Published in final edited form as:
*J Stroke Cerebrovasc Dis*. 2013 November ; 22(8): . doi:10.1016/j.jstrokecerebrovasdis.2011.06.010.

# Sleep Apnea Treatment after Stroke (SATS) Trial: Is it feasible?

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## Abstract

**Goal—**Sleep apnea affects over half of acute ischemic stroke patients and is associated with poor stroke outcomes. This pilot study assessed the feasibility of a randomized, sham-controlled continuous positive airway pressure trial in acute ischemic stroke patients.

**Methods—**Subjects identified to have sleep apnea based on an apnea-hypopnea index ≥ 5 on overnight polysomnography or portable respiratory monitoring within 7 days of stroke symptom onset were randomized to receive active or sham continuous positive airway pressure for 3 months. Objective usage was ascertained by compliance data cards. Subjects, treating physicians, and outcome assessors were masked to intervention allocation.

**Findings—**Among 87 consented subjects, 74 were able to complete sleep apnea screening, 54 (73%) of whom had sleep apnea; 32 agreed to randomization. Of the 15 who commenced active titration, 11 (73%) took the device home, and 8 (53%) completed the 3 month follow-up. Of the 17 subjects who commenced sham titration, 11 (65%) took the sham device home and completed the 3 month follow-up. The median cumulative usage hours over the 90 days were similar in the



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active group (53 hours (IQR: 22, 173)) and the sham group (74 hours (17, 94)) and blinding to condition was successfully maintained.

**Conclusion—**This first-ever, randomized, sham-controlled trial of continuous positive airway pressure in patients with recent stroke and sleep apnea showed that sham treatment can be an effective placebo.

## INTRODUCTION

Sleep apnea has a prevalence greater than 50% in ischemic stroke patients,(1) and is associated with poor functional outcome and increased dependence after stroke,(2) even when adjustment is made for baseline neurological dysfunction.(3) Sleep apnea has also been shown to predict longer hospital stays in acute rehabilitation and poorer functional outcome at the time of both admission and discharge from rehabilitation.(4) Furthermore, with adjustment for multiple confounders, several studies have shown an association between sleep apnea and post stroke mortality.(2,5) The relationship between sleep apnea and poor stroke outcomes highlights the need to study the effects of sleep apnea treatment on stroke outcomes. If proven effective, such an intervention should have great public health importance. However, no definitive study has tested the effects of continuous positive airway pressure (CPAP), the standard treatment for sleep apnea, on stroke outcomes.

The most rigorous clinical trial design for CPAP trials includes a sham CPAP control group.(6,7) Sham CPAP, with < 1 cm $H_2O$ pressure at the mask, is an ineffective treatment for apneas,(6,8) is tolerated by non-stroke subjects,(8) and is associated with a placebo effect.(9) However, the tolerance and adherence of stroke patients to sham CPAP is unknown, and whether stroke patients identified to have sleep apnea would be willing to enroll in a randomized, sham-controlled trial soon after stroke is unknown. The purpose of this study, therefore, was to assess the feasibility of a randomized, sham-controlled CPAP trial in ischemic stroke patients and to generate data needed to plan a large, multicenter study of this type.

## METHODS AND MATERIALS

### Study design

The Sleep Apnea Treatment after Stroke study (SATS) was a single-center, pilot, prospective, randomized, sham-controlled trial of CPAP in stroke patients where subjects, treating physicians, and outcome assessors were masked to intervention allocation. Subjects were enrolled between September 2004 and March 2010 from the inpatient neurology service at the University of Michigan. Adult subjects were eligible if they had an ischemic stroke, based on clinical criteria,(10) within 7 days of the planned sleep apnea assessment, and had a modified Rankin Scale score >1. Subjects were excluded for conditions where CPAP may cause harm, such as previous pneumothorax, bullous emphysema, a requirement for bilevel positive pressure, acute sinus or ear infection, and for conditions such as decompensated heart failure, cardiac or respiratory arrest within the past 3 months, myocardial infarction within the past 3 months, severe pneumonia, or hypertension refractory to treatment, where short term deferral of CPAP may be more controversial. Subjects were also excluded for any prior CPAP use, given the use of a sham CPAP, or any other unstable medical condition thought likely to interfere with participation.

