up before discharge
- Send reminder letter/portal message about appt date/time

Staff Documents: Randomized subjects

- Follow-up visit reminder letter: use to remind subjects of upcoming 3- and 6-month assessments
- Unable to reach letter template: can use if unable to reach subject to schedule 3- or 6-month follow-up appointment.
- Lost to follow-up letter: can use as last ditch effort to reach subject for 6-month follow-up appointment
- PCP letter template: can use to convey secondary stroke prevention recommendations
- Informational sheet for CPAP and the Nox T3: may be placed in the participant’s room to remind nurses of the person’s study participation and how to seek assistance regarding it.
- CPAP Resources page: can be used to transmit information about the study to the rehabilitation facility or nursing home where the participant may be transferred after the acute stroke hospitalization.
- Rehab letter template

Unable to reach letter template

Sleep SMART

Sleep for Stroke Management and Recovery Trial

Date: _____
[Date]

Patient's address:_____
[Participant's Address]

Dear _____,
[Participant's Name]

On _____, you enrolled in the Sleep SMART research study at
[Date]

_____.
[Location of enrollment]

The purpose of the study is to determine whether treatment of obstructive sleep apnea (OSA) with continuous positive airway pressure improves recovery after stroke and helps prevent stroke, heart attack, and mortality. It is important that we follow your health status while you are enrolled in this study.

We have not been able to reach you to schedule your follow-up assessment.

Please call my office at the number below, so we can discuss follow-up.

I can be reached at_____.
[trial staff phone number]

If I am not available when you call, please leave a detailed message including phone number and best time to reach you. I will return your call as soon as possible.

I want to personally thank you for your participation in Sleep SMART and I look forward to hearing from you soon.

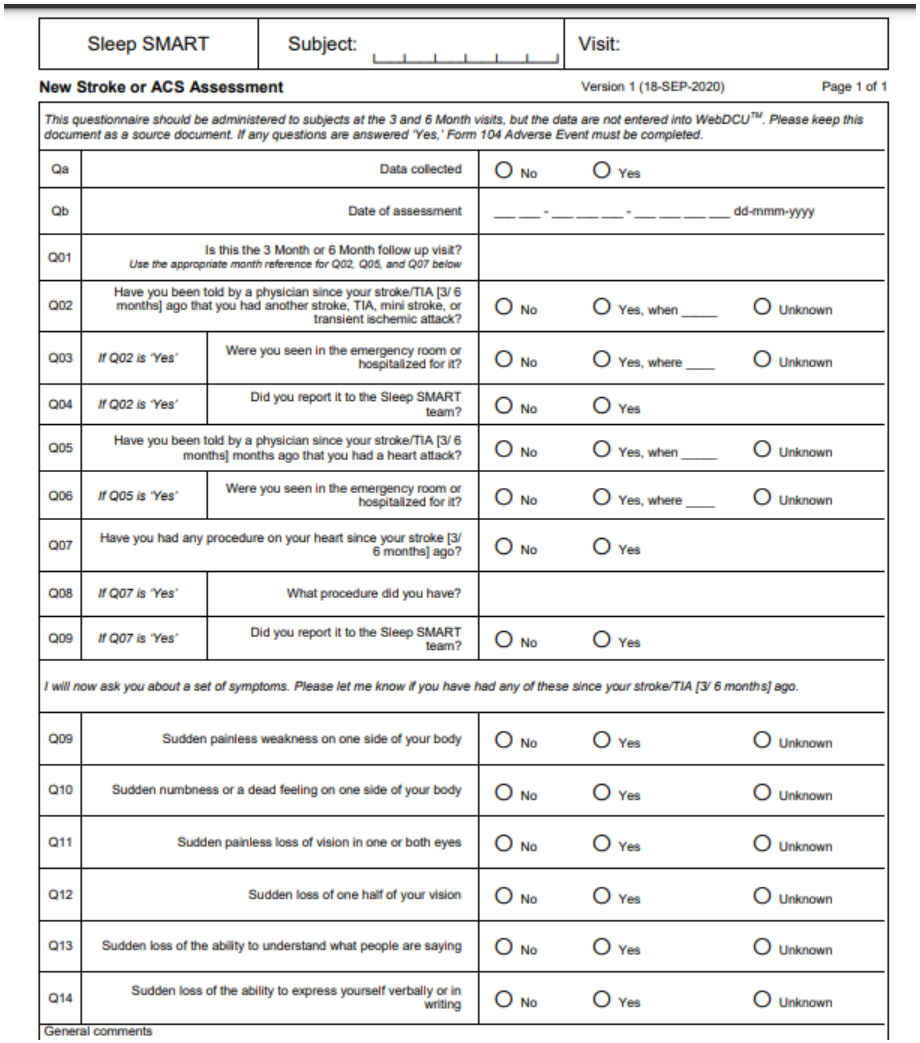
Sincerely,

[Name of site PI, other investigator, or Research Coordinator]

