CPAP Treatment of Sleepy Patients with Milder OSA: Results of the CATNAP Randomized Clinical Trial

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Web Supplement

Reading Level Assessment

The ability to write and read in English at the fifth grade level was evaluated using a brief passage regarding the risks of daytime sleepiness written at the fifth grade reading level as determined by the Flesch-Kincaid assessment.(1) All participants were asked to read the passage as part of the informed consent process and respond to a series of questions evaluating their comprehension.

Primary Endpoint

Functional Outcome of Sleep Questionnaire (FOSQ): FOSQ is a validated 30-item, self-report, disease-specific, functionally-based gold standard measure designed to assess the impact of disorders of excessive sleepiness on functional status.(2) Factor analysis of the FOSQ was conducted with 133 subjects seeking medical attention at two different sleep disorders centers and 20 normal controls (to enhance the variability of responses).(2) This analysis yielded five factors (subscales): Activity Level, Vigilance, Intimacy and Sexual Relationships, General Productivity, and Social Outcome. Internal reliability of the measure was excellent for both the subscales (α=0.70 to α=0.92) and for the total scale (α=0.96). Test-retest reliability of the FOSQ yielded coefficients ranging from r=0.74 to r=0.88 for the five subscales, and r=0.91 for the total measure. The normal value on the FOSQ Total score is 17.9, determined in a sample of normal

individuals free of sleep disorders as verified by polysomnograpy.(3-5)**Secondary Endpoints**

Epworth Sleepiness Scale (ESS): The ESS is a self administered questionnaire that evaluates subjective sleepiness.(6) This scale rates the likelihood of falling asleep in eight soporific situations using a four-point Likert scale ranging from never dozing to high chance of dozing. The ESS significantly correlates with the frequency of apneas and has been used extensively in clinical assessment and sleep apnea research.

Psychomotor Vigilance Task (PVT): The PVT is an objective assessment of sleepiness and measures decrements in neurobehavioral performance due to sleepiness, i.e., ability to sustain attention and respond in a timely manner to salient signals.(7) The PVT yields five highly informative metrics on the capacity for sustained attention and vigilance performance: frequency of lapses, duration of lapse domain, optimum response time, vigilance decrement function, false response frequency. We applied this conceptually valid, relatively short duration, reliable task with known psychometric properties and minimal practice/learning curves to document attentional lapses (response times > 500 msec) in performance. A component of the PVT, the Visual Analog Scale (VAS) asks respondents to indicate on a line the location that best reflects their degree of sleepiness with the anchors “not sleepy”, “very sleepy”.

Medical Outcomes Study Short Form-36 (SF-36): The SF-36 is a 36-item questionnaire that assesses eight health concepts: physical functioning, bodily pain, role limitations due to physical problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions.(8)

Profile of Mood States (POMS): The POMS measures self-reported mood during the daytime.(9) The POMS is a reliable and valid measure of mood states that consists of 65 adjectives on which subjects' rate themselves as they feel "today" using a five-point scale. There are six mood or affective states on this test derived through factor analysis: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment. There is also a summary Total Mood Disturbance (TMD) score that gives a Total estimate of affective state. The POMS test requires 3 to 5 minutes for most subjects to complete.

Ambulatory Blood Pressure: Ambulatory blood pressure was measured using the Spacelabs™ ambulatory blood pressure cuff and monitoring system. Systolic blood pressure (BP), diastolic BP, and 48-hour mean ambulatory arterial BP during the day, during the night and their difference were measured.

Diagnostic and Titration Polysomnography and Scoring

To standardize data collection across sites, the same polysomnograph (PSG) signals were recorded at each site during both the diagnostic and sham-CPAP PSGs including: electroencephalograms (C3M2, C4M1, O2M1), bilateral electrooculograms, electromyograms of the chin muscles and right and left anterior tibialis, movement of the rib cage and abdomen (piezoelectric crystal), oxygen saturation (SaO2) by pulse oximetry, electrocardiogram (Lead 1), and body position. For the diagnostic PSG, nasal pressure (ProTech PTAF2™) was the surrogate airflow signal, and mask pressure (ProTech PTAF2™) was used as the airflow signal on the sham-CPAP studies. The only equipment that was standardized across all sites was the amplifier for the nasal pressure signal (Pro-Tech Services, Inc., Mukilteo, WA). The airflow signal from the

CPAP machine could not be used since the large expiratory leak and orifice restrictor in the sham-CPAP circuit prevented the signal from being received by the machine's sensors. Each site adhered to uniform criteria for signal processing (e.g., digitization rates and alternating current [AC] filters).

Polysomnographic files were electronically transmitted to the central scoring laboratory at the University of Pennsylvania by means of the CATNAP web portal or File Transfer Protocol (FTP) for centralized manual, computer software-assisted scoring (Sandman NT™ software [Embla, Ottawa, Ontario, Canada]). Three of the clinical sites recorded the PSGs using software different from that used by the scoring lab. In order for these recordings to be analyzed, the files were converted into European Data Format prior to being transmitted to the scoring lab. Since electronic tags on the files were lost when the files were converted to European Data Format, the technologists used a standardized PSG event log to record events during the studies.

Sleep stages were characterized by Rechtschaffen and Kales criteria.(10) Arousals were characterized by the AASM criteria.(11) An arousal was associated with a respiratory event if it began within 3 seconds of the termination of the event. Apneas were identified if the airflow signal was flat or nearly flat (i.e., below at least 10% of baseline) and the decrease lasted for > 10 seconds. Apneas associated with respiratory effort were scored as obstructive apneas. Apneas that were not associated with respiratory effort were scored as central apneas. Mixed apneas were scored as obstructive apneas. A decrease in amplitude of a respiratory signal for at least 10 seconds that was associated with a greater than 3% oxygen desaturation was scored

as a hypoponea. The AHI was calculated as the mean number of apneas and hypopneas per hour of sleep.

Placebo Device and Sham Titration

The sham CPAP apparatus (RemStar Pro, Respironics, Inc., Murrysville, PA) consisted of an enlarged air leak incorporated into the exhalation valve (WhisperSwivel®, Respironics, Inc.) between the mask and the CPAP tubing and an orifice restrictor in the CPAP circuit.(12) When fully assembled, this modification in the exhalation valve was not visibly perceptible. Participants randomized to the placebo intervention were fitted with one of the following nasal mask interfaces: Comfort Gel, Comfort Classic, Comfort Select, and Profile Lite (Respironics, Inc.) During the sham CPAP PSG, the technologists used the sleep centers' remotely controlled CPAP machines as the sham-CPAP device to avoid the possibility of unblinding participants. The laboratory CPAP machine was converted into a sham device by inserting the orifice restrictor into the circuit at the point where the CPAP tubing connected to the machine. With the machine set at 10 cm H2O throughout the night and the sham expiratory valve and external orifice resistor in the circuit, the pressure at the mask interface was less than 1 cm H2O. The sham-CPAP apparatus (Respironics, Inc.) distributed to the participants for home use had the same circuit as that used during the PSG with sham-CPAP, except that the orifice restrictor was contained in the CPAP machine so that it was not visible and the machine looked identical to that used by participants randomized to active CPAP treatment.