At the time of enrollment, the Sleep Disorders Questionnaire-sleep apnea portion(11) was administered and the National Institutes of Health (NIH) Stroke Scale was performed by certified study personnel. Subjects were tested for sleep apnea and those who tested positive were randomized in a 1:1 fashion to CPAP or sham CPAP for 3 months. Study personnel provided subjects with instruction on the operation of the device. Subjects were called at 1,

2, 4, 6, 8, and 10 weeks after intervention initiation to encourage compliance and help troubleshoot problems. At the 3-month follow-up visit, compensated with $20, the Epworth Sleepiness Scale,(12) Patient Health Questionnaire-9,(13) Fatigue Severity Scale,(14) modified Rankin Score,(15) and Barthel Index(16) were administered and the NIH Stroke Scale(17) was repeated. A CPAP questionnaire queried the subjects' belief in intervention allocation. Responses included "definitely real," "probably real," "uncertain," "probably pretend," and "definitely pretend."

Subjects were also asked about average nights of CPAP use per week, average number of hours of CPAP use on nights used, and specific problems experienced with CPAP. We revised this CPAP problems questionnaire to include more specific examples during the study, hence the number of responses available to specific questions varied. Compliance cards were downloaded to ascertain objective usage data. The study was approved by the University of Michigan Institutional Review Board and was registered on ClinicalTrials.gov (NCT00282815). Written informed consent was provided by the patient or proxy.

## Sleep apnea screening

**Polysomnography—**For the first 46 subjects, sleep apnea was screened by full nocturnal polysomnography. Each polysomnogram was reviewed by a board-certified sleep medicine physician. Full nocturnal polysomnography was attended by an experienced sleep technologist in the subjects' hospital room, or during a readmission to the General Clinical Research Center at the University of Michigan. Polysomnograms included four EEG leads (C3-A2, C4-A1, O1-A2, O2-A1 of the International Electrode Placement System), two electro-oculographic leads, chin and bilateral anterior tibialis surface electromyograms, three ECG leads, nasal and oral thermocouples, nasal pressure cannula, thoracic and abdominal excursion piezo-electric bands, and finger pulse oximetry. An apnea was defined as ≥ 10 seconds of complete airflow cessation. In the presence of continued chest or abdominal movement, the apnea was designated as obstructive. If such movements were not present, the event was scored as a central apnea. An hypopnea was defined as a ≥ 30% reduction in airflow, chest excursion, or abdominal excursion that led to ≥ 4% oxygen desaturation, awakening, or arousal.(18)

**Portable respiratory monitor—**Due to intolerance of polysomnography and to logistical challenges inherent in testing after acute stroke (see Results), polysomnography was discontinued and screening for sleep apnea was performed with a portable respiratory monitor, the ApneaLink™ (Resmed, Inc), for subject number 47 and beyond. The ApneaLink™ monitors nasal pressure with a nasal cannula, and oxygen saturation and pulse with a flexible oxygen saturation probe. An apnea was defined as a reduction in airflow by ≥ 80% for ≥ 10 seconds; an hypopnea was defined as a reduction of airflow by ≥ 30% for ≥ 10 seconds associated with an oxygen desaturation of ≥ 4%, to approximate consensus recommendations.(18) This device has been validated against full polysomnography as a one-channel (nasal pressure) device.(19–26) Sleep apnea screening studies were downloaded from the recorder using the ApneaLink™ software. The raw tracings were edited manually by a trained professional to eliminate artifacts and poor quality data, and adjusted for start and stop times both based on subjective information obtained from the patient and as suggested by review of the recorded data. The previously validated(20,27) ApneaLink™ software analyzed the adjusted recordings.

Sleep apnea severity was measured by the AHI, calculated as the total number of apneas and hypopneas per hour of recorded time (ApneaLink™) or sleep time (polysomnography). Published studies suggest that these two numbers, though calculated from slightly different time bases, are extremely close.(20,27) An AHI ≥ 5 established the diagnosis of sleep apnea

in the ApneaLink™ group, while an AHI ≥ 5 where obstructive exceeded central events established the diagnosis in the polysomnography group.(18). Initially, subjects with an AHI > 60 or a minimum oxygen saturation < 65% on sleep apnea screening were considered too severe to be randomized into a placebo-controlled trial and were excluded from randomization. The AHI cutoff was raised to >100 later in the trial.