Prevention Outcomes

- Ischemic stroke:
  - Focal neuro symptoms ≥24 hours thought to be from cerebral ischemia, irrespective of presence of acute infarction
  - Focal neuro symptoms <24 hours thought to be from cerebral ischemia, if in the setting of thrombolytic or endovascular treatment, irrespective of presence of acute infarction
  - Focal neuro symptoms thought to be from cerebral ischemia <24 hours, and plausibly associated brain infarction
- ACS
  - STEMI
  - NSTEMI
  - Unstable angina
- Mortality
  - Obtain medical records, assess for any preceding stroke or ACS not otherwise identified

Prevention Outcomes – complete "New Stroke or ACS Assessment" as worksheet



Sleep SMART	Subject: _____	Visit:

New Stroke or ACS Assessment Version 1 (18-SEP-2020) Page 1 of 1

This questionnaire should be administered to subjects at the 3 and 6 Month visits, but the data are not entered into WebDCU™. Please keep this document as a source document. If any questions are answered 'Yes,' Form 104 Adverse Event must be completed.

Qa		Data collected	○ No ○ Yes
Qb		Date of assessment	__ __ - __ __ __ - __ __ __ __ dd-mmm-yyyy
Q01		Is this the 3 Month or 6 Month follow up visit? *Use the appropriate month reference for Q02, Q05, and Q07 below*	
Q02		Have you been told by a physician since your stroke/TIA [3/ 6 months] ago that you had another stroke, TIA, mini stroke, or transient ischemic attack?	○ No ○ Yes, when ____ ○ Unknown
Q03	*If Q02 is 'Yes'*	Were you seen in the emergency room or hospitalized for it?	○ No ○ Yes, where ____ ○ Unknown
Q04	*If Q02 is 'Yes'*	Did you report it to the Sleep SMART team?	○ No ○ Yes
Q05		Have you been told by a physician since your stroke/TIA [3/ 6 months] months ago that you had a heart attack?	○ No ○ Yes, when ____ ○ Unknown
Q06	*If Q05 is 'Yes'*	Were you seen in the emergency room or hospitalized for it?	○ No ○ Yes, where ____ ○ Unknown
Q07		Have you had any procedure on your heart since your stroke [3/ 6 months] ago?	○ No ○ Yes
Q08	*If Q07 is 'Yes'*	What procedure did you have?	
Q09	*If Q07 is 'Yes'*	Did you report it to the Sleep SMART team?	○ No ○ Yes

I will now ask you about a set of symptoms. Please let me know if you have had any of these since your stroke/TIA [3/ 6 months] ago.

Q09	Sudden painless weakness on one side of your body	○ No ○ Yes ○ Unknown
Q10	Sudden numbness or a dead feeling on one side of your body	○ No ○ Yes ○ Unknown
Q11	Sudden painless loss of vision in one or both eyes	○ No ○ Yes ○ Unknown
Q12	Sudden loss of one half of your vision	○ No ○ Yes ○ Unknown
Q13	Sudden loss of the ability to understand what people are saying	○ No ○ Yes ○ Unknown
Q14	Sudden loss of the ability to express yourself verbally or in writing	○ No ○ Yes ○ Unknown

General comments

Outcomes: alternative administration

3 and 6 Month Assessments Guide

Assessments that can be done via proxy

- F151 Short SSQOL
- F241 Epworth Sleepiness Scale
- F292 Modified Rankin Scale - 9Q
- F502 Sleep Duration Questionnaire
- 3 and 6 Month New Stroke and ACS Assessment

Assessments that can be done via telephone

- F139 HADS-D
- F151 Short SSQOL
- F167 Short MoCA
- F209 Clinical Management and Medication Adherence
- F241 Epworth Sleepiness Scale
- F255 PROMIS Global Health
- F292 Modified Rankin Scale - 9Q
- F502 Sleep Duration Questionnaire
- 3 and 6 Month New Stroke and ACS Assessment