CPAP Set-up and Education

Before CPAP set-up by the PSG technologist, all participants received a standardized education session with their bed partner designed to improve their CPAP adherence. They also received data cards for their device that documented mask on time. Each participant received an educational brochure, which was reviewed by the unblinded technologist. In addition to motivational content to promote adherence, the brochure covered what CPAP was, why regular use was important, care and daily cleaning of the mask, how to troubleshoot mask-related problems, how to perform weekly cleaning of the mask and the device, care and cleaning of the humidifier, and general care of the device. In conjunction with reviewing the brochure, the unblinded technologist also demonstrated the described techniques using an unpowered unit. Participants received weekly telephone calls to encourage device use.

Inclusion/exclusion Criteria

The determination of alcohol abuse based on the CAGE questionnaire score was changed after the study commenced to better reflect the conceptual definition.

Randomization and Masking

Participants and all members of the research team were blinded to intervention except for the site polysomnographic technologist who performed the polysomnogram and CPAP set-ups based on the assigned intervention. Study personnel at the PSG Reading Center who scored and interpreted the polysomnograms were also unblinded.

Randomisation was performed by computer centrally for each site by the Data Coordinating Center at the University of Pennsylvania. For enrolled participants, a computer-generated randomization number was obtained by the research coordinator and communicated to the PSG technologist who matched it with a sealed envelope,

kept in a locked box, containing the treatment allocation. The appropriate device was then selected by the PSG technologist who distributed it to the research coordinator for distribution in a sealed black bag.

Role of the Funding Source

The sponsors of this study had no role in developing the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all study data and had final responsibility for the decision to submit this study for publication.

Statistical Analysis

Age (<60, ≥ 60), race (white, other), and sex main effects and interactions with treatment as well as group differences in baseline FOSQ Total score and baseline factors with significant group differences found to be associated with change in FOSQ Total score were applied as covariates in the analysis of covariance. Interim analysis for safety was performed when half of the sample had completed the protocol.

Weekly FOSQ score

FOSQ data were obtained weekly from the smartcard download. These data were used in LOCF to provide a follow up FOSQ Total score for participants who failed to return for their final 8-wk assessment. Table E1 displays the weekly data for each group. There were significant difference between weeks within group ($F_{86.39}$, $p<0.001$), but no differences between groups overall ($F_{0.14}$, $p = 0.714$) an no interaction of group by week ($F_{1.69}$, $p = 0.097$).

Adverse Events

There were few important adverse events and no significant differences between groups (Table E2).

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SUPPLEMENTARY TABLE E1. WEEKLY FOSQ TOTAL SCORE FOR ACTIVE AND SHAM CPAP GROUPS

Week	N	MEAN ± SD	N	MEAN ± SD
	ACTIVE CPAP*		SHAM CPAP*	
1	30	7.09 ± 3.68	25	6.21 ± 1.96
2	44	11.21 ± 5.13	44	11.56 ± 4.34
3	64	13.09 ± 4.32	63	13.58 ± 2.87
4	69	13.62 ± 4.22	73	13.34 ± 3.42
5	71	13.91 ± 4.05	81	14.11 ± 3.40
6	79	14.57 ± 3.97	76	13.53 ± 3.65
7	70	13.96 ± 3.95	78	13.59 ± 3.58
8	74	14.11 ± 3.99	76	14.12 ± 2.98
9 (FOLLOW UP)	81	14.45 ± 3.94	73	13.91 ± 3.33

*Within group effect by week p<0.0001

SUPPLEMENTARY TABLE E2. SUMMARY OF CLINICAL ADVERSE EXPERIENCES DURING THE POST-RANDOMIZATION TREATMENT PERIOD PRIMARY SAFETY SAMPLE[1]

Characteristic of Events	**Active N = 121**		**Sham N = 118**		
Number (%) of Patients	*n*	%	*n*	%	*p* value[4]
With No Adverse Experiences	28	23.1	26	22.0	
With One or More Adverse Experiences	93	76.9	92	78.0	.88
With Study-Related Adverse Experiences[2]	46	38.0	42	35.6	.79
With Device-Related Adverse Experiences[3]	50	41.3	39	33.1	.23
With Serious Adverse Experiences	5	4.1	9	7.6	.28
-With Serious Study-Related Adverse Experiences[2]	0	0	1	.8	.49
-With Serious Device-Related Adverse Experiences[3]	0	0	1	.8	.49
Who Died	0	0	0	0	1.00
Discontinued Study Due to an Adverse Experience	0	0	0	0	1.00
Discontinued Treatment Due to an Adverse Experience	1	.8	0	0	1.00
Discontinued Study or Treatment Due to an Adverse Experience	1	.8	0	0	1.00
-Discontinued Study or Treatment Due to a Study-Related Adverse Experiences[2]	1	.8	0	0	1.00

-Discontinued Study or Treatment Due to a Device-Related Adverse Experiences[3]	1	.8	0	0	1.00
-Discontinued Study or Treatment Due to a Serious Adverse Experience	0	0	0	0	1.00

Notes:

[1]The Primary Safety Sample includes all patients exposed to CPAP or Sham treatment status.

[2]Study-related includes possibly, probably, definitely, and those with unknown/undetermined

(documented exposure of at least 20 minutes) during the post-randomization.

[3]Device-related includes possibly, probably, definitely, and those with unknown/undetermined status.

[4]Fisher's Exact 2-tailed test.

SUPPLEMENTARY TABLE E3A. NUMBER (%) OF RANDOMIZED AND EXPOSED PARTICIPANTS EXPERIENCING A LIFE TIME MEDICAL CONDITION BY TREATMENT

	Active		Sham		
Factor	**n**	**%**	**n**	**%**	**p-value[1]**
Any other life time medical condition	118	97.5	110	93.2	.13
No other life time medical condition	3	2.5	8	6.8	.13
More than one other medical condition	87	71.9	84	71.2	1
Diabetes	16	13.2	19	15.4	.71
Chronic Bronchitis	2	1.7	5	4.3	.27
Emphysema/COPD	1	.8	4	3.4	.21
Asthma	16	13.2	21	17.9	.37
Other Lung Disease	6	5.0	5	4.3	1
High Blood Pressure	49	40.5	46	39.3	.90
Pulmonary Hypertension	0	0	0	0	NVT
Angina	5	4.1	7	6	.57
Heart Attack	3	2.5	5	4.3	.49