### CPAP and sham CPAP titration and treatment

**Active titration and treatment—**For subjects 1–46, active CPAP was titrated to eliminate respiratory events by a registered sleep technologist during a second night of polysomnography, or during the second half of the initial night of testing if the AHI was ≥ 20 during the first half of the night. For subjects 47+, an autotitrating device (AutoSet Vantage or AutoSet II, Resmed Inc.) was used to titrate subjects. Several studies have shown that automatic titration leads to outcomes that are at least equal to those obtained by more common (but less feasible, after stroke) sleep-laboratory-based manual titrations.(28,29) For all subjects randomized to active CPAP, the RemStar Pro (Respironics, Inc) with heated humidification was set to deliver a fixed pressure based on the pressure determined by the attended CPAP titration or autotitration.

**Sham titration and treatment—**Subjects 1–46, if randomized to sham CPAP, had a titration study simulated by the sleep technologist during polysomnography as above. Subjects 47+, if randomized to sham CPAP, were initiated on sham CPAP on the night following the ApneaLink™ study. Sham CPAP was delivered by a RemStar Pro (Respironics, Inc) modified to include an internal flow resistor, placed by Respironics' engineers, and an augmented leak port at the mask adaptor or on the nasal interface.(30) Each sham unit delivered less than 1 cm $H_2O$ pressure at the level of the mask. The active and sham CPAP units were identical in appearance, with the exception of the barely discernable augmented leak port, and sounded similar.

**Nasal interfaces and headgear—**Respironics' Premium Headgear (Philips) with the appropriate size comfort gel nasal mask was exclusively used at trial onset. After difficulties were reported with one-handed removal and application of the headgear and mask,(31) we expanded options to include Puritan Bennett's Breeze® SleepGear® (Covidian), a single piece head frame, with the DreamSeal standard size nasal mask or appropriately sized nasal pillows.

**Statistical analysis:** Medians and interquartile ranges (IQR), and numbers and percentages were calculated for baseline characteristics. Objective usage data, the primary outcome, were compared between intervention groups using Wilcoxon Rank Sum tests. Perceived treatment allocation was dichotomized into "definitely active" and "probably active" versus all others, and compared using Fisher's exact test. Analyses were performed using Spotfire S + 8.1 for Windows (TIBCO Software Inc., Palo Alto, Ca).

## RESULTS

Seventy-four of the 87 consented subjects completed sleep apnea screening (see Figure). Among the 40 subjects who initiated polysomnography, 4 (10%) could not tolerate the procedure and abandoned the study during the night. Only one subject had an AHI ≥ 5 with more central than obstructive apneas. Twenty-four (60%) of the 40 had OSA defined as an AHI ≥ 5 with more obstructive than central apneas. Five were excluded off protocol. In one study, the sleep physician thought the respiratory events were of unclear significance. In two others, the sleep technologist scored the AHI < 5 while the sleep physician later scored it as ≥ 5. An additional two were excluded because the AHI determined by the sleep technologist

was > 60, but was < 60 when reviewed by the sleep medicine physician. Six of the others (15%) were excluded due to severity. Therefore 13 qualified for randomization and were randomized. Of the 40 subjects who initiated the ApneaLink™ testing, 2 (5%) could not tolerate the testing. Twenty-eight (74%) had an AHI ≥ 5. One (3%) was excluded due to severity. Therefore 27 were available for randomization, of whom 19 were randomized. Collectively, 32 eligible subjects agreed to randomization. Baseline characteristics of the active (n=15) and sham (n=17) CPAP groups, those who qualified for randomization but did not initiate titration, and those who returned for the 3 month visit (n=19) are found in Table 1. The median time from stroke onset to CPAP or sham CPAP titration was 4 days.

### Active CPAP group

Of the 15 subjects who commenced active titration, 3 (20%) did not tolerate titration, and 1 (7%) declined to take CPAP home. Of the 11 who took CPAP home, 3 (20%) dropped out and did not return for the 3 month follow-up. Eight (53%) completed the 3 month follow-up.