Learned with experience: 3-month outcome

- Always schedule 3-mos outcome before subject leaves inpatient setting
- Always have multiple avenues to reach subject, and designated family member or caregiver as back-up
- Combine 3-month assessment with clinical visit if possible (3-month window is wide to accommodate)
- Schedule for early in window in case must be rescheduled

AEs

Between consent and randomization	After randomization
SAEs and non-serious AEs of special interest that are definitely related or stand a reasonable possibility to be related to the Nox T3 sleep apnea test or the aCPAP run-in night procedures	All SAEs
Recurrent stroke and ACS	All non serious AEs of special interest

AEs of special interest (serious or not): COVID-19 (symptomatic or asymptomatic), pneumonia, pneumothorax, car crash or other physical injury related to sleepiness, or skin infection on face

Points about follow-up

- Cross-over from control to CPAP rare and does not constitute study withdrawal
- Subject has withdrawn only if the subject withdraws consent
- If a new stroke or ACS occurs before the 6-month assessment, the subject should continue in his/her treatment group until the 6-month assessment (secondary outcomes)
- Intervention subjects should be instructed to take their aCPAP with them for any subsequent hospitalization, travel, etc
- MRI for new focal findings should be standard

After Sleep SMART participation concludes

- Intervention subjects: may keep their aCPAP and equipment
- Must suggest continued care under sleep medicine practitioner for those who continue use after the trial
- Offer referral to sleep medicine practitioner at conclusion of subject's participation – applies to both treatment groups

Study Intervention

Intervention: Autoadjusting continuous positive airway pressure (aCPAP) delivered with the ResMed Airsense 10 autoset.

- If bilevel PAP needed – FusionHealth
- Another type of PAP – local assistance

Control: Usual care.

Nox T3

ResMed AirSense 10

Mask type

- For those with decreased mental status, on tube feeds, or unable to remove the mask without assistance, **do not use full face mask**
  - May use chin strap if subject otherwise best suited for full face mask – mouth breather
- Decreased LOC or appears to be asleep for long periods of time
  - If CPAP to be administered for >12 hours at a time, alternate between nasal pillows and nasal mask.
  - An initial 48 period of CPAP should be attempted with intermittent inspection of skin and mask fit

Building your dream team

- Primary study coordinator – all but outcome assessment
- Secondary study coordinator – masked to treatment assignment, performs outcome assessment
- Site PI – overall responsibility, oversight of AE collection, assures guideline concordant care, assures letter sent to PCP about secondary prevention
- Other investigators – may assist or perform blinded outcome assessments
- RTs (or sleep techs) – perform mask fit, help troubleshoot aCPAP during hospitalization
- Sleep medicine physician – not required. May be helpful if adherence is particularly challenging, or if care goes beyond Fusion Health's scope