Arrhythmia	8	6.6	17	14.5	.06
Heart Failure	2	1.7	2	1.7	1
Syncope	11	9.1	2	1.7	.02
Stroke	6	5	4	3.4	.75
Other Heart Disease	11	9.1	5	4.3	.20
Thyroid Disease	13	10.7	12	10.3	1
Sinus Disease	13	10.7	19	16.2	.26
Hay Fever	21	17.4	27	23.1	.33
Deviated Nasal Septum	15	12.4	13	11.1	.84
Seizure Disorder	3	2.5	0	0	.25
Impotence	5	4.1	2	1.7	.45
Arthritis	29	24	3	28.2	.46
Depression	39	32.2	39	33.3	.89
Other Psychiatric Conditions	11	9.4	9	7.8	.82
Other Conditions	63	55.8	55	47.8	.24
Notes: [1]Fisher's Exact Test; NVT-No valid test					

SUPPLEMENTARY TABLE E3B. NUMBER (%) OF RANDOMIZED AND EXPOSED PARTICIPANTS EXPERIENCING A CURRENT MEDICAL CONDITION BY TREATMENT GROUP

	Active		Sham		
Factor	**n**	**%**	**n**	**%**	**p-value[1]**
Any current medical condition	116	95.9	106	89.8	.08
No other current medical condition	5	4.1	12	10.2	.08
More than one current medical condition	76	62.8	77	65.3	.79
Diabetes	15	12.4	18	15.3	.58
Chronic Bronchitis	2	1.7	2	1.7	1
Emphysema/COPD	1	.8	3	2.5	.37
Asthma	13	10.7	16	13.6	.56
Other Lung Disease	2	1.7	3	2.5	.68
High Blood Pressure	49	40.5	45	38.1	.79
Pulmonary Hypertension	0	0	0	0	NVT
Angina	3	2.5	5	4.2	.50
Heart Attack	2	1.7	2	1.7	1
Arrhythmia	5	4.1	12	10.	.08

				2	
Heart Failure	1	.8	2	1.7	.62
Syncope	2	1.7	0	0	.50
Stroke	2	1.7	0	0	.50
Other Heart Disease	6	5	1	.8	.12
Thyroid Disease	11	9.1	10	8.5	1
Sinus Disease	12	9.9	17	14.4	.33
Hay Fever	21	17.4	27	22.9	.33
Deviated Nasal Septum	13	10.7	10	8.5	.66
Seizure Disorder	1	.8	0	0	1
Impotence	5	4.1	2	1.7	.45
Arthritis	29	24	32	27.1	.66
Depression	31	25.6	33	28	.77
Other Psychiatric Conditions	10	8.3	7	5.9	.62
Other Conditions	61	50.4	47	39.8	.12
Notes: [1]Fisher's Exact Test; NVT-No valid test					

SUPPLEMENTTABLE E4 NUMBER (%) OF RANDOMIZED AND EXPOSED PARTICIPANTS WITH SPECIFIC CONCOMITANT MEDICATIONS BY GROUP.

	Active (n=121)		**Sham (n=118)**	
	n	**%**	**n**	**%**
With no concomitant medications	3	2.5	8	6.8
With one or more concomitant medications	118	97.5	110	93.2
AA/LIVER-SPLEEN SHEEP EXTRACT	1	0.8	0	0.0
ACETAMINOPHEN	51	42.1	55	46.6
ACETAMINOPHEN WITH CODEINE	6	5.0	8	6.8
ACETAMINOPHEN/CAFFEINE	1	0.8	1	0.8
ACETAMINOPHEN/CHLOR-MAL	0	0.0	1	0.8
ACETAMINOPHEN/DP-HYDRAM HCL	2	1.7	1	0.8
ACIDOPHILUS/BIFIDO LONGUM	1	0.8	0	0.0
ACITRETIN	0	0.0	1	0.8
ALBUTEROL	11	9.1	10	8.5
ALBUTEROL SULFATE	1	0.8	2	1.7
ALBUTEROL SULFATE/IPRATROPIUM	0	0.0	1	0.8
ALENDRONATE SODIUM	0	0.0	1	0.8
ALLERGENIC EXTRACTS	0	0.0	1	0.8
ALLOPURINOL	3	2.5	5	4.2
ALPRAZOLAM	4	3.3	1	0.8
AMILORIDE/HYDROCHLOROTHIAZIDE	1	0.8	1	0.8
AMINO ACIDS/VITAMIN B COMPLEX	0	0.0	1	0.8
AMITRIP HCL/CHLORDIAZEPOXIDE	0	0.0	1	0.8

AMITRIPTYLINE HCL	2	1.7	4	3.4
AMLODIPINE BESYLATE	9	7.4	7	5.9
AMLODIPINE BESYLATE/BENAZEPRIL	3	2.5	0	0.0
AMLODIPINE/ATORVAST CAL	0	0.0	1	0.8
AMMONIUM CH/PE/HYDROCODONE/PYR	0	0.0	1	0.8
AMOX TR/POTASSIUM CLAVULANATE	0	0.0	1	0.8
AMOXICILLIN TRIHYDRATE	2	1.7	7	5.9
ANESTHESIA TRAY	0	0.0	1	0.8
ASA/CALCIUM CARB/MAG/AL HYDROX	1	0.8	0	0.0
ASCORBATE CALCIUM	1	0.8	2	1.7
ASCORBIC ACID	4	3.3	3	2.5
ASCORBIC ACID/ZINC	0	0.0	1	0.8
ASPIRIN	28	23.1	40	33.9
ASPIRIN/ACETAMINOPHEN/CAFFEINE	6	5.0	0	0.0
ASPIRIN/CAFFEINE	0	0.0	1	0.8
ASPIRIN/CALCIUM CARBONATE/MAG	0	0.0	1	0.8
ASPIRIN/SOD BICARB/CITRIC ACID	0	0.0	1	0.8
ATENOLOL	8	6.6	7	5.9
ATENOLOL/CHLORTHALIDONE	0	0.0	1	0.8
ATORVASTATIN CALCIUM	23	19.0	22	18.6
ATOVAQUONE/PROGUANIL HCL	1	0.8	0	0.0
AZELASTINE HCL	1	0.8	2	1.7
AZITHROMYCIN	2	1.7	6	5.1
BACITRACIN	0	0.0	1	0.8
BACITRACIN/POLYMYXIN B SULFATE	0	0.0	1	0.8
BECLOMETHASONE DIPROPIONATE	0	0.0	1	0.8

BEE POLLEN	1	0.8	0	0.0
BENAZEPRIL HCL	0	0.0	1	0.8
BENZOCAINE	1	0.8	0	0.0
BENZOCAINE/MENTH/CETYLPYRD CL	0	0.0	2	1.7
BENZONATATE	3	2.5	0	0.0
BETA-CAROTENE	0	0.0	1	0.8
BETAMETHASONE VALERATE	0	0.0	2	1.7
BEVACIZUMAB	1	0.8	0	0.0
BISMUTH SUBSALICYLATE	2	1.7	5	4.2
BLACK COHOSH	1	0.8	0	0.0
BLOOD SUGAR DIAGNOSTIC	1	0.8	0	0.0
BRIMONIDINE TARTRATE	0	0.0	1	0.8
BRINZOLAMIDE	0	0.0	1	0.8
BUDESONIDE	3	2.5	0	0.0
BUDESONIDE/FORMOTEROL FUMARATE	0	0.0	1	0.8
BUPROPION HCL	8	6.6	4	3.4
BUSPIRONE HCL	2	1.7	1	0.8
CA CARBONATE/MAG OXIDE/CU/ZNOX	1	0.8	0	0.0
CA CARBONATE/MAG/VITAMIN D2	0	0.0	1	0.8
CA CARBONATE/VITAMIN D3/VIT K	2	1.7	1	0.8
CALCIUM	3	2.5	1	0.8
CALCIUM CARB/VIT D3/MINERALS	1	0.8	0	0.0
CALCIUM CARBONATE	4	3.3	3	2.5
CALCIUM CARBONATE/MULTIVIT	1	0.8	0	0.0
CALCIUM CARBONATE/VITAMIN D2	4	3.3	4	3.4
CALCIUM GLUCONATE	1	0.8	0	0.0