### Sham CPAP group

Of the 17 subjects who commenced sham titration, 1 (6%) did not tolerate titration, 2 withdrew after titration and before discharge home due to sham CPAP intolerance, 1 was withdrawn by the clinical rehabilitation team, one was withdrawn by the study team after exposure to active CPAP by the clinical team while hospitalized for rehabilitation, and one died before hospital discharge. The remaining 11 (65%) took the sham CPAP home and completed the 3 month follow-up.

### Active and sham CPAP usage and belief in intervention allocation

Objective data on active and sham CPAP usage for subjects who returned for the 3 month follow-up visit are found in Table 2. Active and sham CPAP groups showed no differences in days with device usage, cumulative usage hours, or average usage on days used. Days with device usage were low in both groups, but on nights when the device was used, it was used for several hours. Subjectively, these same subjects described use of CPAP on a median of 5 (IQR: 4, 6) nights per week in the active CPAP group and 7 (1, 7) nights per week in the sham CPAP group. The median of the reported average nightly hours of use per night of use was 4 (3, 6) in the active group and 6 (2, 8) in the sham group. Table 3 summarizes subjective CPAP use and responses to the CPAP problems questionnaire. A variety of problems were endorsed by subjects. Belief of subjects in intervention allocation by actual group assignment among those who returned for the 3 month follow-up visit is found in Table 4. There was no difference between groups ($p>0.99$).

### Outcomes

Comparison of clinical outcome measures between active and sham CPAP groups, for subjects who returned for the 3 month follow-up visit, are found in Table 5. Interquartile ranges overlapped for sleepiness, fatigue, functional outcome, activities of daily living, and neurological outcomes. The depression measure was worse in the active CPAP group.

## DISCUSSION

This first-ever, randomized, sham-controlled trial of CPAP in patients with very recent stroke and sleep apnea shows that sham CPAP can be an effective placebo even during the challenging immediate aftermath of ischemic stroke. In this trial, sham CPAP was at least as tolerable and believable as active CPAP. However, this rigorously designed and documented pilot randomized controlled trial also highlights challenges that need to be addressed to ensure the success of a full-scale, definitive trial. Despite active attempts to adapt the design

to improve feasibility, including expansion of enrollment criteria, use of alternative headgear systems and interfaces, the switch from full polysomnography to a simpler device, and the change from attended titration studies to autotitrations, both active and sham CPAP were rejected by a significant minority of subjects, and used suboptimally by the remainder. Recruitment of subjects also proved less than simple, as evidenced by 50% of eligible patients' refusal to participate. Prior controlled CPAP trials in stroke patients, though without sham CPAP and focused on a later recruitment time window, were published during the conduct of the current study and also reported difficulties with identification of appropriate subjects and agreement to participate, with approximately 25–50% refusals.(32,33) Therefore, CPAP trials in subjects with recent stroke may need to plan for this challenge whether or not sham CPAP is used.

Interestingly, our results suggest that the problem with low CPAP adherence results more from the low number of nights treatment was attempted, more than the number of hours used per night. This may imply a lack of motivation rather than a more easily addressed specific adverse effect of CPAP. Our results also highlight the need to ascertain objective usage data, as subjects' self-report of nights used was overestimated. Prior randomized trials of CPAP in stroke patients have shown varied CPAP adherence. In two trials,(32,34) CPAP was initiated approximately 2–4 weeks after stroke onset and adherence was again poor. The average duration of CPAP use was only 1.4 hours per night over 8 weeks, despite intensive attempts at compliance management in one trial.(32) Our adherence was even lower, possibly because of the significantly earlier initiation of therapy. Two other trials reported higher CPAP usage: one in the subacute period(33) that excluded more severely affected stroke patients, and the other in the acute stroke period which limited enrollment to those less than age 75.(35) The more inclusive enrollment criteria of our study, including more severely affected, older stroke patients, and less severe OSA, may have contributed to our lower CPAP usage. Other observational studies with broader enrollment criteria have also shown poor CPAP usage in stroke patients.(1,36–38)