Tools

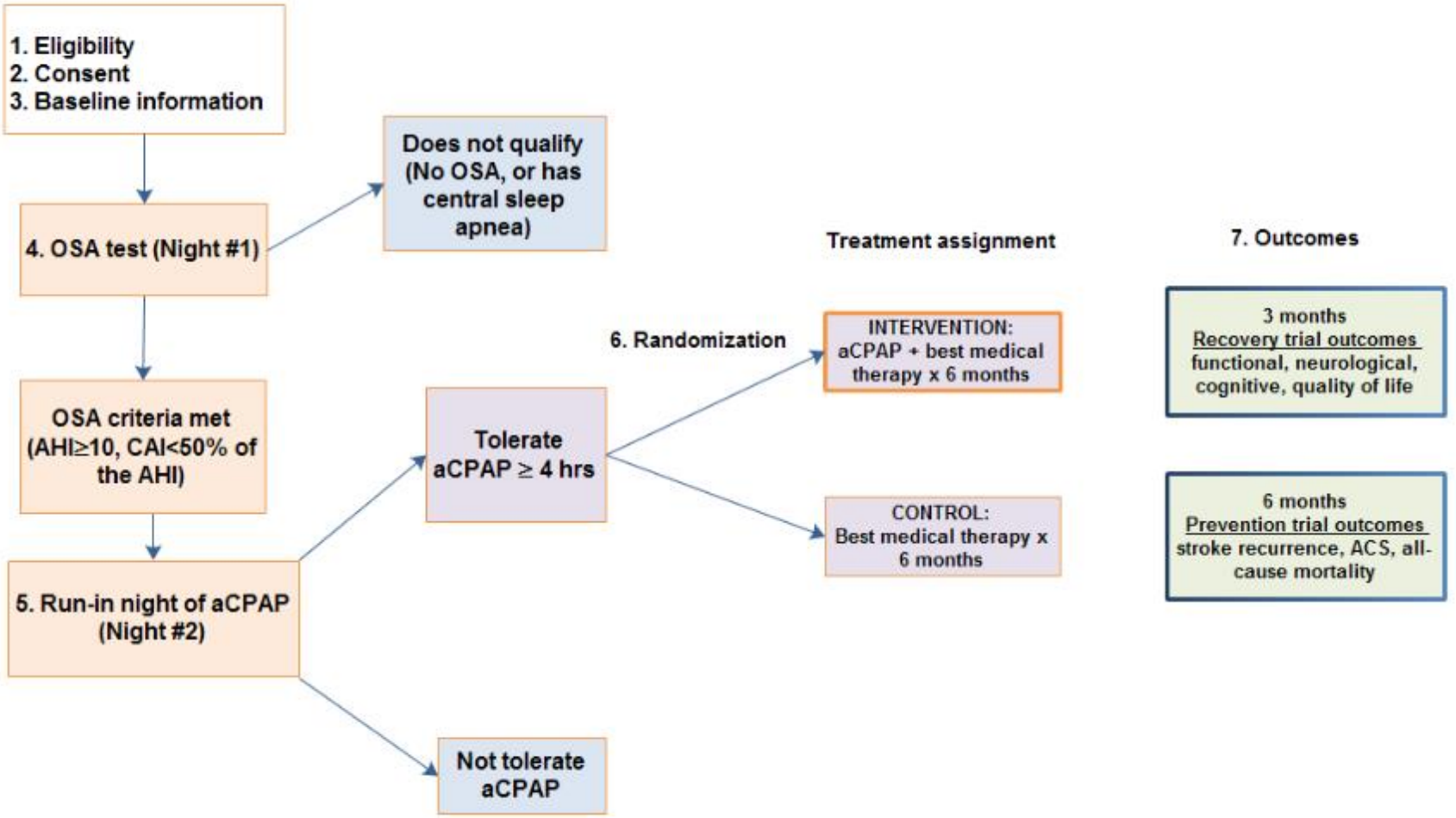
- Please visit our website: www.nihstrokenet.org/sleep-smart-trial/research-team
  - Study brochures
  - Recruitment video
  - Enrollment criteria pocket card
  - Step-by-step pocket card
  - Slide set to provide overview to nurses
  - Mask fit, Nox T3, aCPAP, KOEO guides on WebDCU
  - FusionHealth videos
  - FAQ document
  - Recruitment challenges and responses
  - Recruitment bullet points
  - Letter templates: f/u appt reminder, unable to reach, lost to follow-up, difficult to use CPAP
  - CPAP order template

Don’t forget about these critical tools available only in WebDCU

- MOP
- Data Collection Guidelines (DCG)
- Protocol

Assistance

- Equipment/Fusion's KOEO system: **888-505-0280 extension 4006**
- Eligibility question: Email: sleepsmart@umich.edu
- WebDCU:
  - Jocelyn Anderson (anderjoc@musc.edu, 843-876-1167), or
  - Faria Khattak (khattak@musc.edu, 984-221-0266)
- Randomization hotline if WebDCU randomization is down: **1-866-450-2016**
- Unsure?: kcgossel@umich.edu or sicklejb@ucmail.uc.edu


1. Eligibility
2. Consent
3. Baseline information
4. OSA test (Night #1)
Does not qualify (No OSA, or has central sleep apnea)
OSA criteria met (AHI≥10, CAI<50% of the AHI)
5. Run-in night of aCPAP (Night #2)
Tolerate aCPAP ≥ 4 hrs
Not tolerate aCPAP
6. Randomization
Treatment assignment
INTERVENTION: aCPAP + best medical therapy x 6 months
CONTROL: Best medical therapy x 6 months
7. Outcomes
3 months
Recovery trial outcomes
functional, neurological, cognitive, quality of life
6 months
Prevention trial outcomes
stroke recurrence, ACS, all-cause mortality

…end of trial

- Prevention (n=3,062)
  - All subjects: ischemic stroke or high risk TIA within prior 14 days

- Recovery (n=1,362)
  - Ischemic stroke within prior 7 days
  - NIHSS ≥1 at time of enrollment

Thank you

- You are now ready to take the Sleep SMART protocol quiz: https://goo.gl/forms/p8j0hvYBqea3dYiK2