CALCIUM/MAGNESIUM	0	0.0	1	0.8
CANDESARTAN CILEXETIL	1	0.8	1	0.8
CANDESARTAN/HYDROCHLOROTHIAZID	1	0.8	0	0.0
CARBAMAZEPINE	2	1.7	0	0.0
CARBOXYMETHYLCELL/HYPROMELLOSE	0	0.0	1	0.8
CARBOXYMETHYLCELLULOSE SODIUM	0	0.0	3	2.5
CARTEOLOL HCL	1	0.8	0	0.0
CARVEDILOL	1	0.8	2	1.7
CASANTHRANOL/DOCUSATE SODIUM	0	0.0	2	1.7
CEFPROZIL	0	0.0	1	0.8
CEFTRIAXONE SODIUM	1	0.8	0	0.0
CEFUROXIME AXETIL	1	0.8	1	0.8
CELECOXIB	3	2.5	3	2.5
CEPHALEXIN MONOHYDRATE	0	0.0	2	1.7
CETIRIZINE HCL	3	2.5	4	3.4
CHLORHEXIDINE GLUCONATE	1	0.8	0	0.0
CHLOROQUINE PHOSPHATE	0	0.0	1	0.8
CHLORPHENIRAMINE MALEATE	2	1.7	0	0.0
CHLORTHALIDONE	1	0.8	3	2.5
CHOLECALCIFEROL	4	3.3	2	1.7
CHOLESTYRAMINE	0	0.0	1	0.8
CIPROFLOXACIN	1	0.8	5	4.2
CITALOPRAM HCL	1	0.8	0	0.0
CITALOPRAM HYDROBROMIDE	6	5.0	7	5.9
CLARITHROMYCIN	2	1.7	2	1.7
CLINDAMYCIN HCL	3	2.5	0	0.0

CLONAZEPAM	0	0.0	1	0.8
CLONIDINE HCL	1	0.8	3	2.5
CLOPIDOGREL BISULFATE	1	0.8	4	3.4
COD LIVER OIL	0	0.0	1	0.8
CODEINE PHOS/ACETAMINOPHEN	7	5.8	6	5.1
CODEINE PHOS/ASPIRIN	0	0.0	1	0.8
COLCHICINE	2	1.7	1	0.8
CORTISONE ACETATE	2	1.7	2	1.7
CROMOLYN SODIUM	1	0.8	0	0.0
CYANOCOBALAMIN	1	0.8	1	0.8
CYCLOBENZAPRINE HCL	0	0.0	2	1.7
D-METHORPHAN HB/ACETAMINOPHEN	8	6.6	0	0.0
D-METHORPHAN HB/P-EPD HCL/APAP	0	0.0	2	1.7
D-METHORPHAN HB/P-EPD HCL/BPM	1	0.8	0	0.0
D-METHORPHAN HB/P-EPHED HCL	0	0.0	1	0.8
D-METHORPHAN HB/P-EPHED HCL/CP	0	0.0	1	0.8
D-METHORPHAN/P-EPHED/ACETAMINP	1	0.8	4	3.4
DALTEPARIN SODIUM,PORCINE	1	0.8	0	0.0
DESLORATADINE	2	1.7	5	4.2
DESMOPRESSIN (NONREFRIGERATED)	0	0.0	1	0.8
DESOGESTREL-ETHINYL ESTRADIOL	1	0.8	0	0.0
DESOXIMETASONE	0	0.0	1	0.8
DEXAMETHASONE	1	0.8	0	0.0
DEXTROMETHORPHAN	0	0.0	4	3.4
DEXTROMETHORPHAN HBR	1	0.8	0	0.0
DHCODEINE BT/ACETAMINOPHN/CAFF	0	0.0	1	0.8

DICLOFENAC SODIUM/MISOPROSTOL	0	0.0	3	2.5
DIETARY SUPPLEMENT	0	0.0	1	0.8
DIFLUNISAL	1	0.8	0	0.0
DIGOXIN	0	0.0	2	1.7
DILTIAZEM HCL	4	3.3	4	3.4
DIMENHYDRINATE	0	0.0	4	3.4
DIPHENHYDRAMINE CITRATE	1	0.8	3	2.5
DIPHENHYDRAMINE HCL	4	3.3	9	7.6
DIVALPROEX SODIUM	1	0.8	1	0.8
DL-ALPHA TOCOPHEROL	3	2.5	0	0.0
DL-ALPHA TOCOPHERYL ACETATE	0	0.0	1	0.8
DM HB/PSEUDOEPHED/ACETAMIN/CP	0	0.0	2	1.7
DOCOSAHEXANOIC ACID/EPA	4	3.3	0	0.0
DOCUSATE SODIUM	2	1.7	2	1.7
DOMPERIDONE	0	0.0	1	0.8
DOXAZOSIN MESYLATE	0	0.0	1	0.8
DOXYCYCLINE HYCLATE	0	0.0	1	0.8
DOXYCYCLINE MONOHYDRATE	0	0.0	3	2.5
DULOXETINE HCL	2	1.7	2	1.7
DUTASTERIDE	1	0.8	0	0.0
ECHINACEA	1	0.8	3	2.5
ECONAZOLE NITRATE	0	0.0	1	0.8
ENALAPRIL MALEATE	3	2.5	0	0.0
EPHEDRINE	0	0.0	1	0.8
ERYTHROMYCIN BASE	0	0.0	1	0.8
ESCITALOPRAM OXALATE	2	1.7	0	0.0