We began the SATS trial using formal portable polysomnography to identify stroke patients with sleep apnea. Unlike routine outpatients, some of our acute stroke patients were unable to tolerate the testing, and preliminary AHI assessments mis-categorized some subjects. Observational studies that have assessed sleep-disordered breathing in acute stroke patients have infrequently used full polysomnography,(39) and much more frequently used portable respiratory recording devices,(1,2,32,34) oximetry,(40) or autotitrating devices.(36,41,42) In the largest observational study of full polysomnography in acute ischemic stroke, 25 (20%) of 128 eligible patients refused to provide consent for the diagnostic sleep study, and an additional 21 (16%) could not be studied in a timely fashion.(39) Given the logistical challenges and limited tolerance of full polysomnography in the acute stroke setting, portable devices, such as the ApneaLink™, appear to be more promising for sleep apnea screening, although polysomnography remains an option.

The three trials that previously randomized subacute stroke subjects (in the 2–4 week range) to CPAP or non-placebo control suggested minimal benefits. The first study randomized 63 ischemic stroke and intracerebral hemorrhage patients with an AHI ≥ 15 for 4 weeks.(34) Mini mental status examination scores, Barthel-ADL index scores, and presence of delirium were unchanged after 28 days of treatment. However, depression scores improved over the 28 days in those randomized to CPAP while the depression scores worsened in those randomized to no CPAP. The second trial randomized 30 subjects with an AHI ≥ 30 for 8 weeks, and showed no benefit in functional outcome, neurological outcome, depression, or blood pressure at 3 months or 6 months.(32) However, this study was underpowered and could not be definitive in regard to these negative outcomes, as the planned sample size was 80. The third trial randomized 22 subjects with an AHI ≥ 15 to each treatment group and

showed more improvement in the CPAP group in the Canadian Neurological Scale but not the Berg Balance Scale, 6 minute walk test, or hand grip, all designated as primary outcomes.(33) An on-treatment analysis of a trial in the acute stroke period suggested improvement in the Canadian Neurological Scale at 1 month, but not at any other time point across the two years of assessments in the 57 subjects randomized to CPAP compared with the 69 randomized to standard therapy alone.(35) Our pilot feasibility study did not have adequate power to assess differences in clinical outcomes. A difference in depression scores was found, though the median score in the active (worse) group was only at the lower end of mild depression, arguing against clinical significance.

This study involved a limited sample size, despite screening 803 stroke patients. This points to an important feasibility issue to consider in future trial planning. Changes in the study protocol during the recruitment phase created a limitation, but also provided critical opportunities to explore methods that might improve study procedures. The limited sample size prevented exploration of CPAP usage predictors to identify eligibility criteria that might maximize CPAP use in future studies. However, trials that target only a small subset of stroke patients would have limited generalizability. Although central apneas were uncommon in our population, the use of an autotitrating device was also a limitation, despite its improved feasibility compared with attended titrations. We also lack data on any change in AHI during the treatment period that may have altered CPAP pressure requirements.

In short, this pilot randomized clinical trial showed that sham CPAP can be as tolerable and believable as active CPAP in the acute stroke setting. The use of a sham control would allow for reduction of bias in future studies as it allows for masking of patients, treating physicians, and outcome assessors. In addition, this trial provides critical observations relevant to the design of a larger, more definitive, multi-center trial of CPAP shortly after ischemic stroke. Our experience suggests that motivation to use CPAP must be maximized, perhaps with mechanisms specifically designed to ensure that the device is used each night at bedtime. Objective use data will clearly be necessary. Intensive, one-on-one assistance of each patient, perhaps from a well-trained family member as well as an investigator, may be necessary to improve on the already ample support provided during the current, well-funded pilot trial. As the large majority of post-stroke apnea is obstructive rather than central, and diagnosis is not generally particularly complex after stroke, better-tolerated cardiorespiratory monitoring appears to offer more promise than full polysomnography for a large randomized trial in this fragile population. Furthermore, autotitrating PAP machines may also remove an important barrier that laboratory-based titration can pose. Finally, a definitive randomized trial clearly will have to approach a sizable number of subjects to recruit, screen, randomize, and successfully treat enough subjects to achieve results that are more definitive than those obtained in a growing number of smaller and still inconclusive studies. Our experience, at an academic center with well-developed stroke and sleep expertise, showed significant fall-out from the protocol at every stage. Nonetheless, sufficient preliminary data exist, in support of the hypothesis that successful treatment of post-stroke OSA could improve stroke outcomes, to warrant every effort to execute a rigorous definitive randomized trial.

## Acknowledgments

**Grant support:**

The work was supported by the National Institutes of Health (K23 NS051202). The project described was also supported by Grant Number M01-RR000042 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NCRR or NIH. Respironics, Inc. (now Philips) and Puritan Bennett (now Covidian) provided materials support but had no role in study design, analysis, or manuscript preparation.

Special thanks to Karen C. Johnston, MD, MSc, Medical Monitor.

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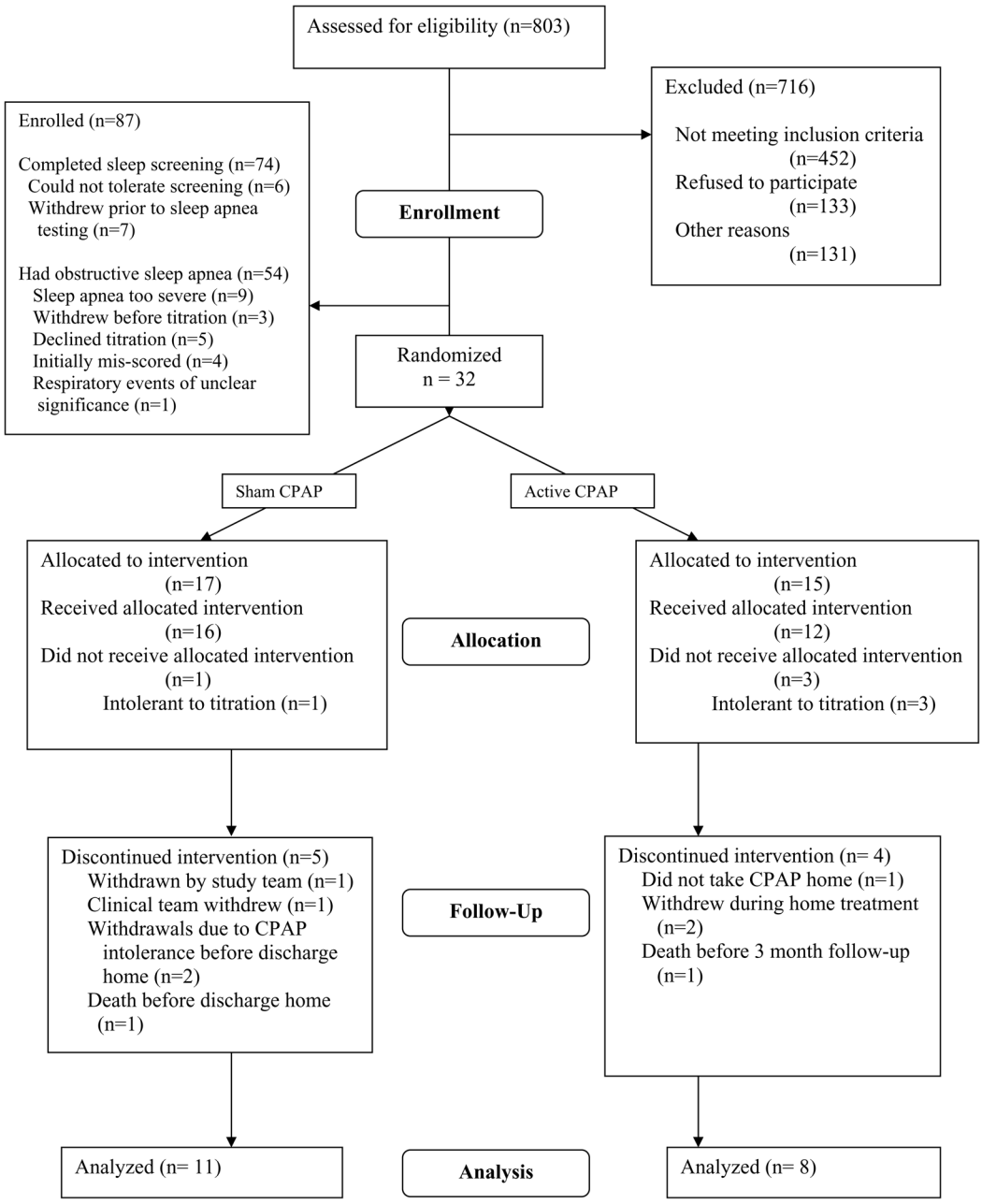