ESOMEPRAZOLE MAG TRIHYDRATE	4	3.3	10	8.5
ESTRADIOL	2	1.7	1	0.8
ESTRADIOL VALERATE	1	0.8	0	0.0
ESTROGEN,CON/M-PROGEST ACET	0	0.0	1	0.8
ESTROGENS,CONJ.,SYNTHETIC A	1	0.8	0	0.0
ESTROGENS,CONJUGATED	1	0.8	5	4.2
ESZOPICLONE	0	0.0	2	1.7
ETIDRONATE DISODIUM	1	0.8	0	0.0
ETODOLAC	2	1.7	1	0.8
EUCALYPT/MEN/CAMP/TURP/PET,WH	1	0.8	0	0.0
EXENATIDE	4	3.3	0	0.0
EZETIMIBE	2	1.7	9	7.6
EZETIMIBE/SIMVASTATIN	0	0.0	4	3.4
FA/MV,CA,FE,MIN/LYCOPENE/LUT	1	0.8	0	0.0
FAMOTIDINE	0	0.0	2	1.7
FELODIPINE	0	0.0	5	4.2
FENOFIBRATE NANOCRYSTALLIZED	2	1.7	1	0.8
FENOFIBRATE,MICRONIZED	1	0.8	2	1.7
FENTANYL	1	0.8	0	0.0
FERROUS FUMARATE	3	2.5	1	0.8
FERROUS SULFATE	3	2.5	1	0.8
FEXOFENADINE HCL	6	5.0	4	3.4
FINASTERIDE	2	1.7	0	0.0
FISH OIL/OMEGA-3 FATTY ACIDS	2	1.7	0	0.0
FLAXSEED OIL	1	0.8	1	0.8
FLUNISOLIDE	1	0.8	0	0.0

FLUOXETINE	3	2.5	1	0.8
FLUOXETINE HCL	3	2.5	6	5.1
FLUTICASONE FUROATE	1	0.8	0	0.0
FLUTICASONE PROPIONATE	6	5.0	11	9.3
FLUTICASONE/SALMETEROL	1	0.8	7	5.9
FLUVASTATIN SODIUM	1	0.8	0	0.0
FOLIC ACID	1	0.8	0	0.0
FOLIC ACID/MV,FE,OTHER MIN	1	0.8	0	0.0
FORMOTEROL FUMARATE	1	0.8	0	0.0
FOSINOPRIL SODIUM	1	0.8	0	0.0
FUROSEMIDE	1	0.8	5	4.2
GABAPENTIN	2	1.7	3	2.5
GARLIC	1	0.8	1	0.8
GEMFIBROZIL	1	0.8	1	0.8
GENTAMICIN IN SALINE, ISO-OSM	1	0.8	0	0.0
GENTAMICIN SULFATE	0	0.0	2	1.7
GENTAMICIN/SODIUM CHLORIDE	0	0.0	1	0.8
GINKGO BILOBA	0	0.0	1	0.8
GINSENG	0	0.0	3	2.5
GLIMEPIRIDE	0	0.0	1	0.8
GLIPIZIDE	2	1.7	3	2.5
GLIPIZIDE/METFORMIN HCL	1	0.8	0	0.0
GLUC HCL/CSA/COLL HY/HYALUR AC	2	1.7	1	0.8
GLUC SU/CHONDR SU A NA/SODIUM	1	0.8	1	0.8
GLUC SU/CHONDRO SU A/VIT C/MN	1	0.8	0	0.0
GLUC SU/CHONDROITIN SULFATE A	1	0.8	0	0.0

GLUCOSAMINE HCL	2	1.7	1	0.8
GLUCOSAMINE HCL/CHONDR SU A NA	1	0.8	0	0.0
GLUCOSAMINE SULFATE	1	0.8	1	0.8
GLYBURIDE	1	0.8	2	1.7
GUAIF/PSE/CODEINE/TRIPROLIDINE	1	0.8	0	0.0
GUAIFEN/PSEUDOEPHED/ACETAMINOP	2	1.7	2	1.7
GUAIFENESIN/D-METHORPHAN HB	0	0.0	3	2.5
GUAIFENESIN/P-EPHED HCL	0	0.0	1	0.8
GUAIFENESIN/PHENYLEPHRINE HCL	1	0.8	0	0.0
HC/MINERAL OIL/PETROLAT,WHT	1	0.8	0	0.0
HEP B VACCINE/HEP A VACCINE	0	0.0	2	1.7
HEPATITIS A & B VACCINE/PF	2	1.7	0	0.0
HERBAL DRUGS	14	11.6	3	2.5
HERBAL DRUGS/PUMPKIN SEED OIL	1	0.8	0	0.0
HUM INSULIN NPH/REG INSULIN HM	1	0.8	0	0.0
HYALURONATE SODIUM	0	0.0	1	0.8
HYDRALAZINE HCL	0	0.0	1	0.8
HYDROCHLOROTHIAZIDE	9	7.4	13	11.0
HYDROCODONE BIT/ACETAMINOPHEN	2	1.7	5	4.2
HYDROCODONE BIT/HOMATROPINE	1	0.8	5	4.2
HYDROCORTISONE	2	1.7	0	0.0
HYDROCORTISONE VALERATE	0	0.0	1	0.8
HYDROCORTISONE/ALOE VERA	0	0.0	1	0.8
HYDROGEN PEROXIDE	1	0.8	0	0.0
HYDROXYZINE HCL	0	0.0	1	0.8
HYOSCYAMINE SULFATE	1	0.8	0	0.0

HYPROMELLOSE/PF	1	0.8	0	0.0
IBANDRONATE SODIUM	1	0.8	0	0.0
IBUPROFEN	62	51.2	56	47.5
IBUPROFEN/P-EPHED HCL/CP	0	0.0	1	0.8
IBUPROFEN/PSEUDOEPHEDRINE HCL	5	4.1	8	6.8
IMIPRAMINE HCL	1	0.8	0	0.0
INDOMETHACIN	1	0.8	2	1.7
INFLUENZA TV-S 05-06 VACCINE	2	1.7	1	0.8
INSULIN DETEMIR	0	0.0	1	0.8
INSULIN GLARGINE,HUM.REC.ANLOG	0	0.0	3	2.5
INSULIN LISPRO,HUMAN REC.ANLOG	0	0.0	2	1.7
INSULIN NPH HUMAN RECOM	1	0.8	0	0.0
INSULIN NPL/INSULIN LISPRO	0	0.0	2	1.7
INSULIN REGULAR, HUMAN	0	0.0	2	1.7
IPRATROPIUM BROMIDE	1	0.8	1	0.8
IRBESARTAN	0	0.0	2	1.7
IRBESARTAN/HYDROCHLOROTHIAZIDE	0	0.0	1	0.8
IRON	1	0.8	1	0.8
KETOPROFEN	0	0.0	1	0.8
LABETALOL HCL	1	0.8	3	2.5
LAMOTRIGINE	2	1.7	0	0.0
LANCETS	0	0.0	1	0.8
LANSOPRAZOLE	1	0.8	1	0.8
LATANOPROST	2	1.7	1	0.8
LEVOFLOXACIN	3	2.5	2	1.7
LEVOTHYROXINE SODIUM	11	9.1	10	8.5

LIDOCAINE HCL	1	0.8	1	0.8
LISINOPRIL	11	9.1	5	4.2
LISINOPRIL/HYDROCHLOROTHIAZIDE	1	0.8	1	0.8
LITHIUM	0	0.0	1	0.8
LITHIUM CARBONATE	2	1.7	3	2.5
LOPERAMIDE HCL	1	0.8	6	5.1
LORATADINE	3	2.5	8	6.8
LORAZEPAM	1	0.8	1	0.8
LOSARTAN POTASSIUM	2	1.7	3	2.5
LOSARTAN/HYDROCHLOROTHIAZIDE	0	0.0	1	0.8
LOVASTATIN	1	0.8	0	0.0
LUBIPROSTONE	1	0.8	0	0.0
LUMIRACOXIB	0	0.0	1	0.8
MAG CARB/AL HYDROX/ALGINIC AC	1	0.8	0	0.0
MECLIZINE HCL	1	0.8	0	0.0
MEDROXYPROGESTERONE ACET	1	0.8	2	1.7
MELOXICAM	3	2.5	3	2.5
MENTHOL/CAMPHOR	0	0.0	1	0.8
MENTHOL/CETYLPYRD CL	0	0.0	1	0.8
MEPERIDINE HCL	1	0.8	0	0.0
METAXALONE	1	0.8	0	0.0
METFORMIN HCL	11	9.1	13	11.0
METHADONE HCL	1	0.8	1	0.8
METHOCARBAMOL	2	1.7	8	6.8
METHOCARBAMOL/ASPIRIN	3	2.5	0	0.0
METHYLPREDNISOLONE ACETATE	0	0.0	1	0.8

METOCLOPRAMIDE HCL	1	0.8	0	0.0
METOPROL/HYDROCHLOROTHIAZIDE	3	2.5	2	1.7
METOPROLOL SUCCINATE	4	3.3	1	0.8
METOPROLOL TARTRATE	2	1.7	3	2.5
METRONIDAZOLE	1	0.8	3	2.5
MIDAZOLAM	1	0.8	0	0.0
MILK THISTLE	1	0.8	0	0.0
MINERAL OIL	1	0.8	0	0.0
MIRTAZAPINE	1	0.8	3	2.5
MOMETASONE FUROATE	6	5.0	11	9.3
MONTELUKAST SODIUM	1	0.8	2	1.7
MORPHINE	1	0.8	0	0.0
MORPHINE SULFATE	0	0.0	2	1.7
MOXIFLOXACIN HCL	3	2.5	2	1.7
MULTIVITAMINS	16	13.2	11	9.3
MULTIVITAMINS W-MINERALS	3	2.5	2	1.7
MULTIVITAMINS W-MINERALS/LUT	1	0.8	1	0.8
MULTIVITS,TH W-CA,FE,OTH MIN	0	0.0	1	0.8
MULTIVITS,THERAP W-FE,HEMATIN	1	0.8	0	0.0
MUPIROCIN CALCIUM	0	0.0	1	0.8
NABUMETONE	1	0.8	1	0.8
NAPHAZOLINE HCL/ANTAZOLINE	0	0.0	1	0.8
NAPROXEN	2	1.7	5	4.2
NAPROXEN SODIUM	7	5.8	3	2.5
NAPROXEN SODIUM/P-EPHED HCL	0	0.0	1	0.8
NATEGLINIDE	0	0.0	1	0.8

NEOMY SULF/BACITRAC ZN/POLY	3	2.5	0	0.0
NEOMYCIN/BACITRA/POLYMYXIN/HC	0	0.0	1	0.8
NIACIN	5	4.1	2	1.7
NIFEDIPINE	4	3.3	1	0.8
NITROFURANTOIN	1	0.8	0	0.0
NITROGLYCERIN	4	3.3	6	5.1
NORETH A-ET ESTRA/FE FUMARATE	2	1.7	0	0.0
NORETHINDRONE	1	0.8	0	0.0
NORFLOXACIN	0	0.0	1	0.8
NORGESTIMATE-ETHINYL ESTRADIOL	1	0.8	0	0.0
NORMAL SALINE	0	0.0	1	0.8
NPH, HUMAN INSULIN ISOPHANE	0	0.0	2	1.7
NYSTATIN/TRIAMCIN	0	0.0	1	0.8
OLMESARTAN MEDOXOMIL	0	0.0	1	0.8
OLOPATADINE HCL	0	0.0	2	1.7
OMEGA-3 FATTY ACIDS	4	3.3	4	3.4
OMEPRAZOLE	5	4.1	7	5.9
OMEPRAZOLE MAGNESIUM	1	0.8	0	0.0
ORLISTAT	1	0.8	0	0.0
OXAZEPAM	1	0.8	0	0.0
OXYCODONE HCL	1	0.8	3	2.5
OXYCODONE HCL/ACETAMINOPHEN	4	3.3	3	2.5
P-EPHED HCL/ACETAMINOPHEN	1	0.8	1	0.8
P-EPHED HCL/ACETAMINOPHN/CP	0	0.0	1	0.8
P-EPHED HCL/ACETAMINOPHN/DPHA	0	0.0	2	1.7
P-EPHED HCL/TRIPROLIDINE HCL	2	1.7	1	0.8

P-EPHED SUL/LORATADINE	0	0.0	3	2.5
PAMIDRONATE DISODIUM	0	0.0	1	0.8
PANTOPRAZOLE SODIUM	1	0.8	1	0.8
PARICALCITOL	1	0.8	0	0.0
PAROXETINE HCL	14	11.6	6	5.1
PE/HYDROCODONE/DEXBROMPHENIRMN	1	0.8	0	0.0
PEN G POT/DEXTROSE-WATER	0	0.0	1	0.8
PENICILLIN V	0	0.0	2	1.7
PENICILLIN V POTASSIUM	0	0.0	2	1.7
PERINDOPRIL ERBUMINE	1	0.8	0	0.0
PHENIRAMINE MALEATE	0	0.0	1	0.8
PHENYLEPHRINE HCL	1	0.8	3	2.5
PHENYLEPHRINE/CHLOR-MAL/SCOP	1	0.8	0	0.0
PHENYTOIN	1	0.8	1	0.8
PIOGLITAZONE HCL	0	0.0	5	4.2
POTASSIUM	1	0.8	0	0.0
POTASSIUM CHLORIDE	0	0.0	3	2.5
POTASSIUM PHOS,M-BASIC-D-BASIC	1	0.8	0	0.0
PRAVASTATIN SODIUM	1	0.8	1	0.8
PREDNISONE	4	3.3	9	7.6
PROGESTERONE	0	0.0	1	0.8
PROMETHAZINE HCL	1	0.8	0	0.0
PROPAFENONE HCL	0	0.0	1	0.8
PROPOXYPHENE/ACETAMINOPHEN	1	0.8	0	0.0
PROPRANOLOL HCL	2	1.7	0	0.0
PROPYLENE GLYCOL/PEG'S	0	0.0	1	0.8

PSEUDOEPHEDRINE HCL	0	0.0	5	4.2
PYRIDOXINE HCL	1	0.8	0	0.0
QUETIAPINE FUMARATE	0	0.0	3	2.5
QUINAPRIL HCL	0	0.0	1	0.8
QUINAPRIL/HYDROCHLOROTHIAZIDE	1	0.8	0	0.0
QUININE SULFATE	0	0.0	1	0.8
RABEPRAZOLE SODIUM	2	1.7	3	2.5
RAMIPRIL	2	1.7	5	4.2
RANITIDINE HCL	5	4.1	1	0.8
RED YEAST RICE EXTRACT	1	0.8	0	0.0
REPAGLINIDE	0	0.0	1	0.8
RIFABUTIN	0	0.0	1	0.8
RISEDRONATE SODIUM	0	0.0	2	1.7
RISPERIDONE	1	0.8	0	0.0
ROFECOXIB	1	0.8	0	0.0
ROPINIROLE HCL	1	0.8	0	0.0
ROSIGLITAZONE MALEATE	2	1.7	2	1.7
ROSIGLITAZONE/METFORMIN HCL	0	0.0	1	0.8
ROSUVASTATIN CALCIUM	7	5.8	2	1.7
SALM OIL/VIT E MIX/SOY/FAT 3	0	0.0	1	0.8
SALMETEROL XINAFOATE	0	0.0	1	0.8
SAW PALMETTO	2	1.7	0	0.0
SERTRALINE HCL	5	4.1	5	4.2
SILDENAFIL CITRATE	0	0.0	2	1.7
SIMVASTATIN	6	5.0	5	4.2
SITAGLIPTIN PHOSPHATE	0	0.0	2	1.7

SODIUM CHLORIDE	1	0.8	1	0.8
SPIRONOLACTONE	0	0.0	1	0.8
SULFAMETHOXAZOLE/TRIMETHOPRIM	1	0.8	0	0.0
SUMATRIPTAN	2	1.7	0	0.0
TADALAFIL	0	0.0	1	0.8
TAMSULOSIN HCL	1	0.8	2	1.7
TEGASEROD HYDROGEN MALEATE	0	0.0	2	1.7
TELMISARTAN	3	2.5	2	1.7
ZOLPIDEM TARTRATE	1	0.8	6	5.1
TELMISARTAN/HYDROCHLOROTHIAZID	1	0.8	0	0.0
TERBUTALINE SULFATE	0	0.0	2	1.7
TESTOSTERONE	2	1.7	1	0.8
TETRACYCLINE	1	0.8	0	0.0
TETRAHYDROZOLINE HCL	0	0.0	1	0.8
TIMOLOL MALEATE	2	1.7	0	0.0
TIOTROPIUM BROMIDE	1	0.8	2	1.7
TOPIRAMATE	1	0.8	1	0.8
TORSEMIDE	1	0.8	0	0.0
TRAMADOL HCL	1	0.8	3	2.5
TRAVOPROST	0	0.0	1	0.8
TRAZODONE HCL	2	1.7	5	4.2
TRIAMCINOLONE ACETONIDE	2	1.7	6	5.1
TRIAMTERENE	0	0.0	2	1.7
TRIAMTERENE/HYDROCHLOROTHIAZID	4	3.3	1	0.8
TRIAZOLAM	0	0.0	1	0.8
TRIHEXYPHENIDYL HCL	1	0.8	0	0.0

UBIDECARENONE	3	2.5	0	0.0
VALACYCLOVIR HCL	3	2.5	0	0.0
VALPROIC ACID	0	0.0	1	0.8
VALSARTAN	6	5.0	1	0.8
VALSARTAN/HYDROCHLOROTHIAZIDE	2	1.7	2	1.7
VENLAFAXINE HCL	5	4.1	4	3.4
VITAMIN B COMPLEX	3	2.5	3	2.5
VITAMIN C	2	1.7	0	0.0
VITAMIN E	1	0.8	0	0.0
WARFARIN SODIUM	1	0.8	4	3.4
XYLOMETAZOLINE HCL	2	1.7	0	0.0
ZINC	1	0.8	0	0.0
ZINC GLUCONATE	0	0.0	1	0.8
ZOPICLONE	4	3.3	0	0.0

SUPPLEMENTARY TABLE E5. BASELINE PARTICIPANT CHARACTERISTICS OF THOSE RANDOMIZED BUT NOT EXPOSED TO CPAP

Variable	N	% or Mean ± Standard Deviation	Median
Percent males	42	60%	
Percent African Americans	42	26.19%	
Percent married	42	52.38%	
Percent high school education	42	23.81%	
Percent work full time	42	64.29%	
Age (years)	42	48.76 ± 12.93	47
FOSQ Total Score	25	15.21 ± 1.88	15.44
ESS Score	25	15.48 ± 4.24	17

SUPPLEMENTARY TABLE E6. EFFICACY CHANGE OF SECONDARY SUBJECTIVE OUTCOMES FROM PRE-TREATMENT BASELINE TO THE END OF THE INITIAL 8-WEEK TREATMENT PERIOD[1] IN THE MODIFIED INTENT TO TREAT SAMPLE[2]

Endpoint	Active Adjusted Mean Change[2]	Sham Adjusted Mean Change[2]	Adjusted Difference in Mean Change[2]	SE	p Value[3]	95% CI for Difference in Mean Changes	
						Lower Bound	Upper Bound
SF-36							
Physical Component	3.89	.04	3.85	1.17	.001	1.53	6.17
Mental Health Component	3.07	2.21	.86	1.42	.546	-1.95	3.67
Physical Functioning	8.97	1.83	7.14	2.35	.003	2.49	11.79
RP Role Physical	11.41	2.05	9.36	5.95	.118	-2.40	21.12
Bodily Pain	9.25	1.13	8.12	2.69	.003	2.81	13.44
General Health	6.27	-.35	6.61	2.42	.007	1.82	11.41
Vitality	12.66	6.07	6.59	3.14	.037	.39	12.80

Social Functioning	7.15	2.95	4.20	2.72	.125	-1.19	9.59
Role Emotional	8.68	7.39	1.29	6.10	.833	-10.77	13.35
Mental Health	4.80	2.27	2.54	2.12	.234	-1.66	6.73
ESS	-2.46	-.68	-1.78	.52	.001	-2.82	-.75
POMS							
Fatigue Score	-2.7	-.5	-2.27	.83	.007	-3.9	-.6
Confusion-Bewilderment	-1.5	-.4	-1.09	.42	.011	-1.9	-.3
Tension-Anxiety Score	-.5	-.8	.30	.52	.565	-.7	1.3
Vigor Score	2.8	-.1	2.89	.75	0	1.4	4.4
Depression-Dejection	-.8	-.4	-.37	.79	.640	-1.9	1.2
Anger-Hostility	-.3	.1	-.35	.62	.574	-1.6	.9
Total Mood Disturbance	-8.9	-1.7	-7.22	2.91	.014	-13	-1.5

Notes:

1 Adjusted mean changes and adjusted differences in mean changes were estimated as site-total-sample-size weighted values controlling for treatment group differences in mean pre treatment baseline values.

[2] The Intent-to-Treat sample includes all randomized patients exposed to active CPAP or sham-CPAP treatment during the post randomization treatment.

[3] P-value from Type II sum of squares estimated by way of analysis of covariance. To produce site weighted comparisons the ANCOVA model included main effects for treatment group, site, and pre-treatment baseline value.

SUPPLEMENTARY TABLE E7. EFFICACY CHANGE OF SECONDARY OBJECTIVE OUTCOMES FROM PRE-TREATMENT BASELINE TO THE END OF THE INITIAL 8-WEEK TREATMENT PERIOD[1] IN THE MODIFIED INTENT TO TREAT SAMPLE[2]

Endpoint	Active Adjusted Mean Change[2]	Sham Adjusted Mean Change[2]	Adjusted Difference in Mean Change[2]	SE	P Value[3]	Lower and Upper Bounds of 95% CI for Difference in Mean Changes	
Psychomotor Vigilance Task							
Lapses/Trial	-2.00	2.33	-4.33	2.78	.121	-9.80	1.15
Median RT (ms)	-13.25	9.86	-23.12	12.93	.0075	-48.62	2.39
Fastest 10% RT (ms)	-4.93	-.26	-4.68	4.36	.285	-13.29	3.93
Slowest 10% 1/RT	.07	-.15	.22	.07	.002	.08	.36
Mood VAS	-1.28	-.17	-1.11	.31	0	-1.73	-.50
Ambulatory 48-hr blood pressure							
Heart rate - day	-0.62	0.20	-0.82	1.10	0.457	-3.0	1.4
Systolic BP - day	0.72	2.04	-1.32	1.58	0.407	-4.5	1.8
Diastolic BP - day	-0.57	1.36	-1.93	0.96	0.048	-3.8	0.0
MAP - day	-0.59	1.17	-1.76	1.03	0.090	-3.8	0.3

Heart rate - night	-0.61	0.03	-0.64	1.01	0.530	-2.6	1.4
Systolic BP - night	-0.10	2.10	-2.21	1.86	0.239	-5.9	1.5
Diastolic BP - night	-0.31	1.21	-1.51	1.23	0.222	-4.0	0.9
MAP – night	-0.60	1.61	-1.77	1.34	0.190	-4.4	0.9
Heart rate - dip	0.10	0.50	-0.40	1.02	0.694	-2.4	1.6
Systolic - dip	-0.46	-0.66	0.20	1.36	0.885	-2.5	2.9
Diastolic - dip	0.49	-0.18	0.66	1.04	0.526	-1.4	2.7
MAP - dip	0.30	-0.49	0.79	1.10	0.474	-1.4	3.0

Notes:

1 Adjusted mean changes and adjusted differences in mean changes were estimated as site-total-sample-size weighted values controlling for treatment group differences in mean pre treatment baseline values.

[2] The Intent-to-Treat sample includes all randomized patients exposed to active CPAP or sham-CPAP treatment during the post randomization treatment.

[3] P-value from Type II sum of squares estimated by way of analysis of covariance. To produce site weighted comparisons the ANCOVA model included main effects for treatment group, site, and pre-treatment baseline value.

SUPPLEMENTARY TABLE E8. PARTICIPANT CHARACTERISTICS OF THE CROSS-OVER COHORT (N=99) JUST PRIOR TO BEGINNING ACTIVE CPAP INTERVENTION, I.E., AT THE 8-WEEK SHAM CPAP FOLLOW-UP ASSESSMENT.

Variable	
Age (years)	49.3 ± 11.1
Percent males	61.8
Percent African Americans	15.7
Body mass index (kg/m^2)	33.3 ± 6.6
Weight (lbs.)	213.8 ± 209.5
FOSQ Total score	14.24 ± 2.75
General productivity	2.99 ± 0.61
Vigilance	2.56 ± 0.64
Social outcome	3.03 ± 0.69
Activity level	2.65 ± 0.64
Intimacy & sexual relationships	3.03 ± 0.98

SUPPLEMENTARY TABLE E9. MEAN CHANGE IN FOSQ TOTAL AND COMPONENT SCORES IN THE CROSS-OVER.

Endpoint	n	Mean ± SD	Min	Max	Effect size	p-value
FOSQ						
Total Score	91	1.73 ± 2.50	-6.95	9.43	0.690	< 0.001
General Productivity	91	0.27 ± 0.52	-0.95	1.86	0.514	< 0.001
Vigilance	90	0.40 ± 0.66	-2.00	2.29	0.613	< 0.001
Social Outcome	88	0.34 ± 0.73	-2.50	3.00	0.465	< 0.001
Activity Level	91	0.38 ± 0.56	-1.25	2.11	0.681	< 0.001
Intimacy & Sexual Relationships	75	0.30 ± 0.66	-1.00	2.50	0.462	< 0.001
ESS	92	-2.29 ± 3.99	-13.0	7.00	-0.575	< 0.001
PVT						
Lapses/trial	80	-3.93 ± 13.46	-70.5	27.0	-0.292	0.0108
PVT Median RT	80	-17.2 ± 46.1	-284.0	75.50	-0.374	0.0012
PVT Fast 10% RT	80	-7.0 ± 17.2	-65.4	44.4	-0.409	0.0005
PVT Slowest 10% 1/RT	80	0.18 ± 0.57	-1.44	1.90	0.323	0.0050
Fatigue score	97	-2.4 ± 6.6	-18.0	14.0	-0.366	0.0005
POMS						
Confusion-bewilderment	97	-1.1 ± 3.2	-9.0	10.0	-0.354	0.0008
Tension-anxiety score	97	-0.1 ± 4.7	-14.0	20.0	-0.023	0.8218

Vigor score	97	3.1 ± 5.6	-16.0	17.0	0.555	0.0000
Depression-dejection	97	-0.7 ± 6.6	-23.6	34.0	-0.101	0.3228
Anger-hostility	97	0.0 ± 4.2	-16.4	12.0	0.008	0.9347
Total mood disturbance	97	-7.4 ± 23.5	-63.0	86.0	-0.314	0.0026
SF36						
Physical Component	62	2.50 ± 7.70	-15.87	26.31	0.324	0.0132
Mental Health Component	62	3.40 ± 8.38	-25.02	29.21	0.406	0.0022
Ambulatory Blood Pressure						
Systolic BP - Day	46	1.80 ± 7.92	-14.67	29.61	0.227	0.1311
Diastolic BP - Day	46	0.21 ± 5.13	-13.13	12.13	0.041	0.7827
MAP - Day	46	0.64 ± 5.21	-12.79	14.73	0.124	0.4060
Systolic BP - Night	46	-1.54 ± 8.99	-17.85	15.48	-0.171	0.2509
Diastolic BP - Night	46	-1.61 ± 5.91	-17.57	11.66	-0.272	0.0712
MAP - Night	46	-1.23 ± 6.36	-15.15	10.48	-0.193	0.1971
Systolic BP - Dip	44	-3.00 ± 9.94	-34.34	12.91	-0.302	0.0518
Diastolic BP - Dip	44	-1.63 ± 6.30	-16.45	11.14	-0.259	0.0935
MAP - Dip	44	-1.71 ± 6.78	-17.46	12.04	-0.252	0.1018