**Figure.**
Patient flow diagram

## Table 1

Baseline characteristics of subjects randomized to active CPAP, randomized to sham CPAP, and eligible for randomization but not randomized.

| | Active (n=15) n (%) or median (IQR) | Sham (n=17) n (%) or median (IQR) | Qualified per protocol, but not randomized (n=13) n (%) or median (IQR) | Completed 3 month protocol (n=19) n (%) or median (IQR) |
|---|---|---|---|---|
| Age | 61 (46, 76) | 74 (55, 81) | 74 (62, 82) | 61 (49, 74) |
| Male | 5 (33) | 13 (76) | 6 (46) | 12 (63) |
| Caucasian | 13 (87) | 15 (88) | 10 (77) | 18 (95) |
| Hypertension | 11 (73) | 13 (76) | 9 (69) | 13 (68) |
| Diabetes | 7 (47) | 5 (29) | 1 (8) | 8 (42) |
| Atrial fibrillation | 3 (20) | 4 (24) | 2 (15) | 4 (21) |
| Prior stroke | 4 (27) | 1 (6) | 1 (8) | 4 (21) |
| Coronary heart disease | 2 (13) | 2 (12) | 0 (0) | 3 (16) |
| Hyperlipidemia | 8 (53) | 14 (82) | 6 (46) | 13 (68) |
| Current smoker | 3 (20) | 3 (18) | 2 (15) | 4 (21) |
| Post stroke baseline Rankin | | | | |
| 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 1 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 2 | 1 (7) | 2 (12) | 1 (8) | 2 (11) |
| 3 | 1 (7) | 4 (24) | 3 (23) | 4 (21) |
| 4 | 11 (73) | 10 (59) | 8 (62) | 11 (58) |
| 5 | 2 (13) | 1 (6) | 1 (8) | 2 (11) |
| BMI | 28 (23, 31) | 29 (28, 32) | 27 (23, 30) | 30 (29, 33) |
| Polysomnography | 5 (33) | 7 (41) | 6 (46) | 6 (32) |
| ApneaLink | 10 (67) | 10 (59) | 7 (54) | 13 (68) |
| SDQ-SA | 31 (27, 36) | 34 (31, 41) | 29 (22, 31) | 36 (30, 41) |
| AHI | 11 (10, 35) | 26 (9, 31) | 16 (9, 36) | 22 (10, 36) |

CPAP: continuous positive airway pressure; BMI: body mass index; SDQ-SA: Sleep Disorders Questionnaire-Sleep apnea; NIHSS: National Institutes of Health Stroke Scale; AHI: apnea-hypopnea index.

## Table 2

Comparison of objective usage data between active and sham CPAP groups.

| | Active CPAP (n=8) median (IQR) | Sham CPAP (n=10*) median (IQR) | p-value |
|---|---|---|---|
| Days with device usage (n) | 16 (6, 40) | 32 (26, 70) | 0.27 |
| Cumulative usage (hours) | 53 (22, 173)† | 74 (17, 94)‡ | 0.92 |
| Average usage on days used (hours) | 4.5 (2.6, 5.5) | 3.5 (1.8, 4.1) | 0.51 |

* Card data for one sham subject not available due to technical issues

† n=7

‡ n=9

## Table 3

Comparison of subjective usage and problems between active and sham CPAP groups in subjects who returned for the 3 month follow-up visit.

| Survey question at 3 months | Active n (%) or median (IQR) | Active n | Sham n (%) or median (IQR) | Sham n |
|---|---|---|---|---|
| On average, how many nights a week do you try to use CPAP when falling asleep? | 5 (4, 6) | 6 | 7 (1,7) | 11 |
| On average, how many hours do you use CPAP per night of use? | 4 (3,6) | 7 | 6 (2, 7.5) | 11 |
| Do you ever take CPAP off in the middle of the night? | 4 (67) | 6 | 5 (71) | 7 |
| How often take off in 7 days | 1 (0, 2) | 6 | 2 (1, 5) | 7 |
| On average, how many nights a week do you take CPAP off and try to sleep more? | 1 (0, 1) | 5 | 1 (0, 7) | 7 |
| How well did you tolerate CPAP | | 7 | | 11 |
| No problems | 2 (29) | | 1 (9) | |
| Minor Problems | 2 (29) | | 3 (27) | |
| Moderate Problems | 2 (29) | | 5 (45) | |
| Severe Problems | 1 (14) | | 2 (18) | |
| Specific problems experienced: | | | | |
| Machine and mask cause nose bleeds | 2 (29) | 7 | 0 (0) | 11 |
| Mask and headgear are difficult to put on | 2 (33) | 6 | 2 (29) | 7 |
| Mask is uncomfortable/painful on face | 3 (43) | 7 | 7 (64) | 11 |
| Mask equipment is too complex | 1 (17) | 6 | 0 (0) | 7 |
| Machine and hose are too complex | 0 (0) | 6 | 0 (0) | 7 |
| Air is uncomfortable on my face | 1 (17) | 6 | 3 (43) | 7 |
| Machine and mask cause nasal congestion or stuffiness | 3 (43) | 7 | 1 (9) | 11 |
| Machine and mask causes dry eyes, nose, mouth and/or throat | 1 (14) | 7 | 3 (27) | 11 |
| Cannot fall asleep with mask on | 3 (50) | 6 | 1 (14) | 7 |
| Cannot stay asleep with mask on | 2 (33) | 6 | 4 (57) | 7 |
| Using CPAP mask and machine is too much of a hassle | 2 (33) | 6 | 4 (57) | 7 |
| Feel claustrophobic with mask on | 1 (17) | 6 | 0 (0) | 7 |
| CPAP makes me feel gassy/nauseous | 0 (0) | 6 | 0 (0) | 7 |
| How do you feel CPAP affects your sleep? | | 6 | | 7 |
| Sleep lighter | 2 (33) | | 1 (14) | |
| Sleep deeper | 1 (17) | | 1 (14) | |
| No change to sleep | 3 (50) | | 5 (71) | |
| How does using CPAP affect your alertness during the day? | | 6 | | 7 |
| Feel more awake | 3 (50) | | 0 (0) | |
| Feel more tired | 0 (0) | | 0 (0) | |
| Does not affect how I feel during the day | 3 (50) | | 7 (100) | |

## Table 4

Comparison of perceived intervention allocation by actual allocation among those who returned for the 3 month follow-up visit.

| | Definitely active | Probably active | Uncertain | Probably pretend | Definitely pretend |
|---|---|---|---|---|---|
| Active CPAP (n=8) | 2 | 2 | 3 | 1 | 0 |
| Sham CPAP (n=11) | 2 | 4 | 3 | 1 | 1 |

## Table 5

Comparison of outcomes at 3 months between active and sham CPAP groups among those subjects who returned for the 3 month follow-up visit.

| | Active (n=8) n (%) or median (IQR) | Sham (n=11) n (%) or median (IQR) |
|---|---|---|
| Fatigue Severity Scale | 2.6 (2.0, 4.1) | 2.4 (1.4, 3.0) |
| Epworth Sleepiness Scale | 8 (6, 9) | 7 (4, 10) |
| PHQ-9 | 5 (4, 6) | 2 (2, 3) |
| Barthel Index | 95 (90, 100) | 100 (95, 100) |
| mRS | 2 (1,3) | 2 (1,2) |
| 0 | 1 (11) | 1 (9) |
| 1 | 2 (22) | 3 (27) |
| 2 | 3 (33) | 5 (45) |
| 3 | 2 (22) | 1 (9) |
| 4 | 1 (11) | 1 (9) |
| 5 | 0 (0) | 0 (0) |
| NIHSS | 1 (0, 4)* | 2 (0, 3)† |

*n= 7

†n=10 PHQ-9: Patient Health Questionnaire; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale.